

Chapter 1 – Introduction

Anecdotal reports of therapeutic benefits for asthma sufferers from chiropractic treatment are evident as the basis of this clinical practice. Previous studies of chiropractic treatment for asthma have been at best inconclusive regarding any therapeutic benefit. Given absence of scientific legitimacy, it is paramount that further research into this area of healthcare be carefully considered. This thesis presents a review of particular evidence of efficacy in chiropractic as a treatment for improving the health of the individual asthma sufferer. It also considers the applicability of research methods that may be adopted to evidence any such benefits.

In this chapter, relevant concepts are reviewed in brief terms. These are introductory to more detailed discussion (refer Chapter 2) which expands on those concepts and factors taken to account in the background planning for, and design of, the research method for the clinical trial forming the subject of this thesis,

The prevalence of asthma is noted.

The complex nature of asthma as a condition is discussed and the potential benefits of chiropractic treatment to an asthma sufferer's quality of life are considered. The condition is reviewed in the context of the individual who suffers from asthma.

Alternative healthcare, referred to as Complementary and Alternative Medicine (CAM), is introduced as an area not well understood and within which chiropractic falls as a health delivery service.

Chiropractic's historical association with asthma is reviewed.

The strengths and weaknesses of current research models used in Evidence-Based Medicine (EBM) and CAM are examined to establish a research method that may allow evidence of efficacy to be examined.

1.1 Asthma

Asthma creates a severe burden to individuals and families and restricts the quality of life for both the asthma sufferer and their carers. It is the most common chronic condition in children. Asthma is a public health problem across the globe; not just for high income nations. Most asthma deaths occur in low and lower middle income countries. It creates a substantial burden to individuals and families and often restricts individuals' activities for a lifetime (1).

The Global Initiative for Asthma (GINA), under the auspices of the WHO, has been established since 1989 to increase global awareness of the epidemic of asthma as a significant global health burden. There will be an estimated 400 million asthma sufferers by the year 2025. It has been suggested in a recent review of asthma over the last 50 years in the UK that there is an increasing prevalence of individuals being given a 'lifetime' diagnosis of asthma across all age groups (2, 3). This 'lifetime' diagnosis is an indication of the social impact of this condition. It is not a disease that can be cured or eradicated. It is a condition that requires individual management and a proactive approach to minimise the occurrence of attacks. It remains a dysfunctional condition of respiratory physiology that is not fully understood and peculiarly involves a unique set of stressors or triggers in each individual. The global strategy for asthma is to promote evidence-based asthma management with asthma self-awareness and education for each asthma sufferer. The WHO seeks to understand and incorporate the local and traditional healthcare systems around the world in this endeavour (4).

Population studies indicate that Australia has one of the highest levels of asthma prevalence in the world. Though morbidity in asthma is decreasing, the burden of ill health, disability and

reduced quality of life has given asthma a ranking of number six in the nation's health priorities (5).

1.2 Defining features of asthma

Asthma is a chronic condition of the lungs, however, being characterised by the reversible nature of an episode in the individual asthma sufferer, it is distinct from a the condition where irreversible lung tissue damage as is seen in the progressive changes of Chronic Obstructive Pulmonary Disease (COPD) (6). This thesis reviews the nature of the underlying pathophysiology of asthma with the intention of advancing understanding as to any plausible biological mechanism that may explain the empirical evidence of chiropractic treatment being of benefit in asthma.

In examining asthma, the history of approaches taken to asthma management is reviewed briefly; observing how medical management has changed as the research of the underlying pathophysiology of asthma has contributed to an understanding of asthma (7).

1.3 Health of the individual with asthma

The WHO's definition of health, adopted since the 1940s, suggests that the mere lack of disease and infirmity does not equate to health in an individual and it is the individual's attitudes, experience and personal beliefs that are all fundamental to the achievement of wellbeing (8). The WHO defines health as: 'health is a state of complete physical emotional and social wellbeing'(9).

The individual asthma sufferer's measure of wellbeing on that definition will vary within the asthma experience. Viewing asthma from the perspective of the individual sufferer, places focus on that individual's own experience of asthma in the context of overall health expression.

An individual diagnosed with asthma can be maintaining an active and healthy life, with the asthma condition managed so as to minimise impact on his or her life. The aim of asthma management for the individual asthma sufferer is to maintain healthy lung function.

An active approach to asthma management has been developed with a focus on the individual asthma sufferer. This approach has introduced in most developed societies a standard care regimen known generically as an Asthma Management Plan (AMP). AMPs have come to be accepted as the ‘gold standard’ of asthma management in most countries (2, 10). Asthma is managed with the prophylactic use of an asthma medication regimen within an AMP. Asthma is classified as well-managed when there is good control of the signs and symptoms. In Australia, individual AMPs have been in use for over 20 years (11, 12).

The AMP requires daily self-monitoring of lung function with active self-management and decision-making within a program of regular medical review. The significant contribution of self-management and educational approaches to the success of the AMP has been observed (13, 14).

1.4 Alternative healthcare – Complementary and Alternative Medicine (CAM)

Alternative healthcare is considered unorthodox when compared to the conventional healthcare traditionally available in the mainstream healthcare systems. Alternative healthcare offers non-conventional treatments, not considered ‘normal’ according to conventional medicine. These healthcare approaches are categorised for the sake of identification and differentiation as Complementary or Alternative Medicine (CAM).

CAM provides a means of classifying non-conventional healthcare systems. However the divisions between alternative medicine and conventional medicine continue with the classification of CAM, non-CAM and mainstream healthcare confusing for the health consumer (15). Individual asthma sufferers are only interested in what is helping them to

breathe better and feel better. They are active in personally registering improvements in their asthma within an AMP.

The increase in the use of CAM is reported as being in addition to conventional therapies rather than as an alternative to them (16). A 2005 review established that this trend in 76.5% of health consumers was due to the CAM offering them a more interactive role in their healthcare and for 78% of the individuals interviewed; CAM was offering a healthcare approach that treated them as a whole person (17). The WHO notes that in some developed countries, the use of CAM is reported by 70% to 80% of the population. In Germany, 46% of consumers use CAM and 49% of people in France choose to involve CAM in their healthcare approach (4). In the United States of America, the choice of CAM reflects individuals' perceptions of health and not their dissatisfaction with conventional medicine. Individual health consumers with a higher level of education report finding CAM to be more in line with their personal health philosophy and concerns of 'poor' health. Approximately 83% of internet users use the internet more than any other source to help them in their health decisions (18).

The WHO and its member countries promote a collaborative approach to support and integrate CAM into national health systems. The WHO acknowledges the use of CAM and aims to ensure its safe and effective delivery within the health systems of the world (4).

There is a trend among individual asthma sufferers to increase their involvement with a non-pharmaceutical approach that they consider appropriate for their circumstances, with 50% of asthma sufferers in Australia reporting use of a CAM healthcare approach (19, 20). Whether or not there is conventional medical evidence to support the practice of unconventional approaches in asthma, the asthma sufferer is increasingly using CAM (20).

Practitioners of conventional western medicine have not historically been educated to understand or take account of CAM's possible benefits for their patients. The emphasis on

practitioners of conventional medicine becoming conversant with CAM practitioners and published CAM papers will avoid any likelihood of their depriving patients of any potential benefit by not providing relevant information (21, 22).

1.5 Chiropractic

Chiropractic is a system of healthcare concerned with the diagnosis, treatment and prevention of mechanical disorders of the musculoskeletal system, and the effects of these disorders on the function of the nervous system and general health (23). The chiropractor is specialised in the assessment and management of spinal dysfunction, and educated at an undergraduate level in medical diagnosis for the purposes of referral to other health providers where appropriate. With a view to the outcome of individual wellness, the delivery of chiropractic treatment requires that each individual understands more about helping themselves with diet, exercise, lifestyle and their own body's innate healing capacities (24).

Australia implemented a national registration scheme of chiropractors as primary care providers in 2010. This national scheme places the chiropractic profession within the developing structures of healthcare delivery in Australia (25).

Chiropractic is seen as alternative medicine around the world and is well used by health consumers for low back pain and other health conditions (26). In Australia, there is acceptance and use of chiropractic as a CAM system by the wider public (27).

Division within the chiropractic profession regarding scope of practice, resulting in differing stands on the politics of chiropractic research and development, only adds to this confusion for the wider healthcare profession (28, 29).

Surveys of general medical practitioners in Australia show that this influential group of health providers has widespread acceptance of CAM and includes chiropractic in this category (30, 31). General medical practitioners also report referring to health providers of massage, chiropractic, acupuncture, meditation, hypnosis, yoga and herbal medicine, but regard only

the non-manipulative and non-medicinal complementary therapies as offering acceptable levels of effectiveness and safety (32).

1.6 Asthma and chiropractic

The need to research the healthcare approach of chiropractic in asthma is driven by increasing use of chiropractic by asthma sufferers in their asthma management. Reasons for choosing to involve chiropractic may be the therapeutic benefits derived from the physical nature of the treatment resulting in improved biomechanics of respiration.

There is a common and established principle for all manipulative and body-based therapies including chiropractic, that in the treatment of asthma, it is the good biomechanical function of the ribcage that promotes healthy lung function (33-41). After orthopaedic examination of the spine and related areas of the ribcage, treatment is given to improve the overall biomechanical function of the area (42). The manipulative and body-based healthcare approach treats dysfunctional relationships of the thoracic vertebrae, ribs, sternum and soft tissue attachments (muscles, ligaments and rib cartilages) (43-48).

Surveys of health consumers show that 27% report an overall improvement in their breathing from chiropractic treatment. Asthma sufferers report improvements in their asthma symptoms and satisfaction with chiropractic treatment, confirming how chiropractic treatment helps them manage their asthma (43).

Chiropractic care in asthma management remains insignificant (48). Yet asthma sufferers continue to consult a chiropractor for help with the management of their condition; and chiropractors continue to treat any signs of spinal dysfunction and any associated peri-articular tissue adhesions and poor respiratory muscular activity in a person with a co-morbidity of asthma (49-51).

Asthma sufferers seek non-medical care as part of their AMP; not because they are disgruntled with their medical care. They see the role of the CAM practitioner as one of

sharing in the 'joint-management' in their asthma, and the use of a CAM as their choice (52). Major asthma support groups offer experienced advice to asthma sufferers enquiring about CAM (53).

1.7 Clinical experience of chiropractic and asthma

The use of chiropractic treatment for asthma is based on empirical evidence over its 100-year history. This evidence is supported in the chiropractic literature with clinical observations of certain spinal levels associated with a co-morbidity of asthma. Specific levels of spinal dysfunction are noted; the spinal levels T2 to T7 have been observed in asthma co-morbidity (54). A UK study of 490 chiropractors in 2007 indicated 64% agree that their practice was effective in the management of asthma (55).

There are unanswered research questions as to what is occurring in chiropractic treatment for asthma sufferers. Two clinical trials of chiropractic treatment and asthma did not demonstrate any therapeutic benefit for asthma from the experimental intervention of chiropractic Spinal Manipulative Therapy (SMT) (56, 57).

The Cochrane Collaboration is an internet-based library and research resource. In 2005, this respected authority reviewed published literature on asthma and the role of manual therapy in its management. This review concluded that there is insufficient evidence to support the use of manual therapies for asthma (58).

EBM requires safety, clinical efficacy and patient satisfaction in considering treatments and clinical interventions. The clinical research of chiropractic is yet to satisfy two of these criteria for EBM to determine the validity of chiropractic treatment for asthma (59).

1.8 Clinical research approaches

The history of healthcare research is reflective of the prevailing paradigm of scientific understanding as to the cause of disease, and of the prevailing agreement as to what is health for the person or population in the research question. The paradigms of reductionist science

and non-reductionist science are at the centre of how these health research questions are then approached.

There is the reductionist examination of a linear construct of biomedical treatment for a disease process or a pathogen. This is contrasted with a newly developing model of inclusion in healthcare research. This is the inclusion of the patient. Included are the many factors inherent in their illness: their health goals, their own responsibilities in management, the providers of their care, whether those providers are operating as a team and the shared responsibility for the patient's clinical outcomes by all these stakeholders in the healthcare.

This is a wholistic approach with a more patient-centred and observational research model gathering more data rather than reducing confounding factors in the research. The current increase of use by health consumers of the internet, the increasing authority of world bodies of health expertise and the public use of 'whole health' approaches offered by CAM are all part of a paradigm shift in health perspectives (60).

Clinical research has a tradition of practical research to further the understanding of health and disease by examining the interactions that occur between patients, populations, observations, diagnosis, intervention and management; the 'whole' of the clinical continuum of data (61). The reality of clinical practice is the reality of how the patient feels. How patients define their own health and relationship they have with their health provider is important. The nature of clinical practice is that the patient and the provider are most interested in clinical improvement not the mechanisms of therapeutic activity (62).

1.9 Healthcare research methodologies

Case records of observational, descriptive, clinical research and some rudimentary statistics were a developing science in the 17th Century. This was from a practised tradition of the observational science that may be seen in the roots of Human Geography; when travelling to distant places and collecting facts and information was for the purpose of sharing knowledge

(63). The first recording of a blinded clinical trial was in 1835. The trial exposed homeopathy as having no therapeutic impact (64).

The double blinded randomised controlled trial has developed from this reductionist approach to examine for evidence of efficacy. This research model has become the 'gold standard' of healthcare research with the growth of EBM since the 1990s. Maximising safety, managing costs and aiming for consumer satisfaction are each driving forces in this emerging health paradigm of developed societies of the world (65, 66).

The reductionist research model of the double blind randomised clinical trial (known generally by the acronym RCT) is designed to control any confounding factors that may influence the research results with 'false' or unrelated factors. The RCT is used in proving the efficacy of pharmaceutical regimens that are examined as biomedical models of treatment. In examining the experimental treatment in a specified population, all confounding factors of individual variations of an illness, personalities, belief systems and placebo effects are removed. A randomised, double-blind, controlled trial is designed to deliver objective results of reproducible internal validity. The external validity or the clinical value of the results of the RCT must then be determined by the statistical inferences regarding the experimental intervention in a specified population. As there is a lack of external validity, a trial of clinical effectiveness may be required to assess the results of the RCT in the clinical reality of practice (67).

Another design of healthcare research methodology comes from the traditions of non-reductionist science. A non-reductionist research approach involves gathering more potentially confounding data. This model is used to examine research questions that cannot be examined in a reductionist method of scientific analysis (68, 69). In healthcare research, qualitative observational studies can be used for research where the health research question is multi-factorial and not able to be reduced to its single components for the clinical trial. This

non-reductionist method of analysis allows all potential relationships to be considered. It may be that such an approach to health research helps address the complexity of individuals and their health, the body to be expressed as a whole and the complex nature of some non-pharmaceutical treatment interventions. The value of this research approach has been the subject of debate (68).

Using a more wholistic synthesis of data allows an individual's experience of illness to be understood and analysed; this may be a more inclusive approach to factors contributing to understanding health, rather than factors confounding the research findings. The venerable discipline of human geography has evolved into many branches of science and epidemiology, including healthcare in the discipline of medical geography. This science, in its original form, still offers a collection of qualitative or observational data, alongside its current discipline of quantitative analysis for many areas of health research. This actively contributes to health policy formation (63, 70, 71).

Objective or laboratory-based research measures are regarded as the 'harder' measures of research trials; they can measure biological processes underlying the therapeutic changes observed, including in CAM clinical research. These harder measures of therapeutic change will override the patient-centred outcomes as a valid evidence of any therapeutic benefit. The use of patient-centred outcomes in research satisfies some healthcare disciplines only; generally considered 'soft measures' of therapeutic benefit.

A research design that is examining for efficacy of an experimental treatment intervention is advised to have 'harder measures' or more objective, laboratory-based findings of physiological mechanisms as research tools. Critically there must be a plausible biological mechanism in place for the selection of the appropriate research tool as the measure. The use of the 'hard' measures of therapeutic benefits in research may then qualify the results of the research as scientific, and its evidence as valid. The results of positive patient-centred

outcomes are deemed as only supportive of these ‘harder measures’. In fact, the patient-centred outcomes or questionnaires alone are seen as ‘anecdotal’ or subjective against the harder laboratory-based research measures.

1.10 Research design: healthcare research and CAM

There is a lack of substantive research evidence of the therapeutic benefits of CAM healthcare. This may be in part due to the lack of development of specific CAM research expertise and experience. CAM healthcare is yet to develop as a discipline in itself for its own purposes (72).

The research discipline of CAM will be assisted by multi-disciplinary research groups sharing research expertise and clinical experience. There is research funding in developed societies focused on epidemics of multi-factorial illnesses such as asthma (73). These conditions are a source of increasing financial and socio-economic burdens, and CAM systems offer complex interventions that appeal to the health consumers affected by these conditions (74). The complex treatment intervention that is the CAM healthcare approach requires the right questions and the right research design.

The first step in choosing research models for examining CAM is asking the question - what the research is examining. Using a RCT designed trial, the CAM must be reproduced as a single biomedical component examined across a randomised group of a specified target population. An important consideration in the choice of research design is whether the CAM system must lose the detail of its complex treatment intervention. Though, this is not the clinical reality of the CAM healthcare in clinical reality, reproducing the CAM as a single component may seemingly enable effective use of the RCT design (75) .

There are considerations for CAM healthcare research design in the selection processes. The options are to keep the RCT’s design, or keep the best of the RCT design and consider the elements that are appropriate for the CAM research question (76, 77). There may be aspects

of the RCT design that prove impossible for effective research of the CAM healthcare approach. There can be influences in the choice of research design for healthcare. These influences are the accepted standards of research to be included in the internet-based research reviews that are the source of information for the healthcare movement known as EBM. The gold standard of RCT is used to filter published research in EBM reviews (78).

The RCT is possible for CAM, though expensive, with a higher level of preparation and preliminary studies required determining effective blinding, placebo and a consistent delivery of the CAM treatment as a single component or biomedical treatment. Reducing the CAM to a single component for the RCT design is therefore possible. However the question then becomes whether one is examining something that is no longer CAM healthcare, but a single component treatment intervention of that healthcare approach.

1.11 Research through clinical trials

The variation of treatment which is the nature of CAM healthcare such as chiropractic is more difficult as a research question for an RCT clinical trial. In the ‘typical’ clinic, chiropractic treatment varies by practitioner and may involve several therapeutic procedures and other ancillary therapy, depending on the issue with which the patient clinically presents (79).

For a chiropractic practice, there are a variety of chiropractic clinical techniques used and these may be varied for each treatment depending on the individual’s presentation on that day. For example, when a person presents with acute pain, the treatment will be different from when a person presents with less pain and the underlying core spinal instability is the focus of the treatment.

The nature of the CAM intervention may be complex, so reducing it one component for research purposes may see a bias in the process of selection and the nature of the research construct as a biomedical intervention. It has been observed in two previous clinical trials of chiropractic treatment for asthma, that the use of a sham of spinal manipulation may have

been an ineffective research design. The group receiving the active spinal manipulation and the group receiving the non-active or sham manipulation showed similar results in the trial's research outcomes. One variation of chiropractic clinical technique and therefore the non-active manipulation may have been considered active treatment according to another variation of chiropractic clinical technique (80).

The variability of the technique used in CAM systems is to be considered in research design. In acupuncture, the use of needles in acupuncture involves insertion and manipulation at certain points of the body. The use of needling techniques is varied. Some schools of acupuncture may use superficial needling whereas some do not see that as the method for therapeutic needling. The handling needles therapeutically can vary according to the practitioner and their school of thought. There has been some research into the validation of a 'sham' within the CAM system of acupuncture for use in clinical trials. Effective research of the complex treatment intervention of CAM healthcare requires a self-critical appraisal of its nature. The research question is whether the 'treatment' is most appropriately examined in the contextual setting of the CAM encounter with the CAM provider as an interactive decision maker with the patient, or as a specified biomedical delivery (77, 78, 81-83).

Chapter 2 - Origins of the clinical trial:

Background to planning; research design; aims and objectives

The background to the clinical trial of chiropractic treatment for asthma is presented. This is a considered review of the processes in selecting the components of research design to be included in the examination of chiropractic treatment for the condition of asthma. Subject areas are explained to provide the critical rationale for their inclusion in the clinical trial.

The treatment in question is chiropractic and the practice of chiropractic merits examination as to its strengths and weaknesses as a healthcare provider. The lack of cohesiveness in its growth as a profession and the infancy of chiropractic as a self-critical research discipline will be introduced in a review of the methods used in the clinical trial. The diversity of clinical techniques is a strength for the clinical reality of practice but divisive in the research of chiropractic. The use of unscientific concepts in clinical communications has historical value due to familiarity, but is divisive in the development of a self-critical research discipline of chiropractic.

Asthma is reviewed as a major epidemic that is a worldwide priority for developed nations in their healthcare policies.

The effective management approach of an Asthma Management Plan (AMP) in developed societies is presented with view to a patient-centred research model for this clinical trial. A concept of health for the individual within asthma, with a quantifying research tool for further understanding of this chronic multi-factorial condition, is introduced as part of the clinical research.

Theories of chiropractic therapeutic mechanisms are introduced in this chapter, specifically in regard to the condition of asthma. The pathophysiological mechanisms of asthma are briefly reviewed. The health of the individual with asthma is considered in the pathophysiology of

asthma with the unique combination of triggers and factors that is the nature of asthma. An altered function of the autonomic nervous system (ANS) is considered in this trial as a plausible mechanism of therapeutic benefits for asthma from chiropractic treatment.

Chiropractic is reviewed as a healthcare approach within the Complementary and Alternative Medicine (CAM) classification of ‘manipulative and body-based’ healthcare approaches. The condition of asthma, the health of the individual with asthma and the nature of chiropractic as a CAM clinical paradigm of healthcare direct the research design for the clinical trial.

The ‘contextual setting’ of CAM healthcare is considered as a research element for the clinical trial to allow the therapeutic aspect of the ‘clinical encounter’ to be involved. A ‘typical’ treatment rather than a specified chiropractic spinal manipulative procedure is introduced as a research method in this research. The decision to have no placebo or sham is reviewed for the purposes of this research trial with review of previous clinical trials’ experiences of research design to examine for efficacy of evidence with a placebo or sham in place. The plausible mechanisms by which there may be therapeutic benefit for asthma and chiropractic are then presented as a review of the research tools that may measure and monitor for any therapeutic benefits of the chiropractic treatment. A series of objective and subjective research tools are reviewed for their appropriateness for this research question.

2.1 Background to planning

2.1.1 Understanding asthma

Asthma is a complex lung condition characterised by variable and recurring symptoms in each individual. Asthma is recognised by an individual’s limited capacity to breathe out. Asthma affects those of all ages and ranges in severity from a mild wheeze to an incapacitating and sometimes life- threatening condition. The severity of asthma ranges from mild, intermittent symptoms, causing few problems for the individual, to severe and persistent wheezing and shortness of breath. In a few people with asthma, the disease has a severe

adverse impact on quality of life. While the underlying causes of asthma are still not well understood, there are a number of factors in each individual that combine as a profile or triggers of their asthma. These episodes can be life-threatening and yet these episodes can also fully resolve, with lung function returning to normal and the individual leading a full and active life once more (84).

Asthma is diagnostically distinguished by the fully or substantially reversible nature of an episode in the individual asthma sufferer, either spontaneously or with treatment. By definition, asthma does not present with irreversible lung tissue pathology as seen in Chronic Obstructive Pulmonary Disease (COPD) (74).

Symptoms

Asthma is characterised by recurrent attacks of breathlessness, coughing and wheezing and a sense of chest tightness. The compromised breathing and airflow obstruction presents with underlying bronchial hyper-responsiveness, mucus production, bronchospasm, tissue swelling and inflammation. Asthma attacks all age groups but often starts in childhood. These attacks vary in severity and frequency from person-to-person. In some individuals, they may occur from hour-to-hour and day-to-day (85).

Diagnosis

An asthma diagnosis is usually made by a medical specialist or general practitioner. The diagnosis will follow a medical review of presenting signs and symptoms such as unexplained wheezing, excessive mucous and/or a persistent cough. The use of a hospital-based pulmonary function laboratory or physician's office, where possible, will provide detailed spirometer readings of lung function testing that assist in the diagnosis. Observations of a response to bronchodilator medications that provide relief from the signs and symptoms of the lung dysfunction may also help confirm that the condition is asthma (42).

Extrinsic and intrinsic asthma

There are two subtypes of asthma: extrinsic and intrinsic asthma. Extrinsic asthma is triggered by stressors from the external environment such as allergens, changes in atmospheric temperature, barometric pressure and the quality of the air. Intrinsic asthma is brought on by a stressor in the individual's internal environment such as physical, emotional and psychosocial upset and excitement.

Of the two classifications, extrinsic asthma is better managed thanks to the current understanding of genetic tendencies, allergy-type asthma and inflammatory pathophysiology. Asthma's intrinsic triggers include psychological and emotional factors, and these underlying mechanisms are less understood. Though asthma cannot be cured, appropriate management can control the disorder and help people enjoy a good quality of life (84, 86).

Progressive airway pathology

The long-term health impact of chronic lung dysfunction is a focus of asthma research. Some research indicates that the airway reshaping or thickening observed over time in the bronchioles of the lungs of the asthma sufferer may be a protective mechanism against pathogen invasion more than advancing tissue pathology (87). In conditions where airways are compromised, the natural production of mucous, as part of the lung tissue defence mechanism, may be pathologically increased and a hyper secretion of mucous occurs. This takes place in asthma, bronchitis, cystic fibrosis and COPD. Chronic mucous production may alter the underlying epithelium in the lungs and cause tissue debilitation with an ongoing cycle of inflammation and mucus production (88).

It is possible that with this cycle of chronic inflammation, a remodelling effect within the lung epithelium takes place. Whether this is designed to protect the epithelium from further infiltration and damage is not yet understood, but the process may contribute to deterioration of the airway patency (89, 90). Indeed, immuno-histochemical analysis shows greater mast cell and lymphocyte infiltration in chronic asthma, where a thickened sub-epithelial

membrane may result in airway remodelling. These tissue changes are only observed in individuals with asthma and not those without this condition.

Asthma and COPD

Asthma may develop into a diagnosis of COPD, with advancing tissue pathology. Risk factors for COPD include exposure to tobacco smoke, occupational dusts and chemicals, and frequent lower respiratory infections during childhood (84).

The underlying mechanism of airway obstruction is assessed with pulmonary function tests and the readings become part of the differential diagnosis. COPD is differentiated from asthma by a number of signs and symptoms. Its hallmark defining feature is that of progressive debilitation. COPD is suspected when the person is middle-aged with excessive sputum production, and a debilitating chronic cough associated with constant fatigue, weight loss and severe unrelenting breathlessness (91, 92).

For pulmonary function testing, a laboratory or clinic environment with spirometer testing is used. The spirometer testing is described in brief: the forced expiratory volume (FEV₁) is the volume exhaled in the first second; following a very precise instruction for the person to inhale maximally and then exhale as hard, and as completely as they can. The total volume at complete exhalation is called the forced vital capacity (FVC). A percentage measure of the two is one of many assessments used to determine the site and degree of airway compromise. In COPD and pulmonary fibrosis, both restrictive lung conditions, both the FEV₁ and the FVC are reduced. In asthma, an obstructive condition, the FEV₁ is reduced much more than the FVC. Pulmonary function tests assist in understanding the nature of the airway obstruction by observing the pattern of lung function, though various patterns overlap these disease entities. Rather than making a diagnosis of either of these conditions of lung dysfunction, spirometer readings are used to follow the progress of chronic lung deterioration in functional capacities and assess the results of the medication regimens (42).

Risk factors

The risk factors for developing asthma as a child include genetic predispositions; a family history with an environmental exposure to inhaled substances and particles which provoke allergic reactions or irritate the airways (93). Symptoms may occur several times in a day or week, and for some, become worse during physical activity or at night. Asthma is a chronic multi-factorial condition and it remains an enigma.

Known asthma triggers include changes in temperature or barometric pressure, hormonal cycles, exercise, infections, gastrointestinal sensitivities or emotional shocks (positive and negative). Exposure to allergenic irritation such as airborne pollens, moulds, dust mites, chemicals, tobacco, animal hair, bacteria, drugs and pollutants can also trigger an episode. Intrinsic triggers predisposing an individual to developing asthma include viral infections, chemical irritations, physical exertion, emotional stress, anxiety, genetics, maternal asthma history, regular childhood antibiotic use, low birth weight and reduced infantile breast feeding (93).

Networks of appropriately modelled pragmatic clinical research trials of asthma to examine the long-term implications of this condition for asthma sufferers, are being encouraged globally by the Medical Research Council (MRC) of the United Kingdom (94).

Global Alliance against Respiratory Diseases

The WHO seeks to address the global burden of chronic respiratory conditions and diseases such as asthma, COPD, allergic rhinitis, sinusitis, bronchiectasis, obstructive sleep apnoea and pulmonary hypertension, with its 'Global Alliance against Respiratory Diseases' (GARD) (95).

2.1.2 Asthma in Australia

Asthma is a significant cause of ill health and poor quality of life. In Australia, one in ten people suffers from asthma (5).

Asthma burden

There are asthma foundations in every state and territory supporting asthma sufferers and their carers. Over two million people in Australia have asthma and over 400 Australians die each year from the condition (96).

Asthma is a major cause of disability, a leading cause of hospitalisation and a declared 'national healthy priority' since 1999. Asthma is considered a high priority, chronic, multi-factorial condition for the Australian healthcare system (97).

Asthma cost the Australian Government an estimated AUD\$615 million during 2000 to 2001 and its effect on the community is similarly high. Asthma results in lost productivity, along with compromised social and physical activity. Morbidity associated with asthma has decreased with the use of the Asthma Management Plan (AMP) for the asthma sufferer; with well-managed asthma a product of this practice in Australia. However, there is anxiety, depression and a reduced quality of life associated with this chronic condition. Asthma sufferers score lower on the global quality of life health questionnaires than the rest of the Australian population (5).

For the 2004 to 2005 financial year, asthma expenditure in Australia was AUD\$606 million (1.2% of the total allocated health expenditure) (84). The greatest proportion of asthma expenditure was attributable to prescription pharmaceuticals. Asthma expenditure consisted of:

- 59% prescription pharmaceuticals
- 23% out-of-hospital costs
- 16% admitted patient costs
- 2% research.

Australians with asthma rate their overall health as worse than those without asthma. They are more likely to have days off work or school, and to have days in which they have reduced activity levels than people without asthma. See Figure 1.

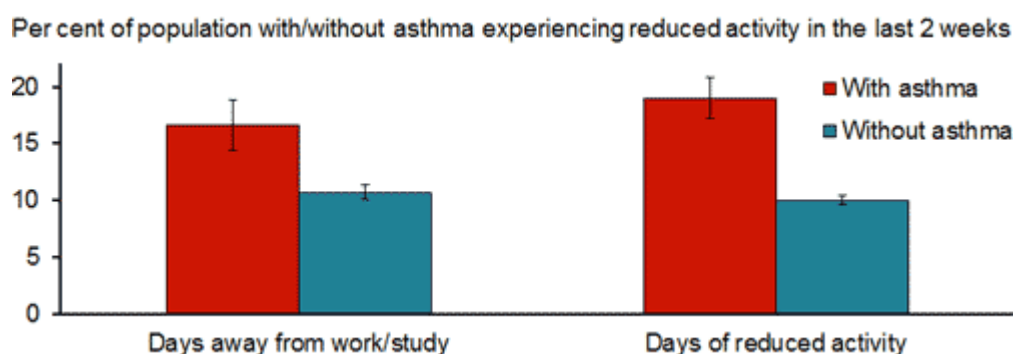


Figure 1: Activity reported in the preceding two weeks of the survey (normal healthy individuals and asthma sufferers)

Notes for Figure 1:

1. Age standardised to the Australian population as at June, 2001
2. Age: five years and over
3. Thin vertical bars attached to the top of each column are 95% confidence intervals. A 95% confidence true value is within the interval depicted.

Source: AIHW analysis of ABS NHS (5).

2.1.3 Medication and asthma management

The use of prescription drugs is the mainstay of asthma management. These medicines control asthma by preventing exacerbations or symptoms, and relieving symptoms when they occur.

Medical approaches

In Australia, the most commonly used medicines for the relief of symptoms are short-acting beta-agonists (salbutamol and terbutaline). However, rapid-onset, long-acting beta-agonists (formoterol) and short-acting anticholinergic drugs (ipratropium) can also be used for this purpose. Inhaled corticosteroids (beclomethasone, budesonide, fluticasone and ciclesonide) are highly effective at controlling symptoms and preventing exacerbations. Inhaled corticosteroids have long been the mainstay of treatment for exacerbations of asthma (5).

Despite the noted improvements in asthma management, episodes of unexplained exacerbations of asthma persist whether or not the asthma is classified as well-controlled (84).

Before these advances in pharmaceutical management, the early approaches to managing asthma over the last century were focused on relieving bronchospasm. Treatments included strong coffee and tea, as well as external applications such as cold baths. ‘Asthma cigarettes’ were still used in the early 20th Century, along with adrenalin (epinephrine) for broncho-dilation in acute asthma. The pharmaceutical preparations for inducing broncho-dilation were followed by new drugs: short-acting beta-agonists (SABAS). These were then developed to be ‘active’ for up to six hours and as long as 24 hours (2).

Allergy-induced asthma became a research focus in the last years of the 20th Century, with anti-inflammatory and anti-allergy approaches to manage the condition. This saw allergy-specific therapy, ‘antihistamine’ preparations, trialled with limited results (98).

Use of synthesised cortisols in asthma

Many diseases are treated with pharmaceutically synthesised cortisols such as cortisone and prednisolone. They are used in asthma management to block the inflammatory response to allergens. The synthetic corticosteroids have an anti-inflammatory action, blocking the early stages and bringing rapid resolution to the inflammatory process. The therapeutic delivery of choice for these pharmaceutically synthesised cortisols, in managing asthma, is in the form of an inhalant. This delivery of the synthetic corticosteroid directly to the lung tissues ensures a speedy response and avoids any unnecessary systemic impact as a result of the oral delivery. The recommendation is for the inhaled synthetic steroids to be kept at the lowest possible dose in long-term or prophylactic asthma regimens, as there is a cumulative dose effect with a risk of side effects. The continued use of synthetic corticosteroids results in a lowered immune response in an asthma sufferer. There may be also be an increased risk of glaucoma, cataracts, slow growth in children, lowered emotional tolerance, mood swings and increased

levels of physical and mental stress with the long-term use of synthetic corticosteroids (96, 99, 100).

Preventer medication

Asthma research is examining the use of longer-acting ‘asthma preventatives’ or anti-inflammatory asthma medications; the focus of asthma medical research is on the inflammatory pathways associated with asthma. This anti-inflammatory approach has resulted in well-managed asthma for the last 20 years. Using a combination of long-lasting bronchodilator (formoterol) with an inhaled corticosteroid (budesonide), twice-daily as a preventative medication, is a typical medication regimen. The use of reliever medication on demand according to chest tightness, wheezing and coughing is advised during the rest of the day. The use of steroid-based inhalant drugs is now the worldwide-accepted prophylactic pharmaceutical regimen for asthma (2, 101).

Global Initiative for Asthma, and well-managed asthma

Guidelines for health practitioners and policy-makers around the world, according to WHO’s Global Initiative for Asthma (GINA), involve a proactive anti-inflammatory approach to treatment so that asthma can be controlled. This is a new focus on ‘well-managed asthma’, used to assess the severity of an individual’s asthma condition as to how well or not it is controlled (3).

According to this approach, in well-controlled asthma, the sufferer experiences no limitation of activities or night-time symptoms and no exacerbation of asthma. Any day-time symptoms occur twice a week or less and the individual uses reliever medication (a bronchodilator) twice a week or less. Under these guidelines, asthma is to be managed by combining the effective use of medication and self-monitoring using a Peak Expiratory Flow Meter, with a healthy lifestyle and an awareness of personal triggers and factors that contribute to an increase in episodes. The Evidence-Based Medicine (EBM) best practice approach is to

combine a regular medical review of the action plan and medication with an AMP for the asthma sufferer to follow at home (102).

Prophylactic pharmaceuticals have had a limited impact on the unpredictable exacerbations that still occur in individual asthma sufferers. These episodes happen despite regular medical reviews, an active AMP and self-monitoring at home (74, 86, 103).

2.1.4 Asthma Management Plans (AMPs)

In Australia, an AMP has been adopted as the approach to asthma management across general medical practice since 1989 (104). The AMP was introduced to enable a more collaborative approach between the medical provider and the asthma sufferer. The focus of the AMP is to see the individual asthma sufferer more responsible and actively self-aware of their asthma, with regular medical reviews. This increased responsibility in monitoring asthma has been a success.

AMP instructions

The AMP includes a list of specific instructions written by a health professional and designed for a person with asthma to read and follow to become educated about their asthma. It includes a regular schedule for medication, as well as actions to take if Peak Flow readings or symptoms become worse than normal. Under all circumstances, the AMP is designed to help flag any potential of severe exacerbation for the asthma sufferer. Life-threatening episodes can happen suddenly, characterised by extreme dyspnoea, cyanosis, exhaustion and sometimes, collapse. The individual is to maintain this daily regimen of medication, often taken daily or twice-daily to prevent symptoms or exacerbation, with reliever medications used as needed to ease asthma symptoms, along with regular medical reviews (105).

Responsible decision-making

An AMP encourages the asthma sufferer to be in control of their asthma, by helping him or her to understand the condition and to recognise changes in signs and symptoms through daily self-monitoring. It gives individual asthma sufferers a sense of self-direction regarding when

to seek additional medical advice or another asthma management intervention. As a result of having an AMP, the asthma sufferer is encouraged to be more self-aware, confident and self-determining (106).

AMPs assist the individual asthma sufferer to:

- Assess the severity of their asthma
- Achieve and monitor their best lung function
- Maintain their best lung function by identifying and avoiding triggers
- Manage their individual asthma presentation with optimal medication
- Actively contribute to decisions and an asthma action plan
- Be increasingly educated about their asthma profile
- Co-operate with a regular asthma medication review (10).

Global Initiative for Asthma (GINA)

GINA is a collaborative body based in the United States of America. Since 1989, GINA has represented the National Institutes for Health (NIH) and the WHO, in establishing worldwide goals in the treatment and care of asthma sufferers. GINA encourages objective assessment, the partnering of physician and patient in the AMP, the individual asthma sufferer's self-awareness and having an established pharmacological therapy in place. This is accepted as the 'gold' standard of asthma management in most countries (2, 3, 7).

2.1.5 Alternative healthcare

Complementary and Alternative Medicine (CAM) is the term now used to refer to many alternative healthcare approaches. These healthcare approaches are used in addition to, or as an alternative to, conventional medicine. For health consumers, alternative healthcare is outside the healthcare system that is most readily available to them.

2.1.6 Complementary and Alternative Medicine (CAM)

CAM exists outside conventional medicine. In 1992, the Office of Alternative Medicine was established in the United States of America, with US\$2 million allocated to researching and

developing CAM and chiropractic healthcare systems. By 2004, funding of CAM research had increased to over US\$116 million.

While it is the subject of healthcare research in developed societies, CAM is not a developed research discipline within itself. This is discussed in this thesis in the context of the clinical trial of asthma and chiropractic, where the asthma sufferer is an active decision-maker in their AMP. A developing healthcare approach that includes CAM with conventional medicine is also discussed.

Some CAM systems are whole health systems

The National Center for Complementary and Alternative Medicine in the United States of America (NCCAM) is now a developing world authority on CAM (107). NCCAM defines a whole health system as being a complete system of theory and practice (107). Some CAM systems are whole health systems, developed in isolation from other systems, and still existing as whole systems of theory and practice. For example, the theory and practice of Traditional Chinese Medicine (TCM) developed from within the non-western cultures of China and Asia and still offers a unique health philosophy. There are also health systems of theory and practice, such as Ayurvedic medicine, that evolved separately and earlier than 'western' or conventional medicine. Yet some whole health systems such as chiropractic and naturopathy developed within western cultures, and have co-existed and grown as whole systems of theory and practice. However, these CAM treatments have grown alongside the Western or conventional medical system and without support from the conventional medical system (15).

Manipulative and body-based practices

CAM is categorised by the NCCAM into three areas: mind-body medicine, energy medicine, and manipulative and body-based practices. Some CAM treatments fit several categories and others do not fit a category at all. Currently, if the treatment is not a pharmaceutical or a conventional medical intervention, it is considered CAM. The lack of understanding of CAM

may benefit from collaborative research by CAM and non-CAM researchers. This may assist in establishing a tradition of research into CAM disciplines. This is beginning to occur within CAM educational institutions. Between 2000 and 2007, the number of CAM researchers grew by 79% (108).

As research into and development of CAM progresses, there may be new categories or classifications that assist in its role in healthcare delivery. As the therapeutic benefits and underlying physiological mechanisms of CAM become better understood, it may become clearer as to how they might contribute to the healthcare system (32, 109).

Use of CAM by health consumers in Australia

A population-based study published in 2007 shows adult Australians may visit CAM practitioners nearly as frequently as medical practitioners. The same study states that half of these Australians always inform their medical practitioner about their use of CAM.

The use of CAM by health consumers in Australia is increasing, with some medical practitioners providing CAM services within their conventional practices. CAM providers have survived in their practices only with the support of health consumers seeking their services and generally without formal inclusion in the conventional healthcare system. The person who chooses CAM as part of their healthcare approach is typically well-educated, 18 to 34-years-old, employed, has private health insurance and is usually female. They are increasingly vocal in what they want for their health, expressing a greater consumer interest in CAM healthcare. Their use of the internet for accessing information, alongside the ability to afford CAM, may be significant (110).

Integration of traditional medicine into primary healthcare systems

The changing landscape of health has been observed by government health funding bodies; the Australian public spends \$600 million on CAM services annually. The National Institute of Complementary Medicine (NICM) is a developing authority on CAM in Australia. NCIM states 50 to 75% of Australians use CAM products and one in four use CAM services (108).

Australia recently contributed to the development of the WHO Beijing Declaration of 2008. This WHO Declaration asked for international agreement in promoting the safe and effective use of traditional medicine and integrating traditional medicine into primary healthcare systems. This is in line with CAM's current use and funding being given to CAM in international trends of government e.g. the United States of America, China, Singapore, Germany, Thailand, North and South Korea, Taiwan and Japan (73).

2.1.7 Co-management of asthma in Australia

The co-management approach to an AMP is about patient empowerment through increased education and understanding. This approach has resulted in an improved control of asthma symptoms and reduced emergency visits to hospitals. It has been noted that co-managed individual asthma sufferers have fewer days absent from work and school, and fewer home visits from the family doctor as a result of their asthma (93).

Co-operative liaison between medical provider and asthma sufferer

Since Australia's national asthma campaign was established in 1990, best practice in asthma management involved a focus on the medical provider and the asthma sufferer working together with an AMP.

This co-operative liaison between medical provider and asthma sufferer focused on self-monitoring and responsible decision-making by the individual asthma sufferer. The AMP co-management approach places the asthma sufferer in a pivotal role in managing their asthma, for the first time in asthma management models. Making a patient more responsible and part of the active decision-making about their health positively affects their sense of control and may assist in their asthma being well-controlled. The AMP has given asthma sufferers the tools to self-monitor and be self-aware; keeping their medical provider informed of their decisions, their sense of health with regards to their asthma and their particular asthma management needs (53).

A collaborative approach is effective in the management of asthma

Asthma is a national health priority for Australia. The AMP has demonstrated how individual asthma sufferers, government authorities and all interested medical parties could work together in a more communicative and effective approach to asthma. This collaboration has had a positive impact on individual asthma sufferers' adherence to their AMPs (111, 112).

Active involvement in an AMP can support a sense of psychological wellbeing for the asthma sufferer – a new sense of empowerment. Thus empowered, the patient will use the media, like-minded consumer groups, disease-specific interest groups, internet resources and other more traditional means of acquiring health information to increase their understanding of the condition, resulting in more informed decision-making.

Decision-making

The asthma sufferer, as a decision-maker in his or her asthma management, may choose to investigate CAM in the context of an AMP. The choice of CAM within a medical model of well-managed asthma gives a safe and effective frame of reference for an individual's own self-awareness of what does and does not help their asthma. This may be considered a patient-activated, co-management health approach. The self-determining asthma sufferer who co-manages their asthma is able to continue their AMP and monitor improvements they may attribute to CAM treatment. This is an expansion of the responsibilities of the asthma sufferer, according to their AMP.

2.1.8 Integrative healthcare and co-management

An effective model for a collaborative co-management focused on integrative health is still to be researched, developed and then measured in terms of its success (113).

Developed nations are facing health budgets severely strained by epidemics of chronic illness and there is great interest in how these escalating health bills may be better-managed. Health systems are increasingly conscious of the economic benefits in placing more responsibility on the population for self-determining health behaviour and self-management of conditions.

No consensus

CAM systems frequently propose a healthier life as a priority, to minimise reliance on the biomedical model when sickness occurs. Health providers, like their patients, are aware of some limitations in relation to biomedical treatments.

There has been no consensus on a model of integrative healthcare delivery. Developed societies are seeking new models that deliver to patients' satisfaction, and are safe and effective. The individual patients, health providers, researchers, health insurers, government health authorities and policy-makers are all stakeholders in this model of healthcare (114).

The well-informed health consumer and their medical provider

In asthma management, medical providers see that asthma patients are well-managed medically, with an AMP in place and the use of prophylactic pharmaceutical regimens. Asthma sufferers nevertheless still present for professional attention, just because they are 'not feeling good'. This may be prompted when a patient conducts research via the internet and/or makes contact with consumer groups. The individual wants to be able to discuss the value of other approaches to their overall health and wellbeing with their medical provider (115).

This well-informed health consumer is aware of current changes in the scientific understanding of how the body works. The internet provides access to innumerable websites with many levels of information for health consumers. New sciences involving 'whole' health, and the science of psychoneuroimmunology, are discussed online and can assist in understanding why a therapy may be helpful. Such health consumers are often already personally aware of the practical benefits of some non-scientific or unproven systems of healthcare such as chiropractic, acupuncture and yoga. It may be that the WHO's definition of health established in the 1940s, is now impacting health consumers in the 21st Century. Their voices are demanding healthcare which doesn't just manage sickness and disease.

Medical providers and CAM providers

In Australia, one in five medical providers, being a general practitioner, uses CAM in medical practice (30). The reasons for this can be more pragmatic than philosophical. In developed nations, there is a patient-centred paradigm developing in healthcare, with an increasing force behind the voice of the health consumer.

Integrative medicine is a term used to describe developing medical practices that include CAM as part of the services they offer. The integrative medical practitioner maintains the conventional medical hierarchy of diagnosis and offers co-ordinated care that includes the use of ‘alternative’ therapies. These therapies are seen as ancillary to the medical treatment and not always directly contributing to medical outcomes.

In Australia, there exist professional bodies of medical providers interested in advancing the use of integrative medicine. The Integrative Medicine Association (IMA), established in the 1990s, seeks to establish collaborative research into, and the development of, ways to include CAM with conventional medical approaches.

Healthcare stakeholders and integrative models

Collaboration between teams of healthcare providers and health consumers may offer the means to develop this model. In this collaborative mode, healthcare stakeholders can contribute to its desired outcomes. Research into the efficacy of integrative healthcare delivery is starting, examining the theories of the integrative model. Further research will follow into the clinical efficacy of its practical delivery (116-118).

Integrative co-management

In integrative healthcare, sharing professional perspectives and knowledge can table differing opinion. Focus is on the patient more than the health disciplines represented by the healthcare team. The focus of the team is less hierarchical in leading diagnoses and care plan decisions. Co-management in the context of integrative health is more about the team of healthcare providers and their interaction regarding the care plan for a patient.

Patient outcomes

The integrative health model has the patient and his or her health outcomes as pivotal. A patient-centric healthcare plan is developed and managed by the team, with patient-centred outcomes central to regular care plan reviews. The questions are still there, whether the CAM is practiced by medical providers effectively or CAM providers are involved in co-management team decision-making. The subsequent question is, can the integrative health team members, as a collaborative group, position their own ‘beliefs’ and professional egos below the shared goals for the patient in their care? Successful solutions to these questions are possible when there is professional understanding across the healthcare disciplines in the team. Success will see effective integration of the various providers, and the working implementation of integrative healthcare and co-management of patient health outcomes, as a team with the patient central to the collaborative focus.

Multi-disciplinary learning

An environment providing more multi-disciplinary experience may assist, starting in the undergraduate years of all health science and medical schooling. Prejudices and bias among the CAM and medical providers will have less potentially adverse impact on collaborative management when healthcare providers have learnt and researched together as students.

2.1.9 Definitions of chiropractic

In Australia, the largest professional association of chiropractors is the Chiropractors’ Association of Australia (CAA). As an authority on chiropractic practice, the CAA offers an understanding of the profession explaining chiropractic as a CAM healthcare system: “Chiropractic is a healthcare discipline based on the scientific premise that the body is a self-regulating, self-healing organism. These important functions are controlled by the brain, spinal cord, and all the nerves of the body. ‘Chiropractic’ comes from the Greek word *Chiropraktikos*, meaning ‘done by hand’.”

The practice of chiropractic focuses on the relationship between structure (primarily the spine, and pelvis) and function (as co-ordinated by the nervous system) and how that relationship affects the preservation and restoration of health.

The skull protects the delicate tissues of the brain. The moving bones of the spine protect the intricate communication pathways of the spinal cord and nerve roots. If these nervous system pathways are impaired, malfunction of the tissue and organ function throughout the body can result.

The chiropractor promotes education about ‘wellness’ described as a lifelong process of assuming personal responsibility that empowers the individual to exercise choice, make informed decisions and take action towards a more balanced, dynamically sustainable and fulfilling existence in all dimensions of life. The chiropractic practice places emphasis on nutrition and exercise, wellness and healthy lifestyle modifications for the long-term health of each person (119).

Manipulative and body-based practices in the history of healthcare

The practice of manipulation, ‘bone-setting’, massage and therapeutic touch are a part of many traditions of healthcare. Historically, joint manipulation has been part of the traditions of many ancient civilisations. There have been manipulative approaches to the body to encourage health and prevent disease in indigenous cultures and folk medicines around the world for over 2000 years. Early Greek physicians used to replace displaced vertebrae by hand to cure disease. ‘Spinal irritation’ was mentioned as a medical entity in 1832, with tenderness of the appropriate vertebra confirming the suspected diseased organ.

Chiropractic as a healthcare system developed in the United States of America over the past 100 years. In 1895, a bone ‘out of place’ was observed in a patient’s spine. This was treated by D.D Palmer – the founder of chiropractic. He observed that there was irritation in the surrounding tissues of the spinal region. The ‘bone of spine’ was an observation of the

vertebral level of the spine being out of alignment with the rest of the spine. According to Palmer's theory of spinal dysfunction, this caused the surrounding tissues of the spinal region to lack healthy and normal function. This state of imbalance in tissue function was introduced as a chiropractic concept of altered 'tone' in the body. It was claimed this would increase the likelihood of disease, according to Palmer's theory (120).

According to the 2010 classification of the National Center for Complementary and Alternative Medicine (NCCAM) in the United States, chiropractic is defined as a 'manipulative and body-based' system – one of four CAM categories (107).

Chiropractic has been registered in Australia since 1979. Today, individuals visit chiropractors more often than any other CAM provider in this country. For example, over a two-week period in 2005, Australians had 433,000 consultations with a chiropractor; 134,000 consultations with a naturopath; and made 90,600 visits to an acupuncturist (119).

The largest CAM provider of 'manipulative and body-based therapy'

Chiropractic is the most frequently accessed health profession after medicine and dentistry.

Registered in 100 countries around the world, chiropractic, for the first time in its history, has the interest of, and is receiving funding from, governments of developed nations.

Chiropractic is the largest CAM system in the NCCIM's category of 'manipulative and body-based therapy'. This position of chiropractic in CAM confirms chiropractic is also the first professional healthcare system with a manipulative and body-based approach. The leadership role that may seem a natural part of worldwide acceptance of chiropractic healthcare is now being challenged. There are increasing numbers of other healthcare providers using 'manipulative and body-based therapy' and no longer are manipulative procedures only found at the chiropractors' clinic (121).

Within the profession there is disunity. There are debates as to whether chiropractic is a CAM whole system of healthcare. Is it a non-medical therapy of spinal care or a style of

manipulative procedure? These questions are strongly debated and are to date, without resolution; conflict is evident and ongoing (110). External to these intra-professional debates are the ongoing questions raised by scientific communities and political interest groups. Issues of chiropractic healthcare legitimacy and arguments regarding unscientific principles are discussed in published literature (122).

Manipulative and body-based healthcare inter-disciplinary research

Chiropractic, as the largest body of CAM providers of manipulative and body-based healthcare, should be leading CAM research in manipulative and body-based healthcare. Chiropractic could promote growth in inter-disciplinary research across the many providers of manipulative and body-based healthcare. As interdisciplinary research develops, chiropractic could contribute to the role of manipulative procedures, spinal care and patient-centred models of integrative health (21, 30).

2.1.10 Research issues in chiropractic

In Australia, in the last 30 years since chiropractors were professionally registered as primary care providers, undergraduate programs for chiropractic education have developed into five-year, university-based programs. Research questions about chiropractic theory and practice are increasing. A chiropractic research discipline is developing in the collaborative research environment of university-based education (123).

Chiropractic research has been influenced by medical research into manual therapies. Chiropractic, as a research discipline, began with collaborative research into manual therapies. A conference in 2005 looked at manual therapies and biological mechanisms, presenting five areas of scientific research and comment on ‘manipulative and body-based therapy’. Discussion centred on neuroscience, biomechanics, endocrinology, imaging and immunology (123). A conclusion was that clinically based research needs day-to-day measures to assess the complex benefits of manipulative and body-based healthcare in an integrative healthcare environment. This clinically based research approach was then supported by laboratory-based,

experimental research to further the understanding the biological mechanisms of the therapeutic benefits observed from ‘manipulative and body-based therapy’.

The chiropractic profession is responding to the EBM movement, health insurers and government health authorities. The profession is under pressure to establish practice guidelines, treatment programs and clinical standards (124).

EBM reviews which support chiropractic in limited cases of musculoskeletal pain syndromes are actually supporting Spinal Manipulative Therapy (SMT). There are many providers of SMT in the healthcare system. SMT is a broad term that covers manipulative procedures used by chiropractors and other providers (125). Manipulation, SMT, mobilisation and other soft tissue manipulative therapies are all procedures used by chiropractors, osteopaths, physiotherapists, physical therapists, some naturopaths, massage therapists and within some traditional Asian therapies in Australia (25).

According to the Cochrane library, SMT is known as a ‘hands-on’ treatment of the spine, which includes both manipulation and mobilisation. In manual mobilisation, therapists move the patient’s spine within their range of motion. They use slow, passive movements, starting with a small range and gradually increasing to a larger range of motion.

Manipulation is a passive technique where the therapist applies a specifically directed manual impulse, or thrust, to a joint, within, at or near the end of its passive (or physiological) range of motion. This is often accompanied by an audible ‘crack’ (126).

The Cochrane reviews of clinical trials of SMT in the management of acute, sub-acute and chronic low back pain are based on quality assessment tools of research evidence that are regularly reviewed. The methods of ‘quality assessment’ used may require research into their validity and reliability within the actual healthcare paradigm they are assessing so as to be considered applicable (127).

These quality assessment tools regarding research evidence are used to examine published literature. One of the criteria used by the Cochrane Back Review 'Quality assessment group' is the use of a sham to assess efficacy in a research design (128). Yet there are no RCTs establishing the biological mechanisms by which SMT offers therapeutic benefit to neck and back pain. Therefore the use of sham may be considered inappropriate for this research purpose. The RCTs of SMT in the Cochrane reviews are clinical trials of comparative effectiveness. Without any established plausible mechanism of benefit for research comparison between SMT techniques or for one style of SMT with a sham, there may be therapeutic benefits from all techniques and all shams; the results may be invalid. These reviews of low back pain and neck pain, and the role of SMT in spinal pain management observe that there is no evidence that manual or physical therapy is any more useful than current regimens of pharmaceutical or non-physical therapy (126, 129).

There are Cochrane reviews of comparative effectiveness that require the 'treatments' across the clinical trials to be grouped, in order to be examined. A recent review grouped medical management, SMT, SMT-sham, 'ineffective' and harmful treatments, and treatments that did not fit the other groupings. This review determined that SMT had benefits only when compared with sham manipulation or the group of treatments considered to be ineffective or harmful. This evidence review concluded that SMT was probably more effective than the sham or placebo, but it depended on the profession of the provider of the SMT (130).

A chiropractic review of SMT in 2005 discussed this physical procedure in terms of its variability of delivery. It suggested that chiropractic treatment is varied by the provider according to the presentation of a patient. This review discussed the experience of 100 years' of chiropractic and the use of SMT in its practice. It was suggested that in clinical presentations of simple joint hypo-mobility, SMT does involve a combination of subtle, passive movements to align the vertebrae as a 'closed pack' and then apply a manipulative

procedure to offer increased range of movement that is not applied into the painful threshold or ‘nociceptive zone’ of the joint. The presentation of more complex joint dysfunctions, as seen often in the practice of chiropractic, can be joint dysfunctions of a three dimensional plane of joint dysfunction. These clinical presentations can involve, for example, non-painful joint dysfunction with unexplained spasm or swelling, trauma, co-morbidities, poor core stability, postural weakness, interrupted joint-end feel and arthritic dysfunction. In these presentations of complex joint dysfunction, chiropractic clinical decisions are then concerned with a ‘clinical physiological’ range of motion. This is suggested as being the clinical presentation of the joint dysfunction; not always hypo-mobility. In practice, there is a chiropractic clinical judgment made of the ‘clinical physiological’ range of motion to decide where, within this ‘clinical physiological’ joint range of motion, the chiropractic treatment is to be applied (79).

There may be an identity crisis for this very diverse and independent group of primary care providers. Are chiropractors point-of-entry physicians, generalists or specialists in the emerging healthcare system?

After chiropractic’s first 30 years’ as a formal, university-based discipline there is still no agreed understanding of any of the chiropractic-specific clinical concepts such as the manipulable lesion and subluxation. Yet these pervasive terms continue to exist without reliability or reproducibility tests (131-133).

As the third most frequently accessed healthcare profession and the largest CAM provider group, chiropractic should be able to contribute to collaborative research of cost-effective, safe and patient-centred healthcare delivery, and help address the worldwide epidemics of chronic multi-factorial illness and escalating healthcare costs. Chiropractic, without further effective research, may be one of many providers of ancillary ‘body- based and manipulative’ therapy (29, 134).

2.1.11 The chiropractic term - 'subluxation'

'Subluxation' has been a term used historically by chiropractors. 'Subluxation' is used in clinical practice by chiropractors, when routinely treating patients, to explain what they are 'treating' when examining the spine. The chiropractor is described as the health professional concerned with 'the preservation and restoration of health, and focuses particular attention on the subluxation' (135).

Historically, this term was used to differentiate the practice of a chiropractor from a medical doctor. Only the chiropractor used the term 'subluxation' in their clinical practice. This term was actually used initially, as a point of differentiation in a defence case about chiropractic, before the courts (136). However, the term continued to be used as a point of differentiation. This has influenced the chiropractic profession. There has been a greater value apportioned to the subluxation as a differentiating factor for chiropractic practice than has ever been validated (118).

According to the WHO, chiropractic is the healthcare profession concerned with the diagnosis, treatment and prevention of disorders of the neuromusculoskeletal system and the effects of those disorders on general health. This respected health authority continues to view the chiropractic profession as using manual techniques, including joint adjustment and/or manipulation, with a particular focus on subluxations (137).

It is suggested that defining the components of this fundamental chiropractic concept may have occurred prematurely. Certainly, the precise nature and pathophysiology of the subluxation construct has confounded many researchers. Given the lack of research evidence that subluxation is something that exists, it may be that the divisible components of this construct are too rigid (118, 138).

A research approach examining what the chiropractor does in clinical practice, without clinical technique jargon, may offer insight into what it is that the chiropractor achieves. The

practice of chiropractic may have more to offer research than the *theory* of chiropractic practice. The use of more patient-centred research tools and a greater range of objective measures appropriate to non-pharmaceutical healthcare may be a part of the research model. Understanding ‘subluxation’ as an undefined concept of clinical practice may find more expression of its nature in the context of the chiropractic clinical encounter. This new approach, using research tools examining non-pharmaceutical treatment and more specific chiropractic patient-centred outcomes, may offer a new understanding of the term as it is found in the practice of chiropractic (139, 140).

The long-term lack of clarity about ‘subluxation’ means the right research question is yet to be posed. While the term served as a concept (unscientific in context) to hold the profession together as a distinct identity in its youth, with 100 years’ of maturity, old concepts can now be reviewed and new research questions posed to address them (139).

A former director of the Foundation for Chiropractic and Education Research (FCER), a major chiropractic body for education and research, suggested that research into the concept of subluxation is best seen as a work in progress. New science brings new understanding in all areas of scientific pursuit; previous models of subluxation will disappear as new constructs are theorised and researched. Chiropractic does not need to abandon the term subluxation; just release a tightly held definition and allow new research to contribute to its meaning (141).

Since the mid-1990s, the Association of Chiropractic Colleges (ACC) in the United States has brought together a wide range of perspectives on chiropractic. The ACC maintains that in clinical practice, subluxation is evaluated, diagnosed and managed through the use of chiropractic procedures based on the best available rational and empirical evidence (139). This body is uniquely positioned as representative of the majority of chiropractic educational institutions in the world, to help define chiropractic practice. Concepts of subluxation are

increasingly reviewed. The combined research activities of the ACC are able to develop new research questions and promote a self-critical discipline of chiropractic research.

A patient-centred healthcare research model would allow clinical practice and the concept of subluxation to be researched together. A research focus on the chiropractor, the patient and the patient's health changes may then assist in understanding what the chiropractor does in clinical practice. Subluxation may be part of the clinical research question but not identified. It is the practice of chiropractic and not the concept of subluxation that will contribute to healthcare systems worldwide.

2.1.12 Clinical techniques used in chiropractic practice

Multiple techniques and diversity

There are many clinical techniques available to chiropractors in treating dysfunction of the spine and related regions. First, there is clinical assessment of the patient as to whether a chiropractic treatment is appropriate. The chiropractor then makes clinical decisions as to the type or variation of clinical technique to be used in combination or alone, and according to the needs of the presenting patient (136).

Clinical techniques for spinal treatment have been developed by chiropractors since the beginning of the profession. A specific vector of direction was developed in the early 1900s as a clinical technique; this was a vectored thrust of high-velocity and low- amplitude, applied to a specific vertebral level of dysfunction. This was called a short lever approach treatment and was developed by D.D. Palmer, known as the founder of chiropractic (121). This early clinical technique of chiropractic practice was developed to directly contact, and with little actual movement of the spinal segment, precisely reposition one segment of the spine (vertebra) in relation to the spinal segments sitting immediately above and below it.

While chiropractors around the world use over 100 techniques, more are being developed – and these new clinical techniques are not replacements for other techniques. They are all

chiropractic clinical techniques that are used in chiropractic practice to greater and lesser degrees (131, 142, 143).

Techniques and technology

With advances in technology, hand-held instruments for chiropractic treatment of spinal dysfunction have been developed. These are commonly used within a defined chiropractic clinical technique. These instruments can control and/or alter the force delivered by the chiropractor in their spinal adjustment, and are usually spring-loaded, velocity-based tools. They have an adjustable feature to alter the impact at each application, to treat spinal and other joint dysfunction.

The clinical option of using a drop-piece table has enabled the chiropractor to deliver a high-velocity and low-amplitude force to spinal segments with a minimum of impact to the patient. The drop-piece table has several pre-set movable pieces in its 'table-like' design for 'dropping' under force. The table can be pre-set with the patient positioned over the movable pieces of the table for treatment. The chiropractor moves in unison with the client as they apply a short thrust to the level of spinal dysfunction. As the patient's body moves away with the drop-piece table, the treatment or correction of the spinal level of dysfunction occurs, with the drop-piece falling a few centimetres in a crisp or sharp movement.

In other chiropractic clinical techniques, there are triangular-shaped blocks or 'postural wedges' positioned under the body to passively de-torque a level of spinal dysfunction. The 'postural wedges' are therapeutically positioned with the patient supine. They force the pelvis in its three bony parts, the ilia and the sacrum to move around the two triangular-shaped blocks, as the patient relaxes with slow, deep breathing.

There are clinical techniques that also use peripheral technical equipment for assessing spinal function and other individual health measurements. An example is the dermo-thermograph. This instrument has been integral in chiropractic clinical technique since the early 20th

Century to assess temperature and other changes in the spinal levels or vertebral segments. The use of X-rays, surface electromyography, thermography and other diagnostic equipment is now common. Such medical imaging technologies are now part of established chiropractic clinical techniques used in practice to confirm the diagnosis of an appropriate chiropractic treatment for a patient.

Joint distraction, traction and mobilisation by hand are all clinical techniques of chiropractic practice and are often combined with therapeutic equipment for the same purpose. ‘Clinically therapeutic machines’ as well as hand-based manipulations are used to greater and lesser degrees by chiropractors. Chiropractic clinical techniques vary according to the experience of the practitioner. There may be several techniques used in any one practice. There may be a ‘complex treatment intervention’ approach, where numerous clinical techniques are used in combination by the chiropractor. In some practices, ancillary procedures are used, routinely or when considered appropriate for a patient. A nutritional supplement and/or an acupuncture treatment may also be used alongside a chiropractic treatment (144).

Technique development and research limitations

Historically, clinical techniques have evolved in response to older clinical techniques. As is normal in healthcare, clinical practice offers the opportunity for clinical observations of which treatments amongst those used achieves results. With cumulative clinical experience, a practitioner may develop a new clinical technique. In the history of chiropractic clinical techniques, such developments have been occasions of great upheaval. Political divides within the chiropractic profession about ‘technique’ bias still exist between chiropractic colleges. Historically, this has been as a result of the strength of conviction of early chiropractors. When they discovered an approach that delivered improved clinical results for patients, not only was it introduced as a new clinical technique, but often a new chiropractic college would be established in which to teach it (143). Students would adopt in practice a

possibly natural bias towards the techniques learned. This may be the case for many professional groups.

In the history of chiropractic, college-based technique allegiances were formed around the clinical techniques of that institution and may have encouraged unnecessary prejudices. Technique allegiance has been politically disruptive and self-limiting for chiropractic; materially limiting research that is not technique-based. A unified professional research agenda requires a common factor of chiropractic that is not dependent on the various schools of clinical techniques. To date, there has been no technique-collaborative clinical research group or clinical research model that has been able to accommodate the diversity of chiropractic clinical techniques in practice today (145).

2.1.13 Use of the clinical terms ‘adjustment’ and ‘manipulation’

Without consistently understood and interpreted terminology, valid within the healthcare being researched, there is confusion in the results. Both ‘adjustment’ and ‘manipulation’ are terms used in chiropractic practice. Each term is used to describe the treatment delivered by the ‘manipulative and therapeutic body-based’ systems of CAM; these all appear under this one banner of CAM (146). Chiropractors, osteopaths, physical therapists and some physiotherapists and general practitioners are all health professionals who administer therapeutic applications to spinal dysfunction and body joints generally. The terminology of treatment may vary.

It may be noted that only chiropractors use the clinical term ‘adjustment’. Many use the term ‘manipulation’ and refuse to use the term ‘adjustment’. There is no current and valid independent principle to differentiate these two terms. Also, there is debate among chiropractors as to what a valid treatment is, in the context of these terms.

The nature of the delivery of an ‘adjustment’ as opposed to the delivery of a ‘manipulation’ may be a differentiating factor. An ‘adjustment’ is delivered using a short lever approach to

the spinal segment or vertebrae. It is delivered by a specific thrust at the transverse or spinous process of that particular vertebra. According to the founders of the chiropractic profession, it is this use of a short lever that defines or distinguishes an ‘adjustment’ (120). Some chiropractors consider only one specific, spinal segmental correction, or the correction of a ‘subluxation’ to be an ‘adjustment’, while others make ‘adjustments’ to any and all osseous articulations, from the atlas, to the sphenoid (skull) and to the talus (foot) (140).

By contrast, a ‘manipulation’ is said to use a long lever approach with less specificity of hand contact on the local tissues of the target area of manipulation. This technique is designed to increase the range of motion within the spinal segments and is often said to be used where spinal segments are considered fixated or hypo-mobile. Then the ‘manipulation’ is applied to move one or more joints and result in an increased range of motion.

Confusing the terms adjustment and manipulation impacts chiropractic research (145). A lack of consensus around clinical practice terminology causes disunity in the chiropractic profession and limits its development as a single body of knowledge. As the oldest of the CAM professions using body-based and manipulative healthcare approaches, chiropractic is in a position to lead into common terminology for research purposes. However, first chiropractors must achieve internal consensus on the nature of their clinical understanding of the terms adjustment and manipulation (79).

A collaborative research group could examine manipulative therapy in its many forms and by its many names, most effectively. Such a group would include the expertise of chiropractors, osteopaths, physiotherapists and other physical therapists (121).

2.1.14 Autonomic nervous system and chiropractic concepts of ‘tone’

The ANS and asthma

The function of the Autonomic Nervous System (ANS) is associated with asthma health. Well-managed asthma requires a healthy, balanced, functioning ANS (147). The

pathophysiological mechanism underlying asthma may be due to factors of inflammation and also unknown ANS abnormalities. Some disordered neural regulation may be related to the pathogenesis of the bronchial hyper-responsiveness and mucus hyper-secretion observed in chronic asthma. This may be due to altered function of the ANS in asthma, though this remains an area of asthma that is not understood.

Asthma is a condition involving an altered responsiveness to the stressors of the internal and external environment in each individual asthma sufferer. The ANS is part of the body's defence system which is activated when confronted with a stressor. Health, in the context of asthma, occurs when the function of the ANS is balanced and healthy, and homeostasis is maintained. Homeostasis requires a highly organised and self-governing environment. The role of the ANS is to respond to the demands of the internal and external environment with appropriate physiological changes (148).

The ANS and research

Early research examined the body's stress response to skin and spinal noxious stimulation. This research observed the function of the ANS via the response of body and internal organ function, when there was noxious skin and spinal stimulation.

This is relevant to what a chiropractor does in practice, in terms of stimulating the spine and related areas of skin in the course of chiropractic treatment. This aspect of chiropractic treatment's clinical approach is discussed with reference to the earliest clinical techniques and the clinical concept of 'tone' (149).

The ANS refers to a combination of the sympathetic and the parasympathetic nervous systems. The sympathetic nervous system is responsible for the body's 'fight or flight' reaction to sudden shock or prolonged stress factors; be they physical, mental or emotional. The parasympathetic nervous system is responsible for regenerating the body; maximising blood to internal organs during digestion and other vital body functions (99). The enteric nervous

system works independently of the ANS, located in the wall of the gut, but may be considered a part of the ANS. There is a complex, interconnected modulation of organ function, by the ANS, that involves its enteric, sympathetic and parasympathetic divisions, as well as systemic, hormonal and chemical mediators of healthy organ function.

The ANS is activated chiefly by centres in the brainstem, spinal cord and hypothalamus. The higher centres of the cortex, and the limbic system or emotional centres of the brain, may also affect the ANS, which could be considered a web that interconnects the brain (CNS) and the rest of the body in all functions (150).

Healthy structure and function

A biomechanically healthy ribcage is vital to the asthma sufferer. Treating the structure of the ribcage has always been one basic and accepted therapeutic benefit from CAM categories of healthcare that are ‘manipulative and body-based approaches’. Viewing the spine as a physical ‘tube of movable segments’, it may be seen to shepherd the nervous system in its functional distribution from the CNS to the rest of the body, and in all co-ordinated activities of the ANS. Levels of spinal dysfunction may be associated with changes in the anterior, posterior and lateral aspects of the spinal cord, in turn disturbing the ANS and altering body function and homeostasis (149).

A study of visceral pain without pathology found that if postural deformity and ‘short leg’ postural compensations were corrected physically, the visceral pain went away. It was hypothesised that this was due to a sympathetic/parasympathetic imbalance of an undetermined nature occurring at the spinal level. There was no visceral pathology and the physical corrections influenced the pathways of perceived organ pain (151).

Another study of chronic vertebral misalignment (CVM) in the thoracic spine, with co-morbidities of allergy and asthma, indicated an association between physically compromised thoracic vertebral segments and symptoms of allergy and asthma. Altered immune function

was the underlying link between the physical compromise of thoracic vertebral levels and the co-morbidities of allergy and asthma (152).

Therapeutic touch

The CAM category of ‘manipulative and body-based approaches’ is about body stimulation. The effects of this may be non-specific, as in massage, or point-precise as in acupuncture, or spinal segment-specific as in chiropractic. Each approach has a therapeutic touch that involves varying forces and applied pressures. The level and type of stimulation differs between individuals, between variations or schools of the CAM system, and across the range of CAM ‘manipulative and body-based approaches’. The body’s responses to stimulation of the skin has been the subject of research since the early 1900s (153).

Studies of somato-sympathetic reflex showed that stimulation of the hind and front paws of full-spine animals (CNS-intact), elicited a heart rate response. This was once more the case when the animals were spinalised (CNS-detached), though it was a weaker response. Stimulation of the thoracolumbar spinal region produced a greater response in the spinalised (CNS-detached) animals, and it was noted that the one side of spinal stimulation as a focused area, produced a greater response in the heart rate. This is yet to be understood (154).

There is limited research into the stimulation of spinal levels, as opposed to skin stimulation in the area of the back. However, research examining somato-autonomic reflexes does demonstrate that stimulating spinal levels specifically results in somato-sympathetic reflex discharges (155-158).

This research into spine and skin stimulation indicated certain levels of the spine are involved in different organ responses. There is evidence that a level of spinal organisation exists in somato-autonomic reflexes and visceral function. The afferent (sensory) autonomic tracts served by cell bodies in the dorsal root ganglion of the spinal nerves, have a crossover with

somatic (body/skin level) sensory fibres. This crossover effect of somato-autonomic reflexes demonstrates that skin stimulation has a direct effect on visceral function (149, 159).

Research into spinal levels of involvement in somato-autonomic reflexes showed stimulating thoracic and lumbar interspinous tissues in animal models, with a capsaicin injection, resulted in increased adrenal sympathetic nerve activity. An adrenal gland response was seen in the stimulation of thoracic vertebrae T7 and T10 in the spinalised animals (CNS-detached), confirming a spinal reflex, not a supra-spinal mediated (CNS) reflex. In organs with a parasympathetic innervation and where the reflex is supra-spinal, there is no clear segmental organisation (160).

This research into skin and spinal level stimulation producing somato-autonomic reflexes and alterations in visceral function suggests that a relationship exists between two seemingly anatomically distinct systems of the body. The systems may appear distinct in function and anatomy, yet they are part of the same body. This is not a surprising idea, as many healthcare approaches of the world, such as acupuncture and meditation, do not separate the body into its parts (159).

A study of an ‘acupuncture-like’ needle insertion in anaesthetised rats produced somato-autonomic reflexes and visceral function, which registered as excitatory gastric motility. The needle stimulation into the rats’ abdomens produced a reflex response with an efferent path to the gastric sympathetic nerves and the reflex centre within the spinal cord. This study also demonstrated a reflex response with needle stimulation of a paw of the animal. Its afferent nerve pathway was via cutaneous and muscle afferent nerves, and its reflex centre required the presence of the brain (CNS-intact) with the efferent nerve pathway, then the gastric vagal efferent nerve (82). This research encourages understanding of the varied nature of stimulation resulting in what may be called the therapeutic benefits from a variety of body-

based manipulative and manual therapies. This supports empirical evidence regarding the use of such therapies.

There have been anecdotal reports of benefits to asthma from chiropractic for some 100 years (161). An early chiropractic clinical technique involved feeling for the 'tone' of tissues and particularly around the spine. Used as an indicator of levels of spinal dysfunction, the finding of a lack of 'tone' may have been an indicator of associated autonomic dysfunction. In the early 1900s, chiropractors were taught to look at signs of the 'tone' of the body. Normal 'tone' is "the condition of the body in which all the functions are performed in a normal degree. When body functions executed in too great or too little a measure, just in that proportion, is there disease (120)". Normal 'tone' was described on the basis of clinical observations, and the experience of the palpation of the spine and related areas. The earliest chiropractic clinical techniques described normal 'tone' as the desired state of health in a patient. This was 'a normal degree of nerve tension' and a healthy function exhibited as 'elasticity, activity, strength and excitability of the organs' (120, 142).

Neurophysiological responses and changes in body function

Scientific research in the early part of last century examined the phenomenon of neurophysiology and body function. There was research into external stimulations of the body and observations of any organ response to such stimulation were made. Experimentation involving the sympathetic and parasympathetic nervous systems frequently used noxious stimulation of limb tissues to elicit changes in heart rate and blood pressure to understand this autonomic response to skin stimulation. These experiments led to the investigation of the somato-autonomic reflex and directly contributed to the model of autonomic response to noxious stimulation. This work was attributed to Walter B. Cannon in the 1920s and characterised as the 'fight/flight' or survival response (148). Noxious stimulation applied to any tissue would elicit a generalised response mediated by the brain (CNS). It was observed that a transection of the cervical spinal cord eliminated somato-sympathetic reflex discharges

and it was assumed, by Cannon and others, that these reflexes were mediated at the supra-spinal level, above the transaction of the cervical spinal cord.

The nature and type of cutaneous or visceral stimulation determines the type of receptor and afferent fibres activated, and the level of autonomic response. With noxious stimulation, receptors transmit sensory information into the dorsal horn of the spinal cord and autonomic dysreflexia occurs via mechanoreceptors and nociceptive free nerve endings. There appears to be an increase in sympathetic fibre ‘sprouting’ in response to the noxious stimulation (162).

There has been much research conducted to understand the impact of noxious and innocuous skin stimulation on the stress response and autonomic dysreflexia, particularly in relation to spinal cord injury (SCI). There is no research into any therapeutic relationship that may exist between noxious and innocuous skin stimulation on or around the spine and health improvements in organs of the body.

Treatment and modulating impact on the ANS

Altered function of the autonomic nervous system (ANS) is suggested to be an underlying abnormality observed in patients with ill health such as asthma (163). There is little research into the impact of ‘manipulative and body-based approaches’ on autonomic reflexes to examine any possible therapeutic benefits. Chiropractic researchers have postulated that chiropractic treatments of the spine and related areas have a modulating impact on the ANS. (163, 164).

If there was such a therapeutic relationship, it may contribute to an understanding of asthma management. The effects of somato-sympathetic or somato-parasympathetic responses and reflex activity of the ANS may be monitored for any modulating impact on the ANS from chiropractic treatment. The functional health of the ANS may be an indicator of an individual asthma sufferer’s responsiveness to their asthma triggers (165).

The science of psychoneuroimmunology in its developments since the 1970s is offering a new understanding of health and illness. The mind and the body are one, the ‘whole’ person seen rather than many systems of body function. Current research developments in these new sciences of neuroendocrinology and psychoneuroimmunology are seeking to understand the relationships of mind, body and the communication systems of the body (166). Clinical research with ‘biomarkers’ of physiological changes in ANS functions may assist in examining the chiropractic practice of treating the spine. Any changes in the health of the ANS in response to chiropractic treatments of the spine may indicate some neurophysiological impact occurring in the ‘whole’ person. These ‘biomarkers’ of physiological change may well be developed for chiropractic clinical research into asthma management (167, 168).

2.1.15 Painless spinal dysfunction and chiropractic concepts of ‘tone’

Assessing tone of spinal tissues

The concept of painless spinal dysfunction is discussed in regards to the early chiropractic clinical technique of assessing the tone of tissues around the spine.

Spinal dysfunction is a lack of normal function of the spine. Chiropractic clinical techniques assess levels of spinal dysfunction and then treat that dysfunction. These techniques can be combined and the skills of palpation, specific testing procedures, differential diagnosis, clinical experience and specific diagnostic instruments can assist in determining the level of spinal dysfunction and observing changes in the nervous system (164, 169).

The earliest chiropractic techniques taught chiropractors to palpate for the tone of the spinal tissues and to feel for ‘a normal degree of nerve tension’. Where there was a lack of ‘normal tone’ in spinal tissues there was dysfunction, and the chiropractor would treat that level of painless spinal dysfunction. The clinical significance of painless dysfunction may involve some of the observed responses of the somato-sympathetic reflex of the early 1920s research into this neurophysiological phenomenon. The painless dysfunction observed by the

chiropractor in examining the spine may produce constant irritation, with a repeated discharge of sensory neurons. This constant irritation may impact parts of the ANS due to the neuro-anatomical relationships of the spine (170).

Spinal segments in body function

There is no suggestion that painless spinal dysfunction causes any systemic ill health. However, painless spinal dysfunction may form part of an imbalance in the ANS. The observation that the practice of chiropractic involves treating levels of painless spinal dysfunction is to be examined in relation to any changes in the functioning of the ANS that may result. Chiropractic treatments are varied; from muscle release, non-specific and involving skin stimulation, to precise spinal segment-specific treatments. It is suggested that a repeated series of chiropractic treatments at the level of painless spinal dysfunction may deliver specific 'sensory' input into the ANS cycling of the viscera-somatic-viscera reflex. The painless dysfunction may not be the causative agent of systemic ill health. However, the mere involvement of the spinal segment via constant stimulation of receptors of spinal dysfunction may be part of the cycle of ill health (171, 172).

Research examining the chiropractic treatment of painless spinal dysfunction and any signs of changes in ANS function that may result will follow this earliest neurophysiological research. There has been some healthcare interest in the neurobiological mechanisms underlying spinal manipulative therapy (SMT) (173). This area of scientific examination has been of interest to medical doctors, osteopaths and chiropractors in the past, though changes in ANS function have been a limited area of research activity in these professions (174) (175). In the future, this may be of interest to any provider of manipulative and body-based healthcare.

Research into SMT has not focused on the biological mechanisms underlying observed benefits. Research into health changes that may occur at the cellular level of the body and may be ANS-mediated would be of value. Activating the physiological mechanisms of homeostasis may occur with chiropractic stimulation of the spine, depending on the state of

health in the presenting patient. Research into the chiropractic treatment of the spine may assist in understanding the continued patient-based reports of therapeutic benefits to asthma, from chiropractic. There is still a lot of scientific knowledge to be gathered about the ANS; how it is regulated, how it responds to therapeutic interventions and how it varies between individuals. This has been an area of limited chiropractic research and is one that may have more to offer in terms of understanding of the chiropractic practice of treating painless spinal dysfunction (139, 172, 176-179).

2.1.16 The MERIC System in chiropractic practice

Early observations of spinal dysfunction

The MERIC System is an autonomic reflex technique developed by early chiropractors, based on their clinical observations. These were early observations of spinal dysfunction associated with clinical presentations of ill health (139). The MERIC System was a clinical technique used as an observational tool to examine any associations between specific levels of the spine and the healthy function of specific organs. The neuro-anatomy of the ANS, its rostral and caudal variations of nerve exit, was systematically reviewed in combination with clinical experience, led to the development of the MERIC System. This was a very early clinical method used by chiropractors in treating painless spinal dysfunction.

The objectives of early clinical techniques in chiropractic practice were to develop skilled and sensitive palpation of the body and para-spinal tissues. This practiced palpation of tissue looked for sensitivity to temperature and tissue changes. This led to an awareness of disturbed 'tone' of para-spinal tissues, where temperature changes or taut and tender fibres at particular spinal levels would indicate levels of spinal dysfunction. This early clinical technique involved 'nerve tracing' when palpating the tissues. These findings would often include areas of pain or other body dysfunction presented to the chiropractor. With these findings recorded time and time again, the MERIC System developed as a clinical protocol. The spinal segments observed were gradually associated with clinical findings of co-morbidities in clinical

practice. This led to an observational science of clinically associated ‘nerve pathways’, or levels of spinal dysfunction and dysfunction in body systems or organs.

Observational science

This phenomenon of a reliable clinical system, based on observed findings, is found in the traditions of many CAM healthcare systems, such as acupuncture and Ayurvedic medicine, where a body of knowledge is built up, with recordings time and time again. The system becomes more and more established by evidence of its efficacy in clinical practice, with these many recordings of clinical observations, experience and results.

Referring to the MERIC System in clinical practice would suggest to the chiropractor several possible levels of involvement of spinal dysfunction, which would then be assessed. The MERIC System referred to the ‘tone’ of the tissues and spinal levels of possible involvement in clinical presentations. A ‘mere’ would refer to the tissue. The stomach was seen as a viscometer of the nerve supply of the fifth through to the eighth thoracic spinal segment. Palpation of these spinal segments would establish involvement by finding ‘taut or tender fibres’ at that particular spinal level. As the chiropractic profession developed, other methods to confirm abnormal findings of spinal segments were progressed. The early use of X-rays as diagnostic spinal X-rays, occurred routinely in chiropractic institutions in 1910, nine years after Roentgen (who discovered the X-ray) received the Nobel Prize in physics (142). Many other diagnostic testing and clinical techniques were developed as clinical tools used to confirm levels of spinal dysfunction (180).

The MERIC System is unscientific as a clinical technique, and only anecdotal in its usefulness. However, this system is part of chiropractic history and may contribute to new paradigms of research to examine what the chiropractor does in clinical practice. It is considered in research models of chiropractic clinical practice; particularly in observing the treatment of painless spinal dysfunction.

The Meric System is illustrated in the Appendix (181).

2.1.17 Clinical recording of spinal findings

In the practice of chiropractic, there is emphasis on the healthy function of the spine. A tenet of chiropractic clinical practice maintains that the healthy function of the spinal segments is linked to the healthy function of the nervous system. There are many clinical techniques used in chiropractic practice to determine levels of spinal dysfunction or lack of healthy function (136).

For practice-based research, ‘what’ a chiropractor does in clinical practice is important. Every chiropractor adopts one or more clinical techniques to use for assessment, treatment and management of the spine and related areas. The chiropractor is educated at an undergraduate level with a clinical technique that often becomes their clinical model of chiropractic practice. One technique might use the term ‘subluxation’ and others refuse to use the term, considering it unscientific or lacking any evidence. The treatment of spinal dysfunction in chiropractic practice is given different names according to chiropractic techniques: a chiropractic lesion, spinal misalignment, spinal fixation, chiropractic manipulable lesion or subluxation. Divisiveness based on clinical techniques and the term ‘subluxation’ is a persistent feature across the chiropractic profession.

Chiropractic research is a relatively new discipline. Experienced chiropractic research scientists are few in number. A self-critical chiropractic research discipline is now starting to emerge. This growth of a more self-critical research discipline is having a greater impact on the internal politics of the chiropractic profession than on the healthcare system. This may be necessary as a prerequisite for the chiropractic profession to have an impact on future healthcare developments (29).

With over 100 clinical techniques used across chiropractic practices, theories of subluxation abound, and technique-specific jargon is common (145). The Diversified Technique, Motion

Palpation, Thompson Table, Applied Kinesiology, Gonstead Technique, Sacro-Occipital Technique, Activator Method and Atlas-Specific are a few examples of chiropractic clinical techniques used around the world.

It may be productive to reconsider research questions concerning subluxation and re-assess a clinical research approach. Appropriate modelling of clinical research that includes a greater emphasis on observational data may be useful. The observations of what the chiropractor does, which spinal levels are treated and what treatment is given in presentations of co-morbidities such as asthma, may contribute to understanding why the anecdotal reports of benefits of chiropractic to asthma persist. Practice-based research allows for observations that may offer insights into the mechanisms of subluxation beyond theory or clinical technique definitions.

Common factors

To advance chiropractic research, it is suggested that common factors be found through observation of all techniques of chiropractic practice. A common imperative of chiropractic clinical techniques is the identification of levels of spinal dysfunction for treatment. This common factor may be able to be quantified for research purposes. A clinical recording sheet of levels of spinal dysfunction may be of use in chiropractic research. The levels of spinal dysfunction treated by the chiropractor makes many chiropractors working together in clinical research, possible. A research model in ‘typical’ practice settings may enable clinical research across many chiropractic clinical techniques. A non-technique specific clinical recording sheet, without jargon, used to record levels of spinal dysfunction was developed for the purposes of the clinical research underlying this thesis.

2.1.18 Previous studies of chiropractic treatment for asthma

Two research clinical trials that examined using chiropractic to treat asthma are discussed here, briefly, for the purposes of the clinical research design.

The Cochrane Collection, an internet-based library, provides regular updates on healthcare research as online reviews of published literature. One Cochrane review listed eight

chiropractic clinical trials as fulfilling the criteria for review. Two of these clinical trials related to asthma (62). The Cochrane review of asthma states that there is no evidence supporting the use of chiropractic in asthma management. Two clinical trials of asthma and chiropractic intervention also worthy of research design discussion were the Neilsen Bronfort and the Balon clinical trials (56) (57) (182).

Chiropractic and asthma research design

The Neilsen Bronfort trial examined asthma and a chiropractic treatment intervention of spinal manipulative therapy (SMT). This study had a sample size of 31 and involved a crossover design of the ‘active’ treatment intervention plus a two-week wash-out period to examine sustained benefits of the chiropractic treatment in the asthma sufferers. The subjects all maintained their medical regimes and two experienced chiropractors administered the ‘active’ treatment and the ‘sham’ treatment. This trial involved a program of eight ‘active’ treatments described as SMT. SMT was applied using the ‘drop-piece’ chiropractic table. The application of the ‘sham’ treatment was a manoeuvre that required the chiropractor to place their hands on the body of the person lying prone on the ‘drop-piece’ chiropractic table, and apply sufficient generalised force with the other hand direct to the ‘drop- piece’ of the table to cause it to drop beneath the person. Thus the ‘sham’ was performed without any direct vector or therapeutic application of force through the spinal area of the body.

‘Sham’ manoeuvre

The second trial was the Balon clinical trial. This trial was conducted with a sample size of 91 and involved 16 weeks of ‘active treatment’. The active treatment was decided by the 11 experienced chiropractors who delivered the treatment. The clinicians delivered a treatment on the basis of what they decided on each clinical occasion of the asthma subjects presenting for treatment. The ‘sham’ treatment involved the chiropractor placing hands on the body of the person with instruction not to apply any therapeutic manoeuvres; that is, to give no

treatment. Interestingly, the asthma subjects in this clinical trial reported being unable to distinguish between the ‘sham’ and active treatment manoeuvres.

Both these studies of chiropractic and asthma used a ‘sham’ treatment manoeuvre for the control of the ‘active’ treatment, for the purpose of examining the experimental intervention for any therapeutic benefit. The results of both clinical trials were inconclusive as to whether there was any benefit attributable to the active chiropractic treatment.

Therapeutic benefits of the ‘sham’

It is possible that both the ‘sham’ used for control of the SMT (defined as non-active treatment), and the SMT used as treatment, had some therapeutic benefit. This is because the nature of chiropractic treatment is as varied as the diversity of chiropractic clinical techniques that may be used for research purposes. The definition of what comprises a chiropractic treatment will differ according to the clinical technique. The amount of force and the degree of movement involved in delivering chiropractic treatment differs across chiropractic clinical techniques. Therefore the ‘sham’ of the chiropractic clinical treatment used in these clinical trials may still have delivered a therapeutic benefit according to a different chiropractic clinical technique. The inconclusive results may in fact be due to the ‘sham’ having had some therapeutic benefit. In fact, the sham may have been considered ‘active’ treatment if the clinical trial had been a research design that used another chiropractic clinical technique.

The placebo effect

In addition, the suggestion in both these clinical trials is that there may be a non-specific therapeutic effect at work. Firstly, this is possibly the therapeutic impact of participating in the clinical trial irrespective of whether the treatment received was active or not, and is unrelated to the chiropractic treatment. The placebo effect, the therapeutic nature of a healthcare exchange or chiropractic clinical encounter, and the Hawthorne effect of enthusiastic participation in the clinical trial, are all confounding factors in the RCT. These factors and any ‘non-specific’ therapeutic effects may be part of the ‘contextual’ setting of

chiropractic healthcare. The development of research designs to include more ‘non-specific’ therapeutic effects of chiropractic and other CAM systems will be of value in understanding the complex nature of CAM healthcare as a clinical intervention.

Participant perceptions

The asthma participants in the Balon clinical trial were unable to discern the difference between the ‘sham’ and the ‘active’ treatment. This means that the research design did have a successful sham from the participants’ point of view. The lack of difference they perceived implies that the placebo effect of the sham treatment did have a therapeutic benefit. This factor may then have contributed to the inconclusive results of these two clinical trials of asthma and chiropractic. Being able to quantify the impact of the placebo effect in chiropractic clinical research may not be possible without a measure of the physiological mechanisms that underpin the benefits of the chiropractic treatment. This measure is then able to quantify the relative impact of the placebo.

Furthermore, a successful ‘sham’ is not only delivering a seemingly identical treatment in the eyes of the caregiver and the participant in the clinical trial. A ‘sham’, if it is a true ‘sham’, is known to deliver a non-therapeutic version of the treatment. There is no conclusive understanding of how, or by what biological mechanism, it is that chiropractic treatment has a therapeutic benefit. Until this is known, there is no way of excluding the possibility that the sham may still be delivering a therapeutic impact.

Any therapeutic impact from the sham occurring in its delivery can make the research design ineffective when examining efficacy. This dilutes the research value of blinding with a ‘sham’ and lessens the value of choosing the respected gold standards of the randomised, controlled research design.

The use of ‘sham’ in this research design contributed to the inconclusive results and it may be that the inclusion of a ‘sham’ is not the best research design for chiropractic and other CAM or non-pharmaceutical clinical research.

Non-pharmaceutical research tools

As the biological mechanisms underlying any therapeutic changes associated with chiropractic treatments are yet to be understood, there are no specific research tools to measure these biological mechanisms.

The research tools used to monitor therapeutic benefits in asthma participants in previous clinical trials of asthma and chiropractic included the use of spirometry as a measure of lung function. Spirometry may be more useful in assessing the efficacy of pharmaceutical preparations in improving lung function in asthma, and monitoring long-term changes in chronic lung disease. Spirometry findings can confirm asthma with a response to oral dosages of bronchodilators and other asthma medications.

The use of the spirometer may be less appropriate when assessing a non-pharmaceutical treatment. Until any mechanisms by which chiropractic treatments benefit asthma sufferers are understood, using spirometry as a research tool may not be appropriate. The use of spirometry as a research tool to examine any therapeutic benefit of chiropractic treatment to the asthma sufferer, may have contributed to finding little difference between the asthma trial participants who received the SMT and those who did not.

Two factors, which may have been significant in these previous clinical trials of asthma and chiropractic, may require consideration for the development of chiropractic clinical research design. The first such factor is that the research did not show evidence of the efficacy of chiropractic treatment, as this required a plausible underlying physiological mechanism that can be examined to explain patient-reported anecdotal benefits. The second factor relates to what it is that a chiropractor does in clinical practice that benefits asthma. These research

questions are arguably as much research questions for chiropractic clinical research design, as measurements of therapeutic benefits observed for asthma. Forming a series of research tools to maximise data collection may be a useful step forward. Such a series of research tools may assist in identifying any biological mechanism, as well as any therapeutic benefit occurring from a series of chiropractic treatments for asthma.

2.1.19 Clinical research methods - randomised controlled trials

Briefly, the randomised, controlled trial (RCT) is considered here in terms of its role in healthcare research.

RCTs are considered the gold standard of healthcare research. Research reviews from the Cochrane library apply filtering criteria in assessing published literature using the RCT design. These reviews are also used as the criteria for published evidence-based medicine (EBM) reviews (65).

Biomedical science has a scientific principle of reducing the body into parts for examination and research. The double-blind, randomised control was designed to assist with controlling all confusing factors that may detract from the research postulate of the RCT. The double-blind, randomised control trial is intended to reduce any impact of confounding factors of individual personalities, belief systems and the chance of spontaneous remissions. Double-blind, randomised controlled trials are most appropriate when used in clinical trials of experimental pharmaceuticals or new medication regimens. The RCT is designed to deliver internal validity through its rigorous protocols and controls, and research constructs of statistical methods to reduce any confounding variables (183, 184).

A pre-established placebo or 'sham' can be created as the control of the known, active treatment in the RCT. It is an effective research design that demonstrates the therapeutic benefits of an experimental intervention against an established 'sham' of no therapeutic benefit. However if the biological mechanisms involved in the therapeutic benefits are not

understood, the use of the ‘sham’ may not be useful. The RCT design cannot prove the experimental intervention or treatment against a placebo or a ‘sham’ when it may have unknown therapeutic benefit (185).

The RCT gold standard can include a single or double-blinding of the patient and/or the doctor or caregiver. The use of the sham in the RCT is designed to demonstrate no change in the expected biological mechanisms. The experimental intervention is demonstrated or proven and all confounding human factors are controlled by the blinding. The RCT has a standing in the healthcare research world of objectivity, in its research design and results. However, there is some suggestion that a bias may exist in concealing research factors because the RCT design decides the factors confounding to the research design of the RCT (78).

2.1.20 Research methods for Evidence Based Medicine and CAM

There are current developments in healthcare research for both the RCT in advancing medical research, and the use of more pragmatic or practice-based research designs, which are more patient-centred. The appropriate choice of different research models for both EBM and CAM is yet to be clearly understood. The strengths and weaknesses, and choices in terms of research design, are discussed in this section. The reasons for choosing one research design over another are introduced as part of the reasoning behind this clinical trial.

The well-informed and measured decision-making of clinical practice has, as its primary focus, patients and their safety and the provider doing no harm. These are healthcare principles that have been suggested from the time of Hippocrates, who is considered the father of medicine (186). Hippocrates also espoused a view of the body as a whole. There has been much debate in health sciences and subsequent research models of design as to whether the body is to be researched as the sum of its parts or as a whole (142).

EBM and RCT

EBM, with its meta-analyses and standing, uses the double-blind, randomised, controlled clinical trial as the gold standard of ‘best practice’ (187).

Following questions concerning conflicts of interest in published research, the identification of all funding sources is now required for all papers reviewed by EBM. A recent study examined the authorship of research and published articles, and found 32% of authors published in the New England Journal of Medicine (NEJM) and the Journal of the American Medical Association (JAMA) may have had some conflict of interest. This was reviewed by American Medical Association (AMA) as relevant to readers in terms of the results of the studies (188).

A regular review of Cochrane filtering criteria, with constant revisiting of any conflicts of interest in research publications, is now considered essential for full disclosure of intent. The availability of all research literature around the world will only grow, thanks to the internet. This growing resource requires constant review for any conflicts of interest, and a regular, full exposure of the filtering criteria of published research. There is concern expressed widely that EBM's recommendations on best practice are becoming both a widely quoted and misquoted aspect of healthcare (75, 189).

A recent review showed many published articles are incorrectly classified as double-blind research trials. The fervour with which the gold standard of RCT has been positioned in research design hierarchy has resulted in it being embraced either intentionally or inadvertently, and misused in research designs (83). Currently, the desire for CAM research to be considered in these systematic, online reviews of EBM may result in inappropriate adoption of the rigour of the RCT for CAM clinical research trials.

This current influence of the RCT as the gold standard of clinical research trials, according to EBM, has seen patient observations, clinical experience and personal observations in healthcare relegated to 'nonsense' and overruled by evidence (190). As CAM advances with its own research discipline, active learning from clinical experience will contribute to appropriate research and development for use in EBM.

CAM as a biomedical treatment

The double-blinding of trial participants and the investigator/doctor is effective if the CAM is a biomedical treatment (therapeutic agent) within the RCT research design. Therapeutic efficacy may be established against a current medication used for the same purpose. This may be seen as a research model of comparative effectiveness and can be used as an RCT design for CAM. There is no examination of the underlying therapeutic mechanism of the experimental treatment. The experimental CAM treatment is defined by the condition or symptom set as the focus of the research. The control of the CAM is an established treatment for that same set condition or symptom. Clinical research into a CAM treatment or substance can thus be an accepted model of a gold standard double-blinding, or placebo pill/sham research against a known therapeutic agent of a specific action. This research design may allow for a valid application of double-blinding of both patient and caregiver. The ‘complementary’ health substance is validated against a known therapeutic agent of a specific action. This CAM research design may then lead to further research of its quantified active chemical constituent. It may also lead to a new pharmaceutical for the biomedical model, which then becomes the ‘active’ constituent and offers a scientific rationale for the biomedical CAM research model. Research into the ‘complementary’ health substance or therapeutic agent of a CAM system is then easily modelled according to the rigour of a double-blind, controlled trial (75).

CAM systems

The National Institute of Complementary Medicine was established in the United States in 2007, in response to the increasing use of CAM. The United States’ government has funded this area of healthcare research for over three years (191).

The National Institute of Health (NIH) was established with the intention of improving human health through scientific research and knowledge-gathering. The NIH defines CAM as “the healing resources that encompass all health systems, modalities and practices and their

accompanying theories and beliefs other than those intrinsic to the politically dominant health system of a particular society or culture in a given historical period” (192).

The ‘integrative medicine’ movement encourages CAM treatments to be used in conventional medical practice after there is validated scientific evidence and research into their safety and effectiveness (107).

The clinical efficacy, patient safety and satisfaction of treatment approach decisions are the focus of EBM. These healthcare principles promote the development of patient-centred research tools and further research studies into the comparative effectiveness of healthcare approaches. The comparative safety and risk-benefit analysis of a healthcare approach or treatment is also required to advance the new healthcare paradigms of developed societies. Patient-focused healthcare is increasing and there is recognition of the role of patient satisfaction and patient-focused outcomes in the consumer-driven healthcare environment (193).

The Australian Institute of Health and Welfare (AIHW) has assisted in the growth and development of CAM in Australia. Several initiatives are in place with the current federal and state governments to further research into CAM systems of healthcare. These government initiatives seek to expand the quality, safety and efficacy of the Australian healthcare system (146).

Health is increasingly being researched as a whole clinical encounter and not a product of biomedical interventions and high technology, or specialised medical care. A combination of subjective and objective research tools are now an expected part of research design in clinical trials. There is an increasing acceptance of a broader research landscape of patient-centred health outcomes and other health change measurements (194).

CAM in context

Developing a manageable system of integrative healthcare to examine CAM and its role in healthcare delivery is the expressed goal of current research funding around the world (73, 191, 195).

Examining CAM as a system of healthcare occurs within a contextual clinical setting, that includes clinical decision-making, CAM therapeutic exchange and treatment provided as a result of that ‘whole practice’ setting. Research methodologies that may be suited to CAM are pragmatic or in the ‘real’ practice settings of CAM. These research designs protect the rights of a patient to receive actual treatment and not be denied the care they expect. Changes to research traditions such as ‘blinding’ in clinical research trials are being discussed for the purposes of a CAM research discipline (196).

A pragmatic research approach may be more appropriate to CAM healthcare. The patient’s right to receive treatment is emphasised; denial is not considered a necessary part of the research approach (21, 197, 198). This patient-centred research has ethical considerations for the patient more than the rigour of the research model. The efficacy of the treatment is to be proven, as much as the statistical analysis can, to be a ‘true’ positive for the identified population of the research trial. With the rigour of the RCT research model, treatment is denied for blinding purposes; minimising bias and removing confounding variables of intent and patient variation are essential to the RCT. However, the new ethics of a patient-centred healthcare paradigm consider the patient the focus of the clinical research, not a potentially confounding factor (199).

Pragmatic and RCT research designs

Researching CAM healthcare requires a new approach. It is suggested that a collaborative research approach may be the best method. Developing a CAM research design may require a new understanding of the clinical trial and the gold standards of the RCT for EBM. The development of a research design that contributes to EBM must show what the therapeutic

benefits are, how to measure and monitor those benefits, and when and why the CAM is used in a healthcare delivery system. The stakeholders to be considered in this research include the patient, clinician and healthcare policy-makers.

A practice-based research model to examine the clinical reality of CAM healthcare is likely to have elements of a practical trial. This research model would be patient-centred, with each CAM approach examined as a complex intervention applied to an equally complex presentation of an individual. The clinical research model best-equipped to investigate this unresolved area of research evidence is a practical trial combined with elements of the RCT design wherever appropriate (196).

A clinical research trial into CAM healthcare will always consider the RCT research model first. Can an absolute difference between the experimental intervention and the placebo or 'sham' be defined with the known physiological mechanisms in place for the purposes of the research? This difference may need to be clearly demonstrated before the clinical research trial is designed and for the applications of the 'sham' to be considered valid.

The double-blind, 'gold standard', RCT clinical trial requires the research investigator/doctor and patient to be blinded, subject to the experimental intervention. In CAM research, blinding the investigator/doctor may not be the most appropriate research method. In hand-delivered therapeutic experimental interventions of CAM healthcare approaches, blinding the investigator/doctor is not possible (83).

Each CAM system has a unique approach to the health of an individual. With a CAM collaborative research group, and with a self-critical research discipline, CAM may then contribute alongside current medical research groups, to the healthcare delivery system of the future (108).

2.1.21 Sham and the option of ‘no treatment’ control in research design

The use of a ‘sham’ or the ‘non-therapeutic’ manoeuvre in CAM clinical research is discussed here. The option of a ‘no treatment’ control of the active treatment is also presented.

A ‘sham’ manoeuvre is a pre-determined intervention administered in a clinical research trial. It is by definition, a physically like intervention to be perceived by trial participants and/or investigators as the same as the experimental intervention. By definition, it is without any therapeutic benefit. The research purpose of the ‘sham’ is to demonstrate whether the effects of the experimental treatment or intervention are real or not.

To establish internal validity or true scientific value, RCT research results need to show an absolute difference between the ‘active’ or experimental intervention and the ‘sham’ manoeuvre with the known biological mechanisms of the active treatment used to define the ‘sham’. Without that plausible biological mechanism in place, the ‘sham’ may be actually providing therapeutic benefit and therefore not acting as a ‘sham’. Not all CAM research models are able to provide a ‘sham’, as the plausible biological mechanisms of therapeutic benefit for the ‘active’ or experimental intervention not established. This means the RCT of the CAM is delivering a false negative. Choosing the rigour of RCT design for research evidence, despite the likelihood of the sham being inappropriate due to a lack of established evidence of efficacy, is a weakness of CAM research.

Deconstructing treatment elements

In CAM, a clinical technique is used. This treatment approach is then defined in the model of research and used as the active treatment intervention. In the RCT, the active treatment intervention is then effectively deconstructed to become non-therapeutic or the ‘sham’ of the active treatment intervention. Firstly, this effective deconstruction of the active treatment only occurs when the therapeutic mechanisms can be removed as is the case with the traditions of the ‘sugar pill’ in research.

Also, different clinical techniques or different schools of that CAM treatment may consider the ‘sham’ an active treatment. For example, SMT is a broad description of spinal manipulative procedures. There are different healthcare professionals who use SMT; each has their own definition and clinical practice of it. In research trials, this difference becomes critical; altering the research results.

‘No treatment’

Instead of the ‘sham’, ‘no treatment’ is an option. This research design enables the active treatment to be controlled without the possibility of the ‘sham’ being similar to some other clinical technique. This form of controlling the active treatment may be highly indicated when the CAM has not yet established any therapeutic efficacy or physiological mechanisms responsible for the therapeutic benefits being researched.

Using a ‘no treatment’ control group rather than a ‘sham’ may be more appropriate in chiropractic research. A true control of the CAM intervention by a ‘no treatment’ group is more likely, when an understanding of the physiological basis of the therapeutic mechanisms is lacking. Ethically, this research design requires more management of the participants in the trial. In the ‘no treatment’ research design, the participants are to be fully informed and managed as to when they receive the ‘treatment’ when this has been promised to them. This research design, in clinical practice, creates a likelihood of normal participant anticipation of care due to them. If participants are fully informed and managed, this encourages a relaxed co-operation during the course of the clinical trial, without any grievances building that perhaps they will not receive any treatment. The participants will be comfortable knowing that even if they have been randomly allocated to the ‘no treatment’ group, they will still receive the same promised treatment, after the trial has been completed (200).

2.1.22 Placebo and ‘clinical encounter’ as research considerations

‘Placebo’ originates from the words ‘to please’. A placebo is ‘inert’, ‘inactive’ or ‘non-specific.’ The placebo has been used and misused in clinical research to explain the

unexplainable, regression to the mean over repeated statistical measurements, spontaneous healing, and natural resolution of illness or even bias in patient-reported benefits (201).

Placebo is the false presentation of something. The idea of placebo has its origins in the paid (and therefore considered false) administering of emotion at funerals in medieval times. The use of a placebo in research comes from a medical tradition of controlling the experimental intervention with an administration, “thought only to comfort the patient without any impact” (202).

The word ‘placebo’ first occurred in a healthcare trial in 1938, designed to demonstrate the value of a ‘cold vaccine’. This experimental healthcare trial had one group which received the ‘cold vaccine’ and a group that did not receive the experimental intervention. The placebo group sustained substantial improvement and negated the ‘experimental intervention’ in the research question of efficacy (64, 203).

This research question of whether an experimental intervention has a greater effect than its placebo has continued to be a factor in healthcare research design. This can be a measure of the experimental intervention with the placebo acting as the false effect; or the placebo can have an enhancing therapeutic effect (204).

Placebo and the RCT

The gold standard of a randomised, double-blind trial with a blinded and placebo-controlled design presumes the measurement of the placebo will be separate to the measurement of efficacy of the ‘active’ treatment. RCT is a rigorously controlled experimental model; it must presume things are to be linear, predictable and unchanging for the course of the clinical trial (67). Strictly speaking, the role of the placebo acting as a control in RCT research design is to prove or disprove the validity of the ‘experimental intervention’. In the RCT, the placebo can provide rigour to prove the efficacy of an experimental intervention where the placebo is

traditionally a non-active pill (a ‘false’ therapy) or a ‘sham manoeuvre’ (physical or technical intervention) (205).

In the RCT, the use of a placebo or sham manoeuvre may only be of value when the mechanisms of therapeutic action are understood clearly. If there is insufficient understanding of these mechanisms, the placebo factor or sham becomes a confounding factor in the research design. The placebo or a sham manoeuvre may have mechanisms in common with the experimental intervention, but this is not yet fully understood by researchers (80).

As clinical research with RCT has developed, the placebo effects have tended to become an explanation for unexplainable findings that fall outside the expected range of outcomes for that experimental intervention and its therapeutic benefits. This issue of placebo is debated in research design. For the RCT, the debate is whether it can be quantified to delineate the effects of the placebo from the effects of the biomedical treatment. For pragmatic clinical research, the placebo will remain a ‘human factor’ that influences all healthcare research. It may be a valuable factor that is examined broadly and not considered confounding to any research results (201, 206).

Placebo and CAM

In non-pharmaceutical healthcare and CAM, there are some inherently different philosophies and treatment approaches to the biomedical model of healthcare delivery. The individual responsiveness of trial participants, the qualities of the CAM or chiropractic treatment provider and the ‘individually determined’ amount of treatment required for a person cannot be examined using a RCT design. Particular clinical interactions may be peculiar to non-pharmaceutical health delivery systems, and ‘blinding’ the caregiver to certain treatment deliveries is impossible in CAM. The experimental intervention, in many CAM approaches, also requires the patient’s cooperation by sheer nature of the intervention. This is clearest in acupuncture or manipulation (108).

Human perception and placebo

The research design of all clinical trials requires considering the participant and their expectations during the trial. One clinical trial reviewed as an example of clinical research design, examined chiropractic and asthma without any established physiological mechanism underlying the expected benefits of the experimental intervention (56). The asthma participants in this clinical trial reported that they did not perceive any difference between the sham ‘non-active’ treatment and the ‘active’ treatment. This lack of perceived difference suggests that a placebo effect would also be active in this clinical trial. This means there may have also been non-specific therapeutic benefits from the placebo effect occurring in the group that received the sham (80). The insignificant difference in results between the two asthma groups in these clinical trials may have been due to the ineffective sham and placebo effects. The combined impact of the placebo effect and the lack of a validated physiological difference between the active manoeuvre and the sham may have resulted in therapeutic benefits from the participants’ involvement in the clinical trial. In any clinical research trial, the patient’s perception of the treatment they receive has an impact on the research outcomes (78).

It is suggested that the patient’s perception of the treatment may be a more important as a factor in the treatment’s therapeutic benefits and needs to be factored into healthcare research. Patients’ perception of the value of the experimental treatment to them may have more direct influence on therapeutic benefits observed than has yet been examined in clinical trials. The placebo effect may encompass ‘the art’ in all therapeutic exchanges and it is now receiving more recognition as a therapeutic factor in health research. From 1977 to 2006, the number of citations for the placebo effect increased from 214 to 1675 (78).

Clinical encounter

Therapeutic impacts occur as a consequence of healthcare relationships. This impact occurs as a result of two individuals in a prescribed clinical encounter with an anticipated therapeutic

exchange. This is a significant factor in clinical research because the healthcare relationship can have a therapeutic impact, as well as the therapy. This therapeutic impact is due to many human factors. There is firstly the enthusiasm of the giver of the therapeutic relationship, coupled with the readiness or receptiveness of the receiver. There is also the ‘whole healthcare encounter’ as an environment of anticipation that there will be therapeutic impact. The Hawthorne effect is recognised in healthcare and other human behavioural research as a participatory factor for involvement in a research trial (207). This has been a confounding factor for research purposes that may now be considered to be another human-to-human effect that is psychologically powerful and contributes to the therapeutic encounter. These human factors are part of the context of research and if better understood, can offer insights into some possible therapeutic benefits that may occur in healthcare environments (208).

It has been suggested that the chiropractic clinical encounter has a therapeutic role; it may provide placebo effects of therapeutic significance. The chiropractic clinical encounter is a worthy focus in clinical research design (208).

Research factors

The clinical encounter in ‘whole’ healthcare systems such as CAM is complex in terms of its potentially impacting elements. These clinical factors require specific research tools. A qualitative research tool may be developed to understand the impact of the clinical encounter in the clinical practice of ‘whole’ health systems. A quantifying research tool may then be developed to examine this factor in appropriate clinical research models (209).

The use of ‘typical’ practices with ‘typical’ CAM treatments as part of their daily practice routines, may start to allow more elements of these ‘typical’ practice settings and ‘typical’ therapeutic interactions to be considered as research factors. A new platform of possibilities for practice-based research could consider the clinical encounter and other elements of ‘typical’ practice settings as factors contributing to the therapeutic benefit measured in the clinical research (210).

2.1.23 Clinical research in a clinical practice setting

Clinical research of ‘whole’ healthcare systems such as CAM may be most productive when a complete clinical encounter is considered. This more wholistic encounter is multi-factorial; the therapeutic exchange is not merely the exchange of the herb, needle or manipulation. The clinical encounter between the individual health consumer and the CAM practitioner only occurs in the ‘real’ or routine practice settings of CAM practitioners in their clinical practice (211).

Whole practice research

Whole practice settings are an evolving dynamic. This dynamism requires research models that take into account the interactions and fit between the developing healthcare approach and research tools. Combined models of RCT and pragmatic or ‘typical’ practice settings offer both quantitative and qualitative data collection and analysis. Health providers and patients alike are considered research factors in this controlled, clinical research design. All those involved in the whole clinical encounter influence the results (212, 213).

RCT in whole practice research

The RCT is a research method used to prove efficacy in a controlled environment. The efficacy of a treatment, seen as its results or findings, is also for a controlled and specified population. Before, during and after a trial, the population is checked to see they conform to the specific population of the original research question. The rigour of the randomisation is checked to ensure consistency with the original specified population of trial participants. This is done by checking a selected number of factors for confounding variables that affect the research outcomes. Non-specific effects such as placebo, bias or intent are considered confounding factors and are to be minimised by, for example, blinding the caregiver. The RCT is considered valid with smaller sample sizes due to the controlled nature of the research environment which is its design. The RCT offers a high level of internal validity but it does not consider the application of results in actual clinical practice. It is not designed to

contribute to clinical guidelines or recommendations on best practices in healthcare due to these research constraints.

A combination of the design features of the RCT with pragmatic aspects may be possible. It is suggested that a research model that examines the real world of clinical practice of chiropractic may provide an appropriate forum for many research questions. Chiropractic and other CAM healthcare may be best examined with research models that allow for more observational data concerning chiropractic practice and individual patients; as is found in the pragmatic or practical trial (172).

Patients as individuals

The RCT design of clinical trials is most suited to examining a ‘single component’ biomedical treatment or a pharmaceutical for a specified target population. Practical clinical trials are most suited to examining CAM’s complex intervention treatment experience for individuals with chronic and complex conditions.

Pragmatic research designs are about ‘whole’ practice, and patients as individuals who do not form a specified target population. The population in this sense is the sum of the individuals as individuals in their experience of the health condition with which they are presenting. It is a research design where individual variations are considered as contributing to the quality of the research.

In the RCT design, the greater the controls of the treatment being examined, the greater the therapeutic benefit of the examination. However, the more control of the treatment in the research design, the less likely the complex nature of a treatment or the ‘contextual setting of the treatment’ will be revealed.

Patient-centred research

In the practical trial, the research model emphasises patient-centred care that is interactive. Observational data about the patient and their health is collected. Individual patient

characteristics are important to review. There is usually no placebo or sham treatment for patients in practical trial research. The patient is not blinded, as they are considered to be a contributor to the research, with their self-determining health behavioural changes as a factor of the research outcomes. The research then allows the more complex healthcare approach, and type of patient who is responding to treatment, to be determined. The practical trial considers non-specific therapeutic effects or the nature of complex clinical practices to be valuable to the results, not confounding. This research design can contribute information about the patterns of behaviour of the patient and may allow for a cost-benefit analysis of the clinical effectiveness of the patient and the CAM healthcare system. The 'whole' systems research model allows the 'whole' of the clinical encounter to be considered as a therapeutic aspect of a CAM system (212).

2.2 Research design selection

The clinical research model used for the trial outlined in this thesis was practical, examining chiropractic treatment in its contextual setting of a 'typical practice', and the multi-factorial condition of asthma. A number of research designs, clinical models and research outcomes were considered. The purpose of the research design selected was to enable broad data collection during the clinical trial, and a number of research outcomes to be fulfilled.

Subjective and objective research tools were selected as appropriate for this clinical trial. A series of patient-centred outcomes tools were used comprising quality of life health questionnaires (HQoL) and disease-specific questionnaires, alongside a scaling system for emotional wellbeing. Peak Flow meters were selected to monitor lung function. Primary or objective measures of health changes in each trial participant's asthma were examined with laboratory-based measurements.

These tools are explained in more detail. In addition, three preliminary studies that were undertaken are briefly reviewed in terms of their contribution to the research design of this

clinical trial. A method of clinically recording the participating chiropractors' treatment in this trial is introduced in explanation of these preliminary studies.

2.2.1 Patient-centred questionnaires

In the late 1940s, the World Health Organisation (WHO) ignited a new way to view health by defining it as a state of optimum wellbeing, not merely the absence of disease. This concept precipitated changes in how health was measured and monitored; it introduced a concept of multi-dimensional levels of health within the idea of 'optimum wellbeing'.

The individual and not the disease was the focus of this new concept. A more comprehensive array of self-perceived health factors included psychological, social and physical functioning, and incorporated positive aspects of health alongside negative aspects of infirmity and death (214).

Health-related quality of life experience

Particularly in health programs for chronic multi-factorial illness, patient-centred measures of health change, evaluated alongside the objective clinical measures expected by a physician, offer a co-operative approach with therapeutic benefits to the patient and the doctor-patient relationship. Fifty years of evaluating cancer therapies based on tumour response and overall survival used clear and objective measures of biomedical success. These healthcare decisions were then influenced by needing to understand a person's sense of wellbeing within this experience of cancer treatment. The health-related quality of life translated into 'quality life years' developed from the experiences of managing individuals with cancer (215).

General healthcare over the last 20 years has become a more humanistic interaction, requiring the wellbeing of the individual to be measured and monitored as much as biomedical success (61). Clinical decision-making has become more patient-centric or inclusive (216).

This health-related 'quality of life' approach aims to ensure patients have a sense of their own health, as much as the clinical measures of improvement known by their physician. This

subjective monitoring, alongside delivering high-quality clinical outcomes of health programs, may also tend to promote in patients greater compliance with such programs (217).

Questionnaires can assist in an individual's understanding of their broader asthma experience. For example, some questionnaires look at 'triggers in asthma', focusing on how the asthma sufferer perceives these (218). In Australia, this focus on the individual experience of health within the context of asthma is advocated by asthma sufferers, health authorities and asthma interest groups. Self-reporting one's health status via focused, quality of life questionnaires seeks to improve asthma management (219).

A tool to measure health changes in specific disease states was developed in the 1970s, using the Sickness Impact Profile (SIP) questionnaire. The SIP has since been used to validate disease-specific measurement tools, specifically those that focus on the condition of asthma (220). Disease-specific measurement tools, with appropriately developed domains of function or health status for a specific disease, have also been developed. These enable an individual to gauge their health within the experience of their particular disease. A combination of patient-centred questionnaires may be used to monitor any health changes from an experimental intervention or proposed treatment regime in clinical research. Disease-specific and health-related 'quality of life' (HQoL) instruments were considered for the research purposes of this clinical trial (221).

2.2.2 Disease-specific asthma profile: signs and symptoms questionnaire

Use of disease-specific questionnaires for asthma research is established (222). The two primary areas of interest are the symptomatic changes to the picture of asthma, and the medications used by an asthma sufferer. Basic questions related to asthma day/night symptoms and the daily use of a bronchodilator or reliever medications were included for this clinical trial. The initial asthma profiling questionnaire contained questions about the

individual's asthma background including details on their age, sex, genetics, family, work and lifestyle, as well as their psycho-social and physical environments (218).

Research examining an individual within the dynamics of their personal asthma environment is underdeveloped. It is suggested that the synthesis of data of the individual can be helpful for that individual in understanding the triggers and factors of their asthma. The awareness of all triggers of asthma within an active asthma management plan (AMP) is an important part of well-managed asthma (22).

There is an increasing expectation in health research to use quality of life healthcare tools in research evaluations. Appropriate healthcare research tools may be used to assess the health of individual asthma sufferers, and increase their health awareness within the context of their asthma condition (223).

2.2.3 SF-36 short form, quality of life: wellbeing questionnaire

The SF-36 short form is the most extensively used and validated self-reporting health instrument in randomised clinical trials. Its improved wording and scoring system have made it the primary tool for measuring generic health status in health research with established validity (224, 225). The SF-36 short form was developed from the SF-36 long form of the Medical Outcomes Study (MOS), with eight domains selected as those most appropriate to assessing an intervention in disease.

The process of validating internal consistency in these self-reporting questionnaires effectively requires that sets of known 'sufferers' in the specific domains of health experience answer the questions and then that these answers be cross-checked with the intention of the question within that domain. The SF-36 short form is a validated questionnaire to measure areas of health, and physical mental and social wellbeing (226).

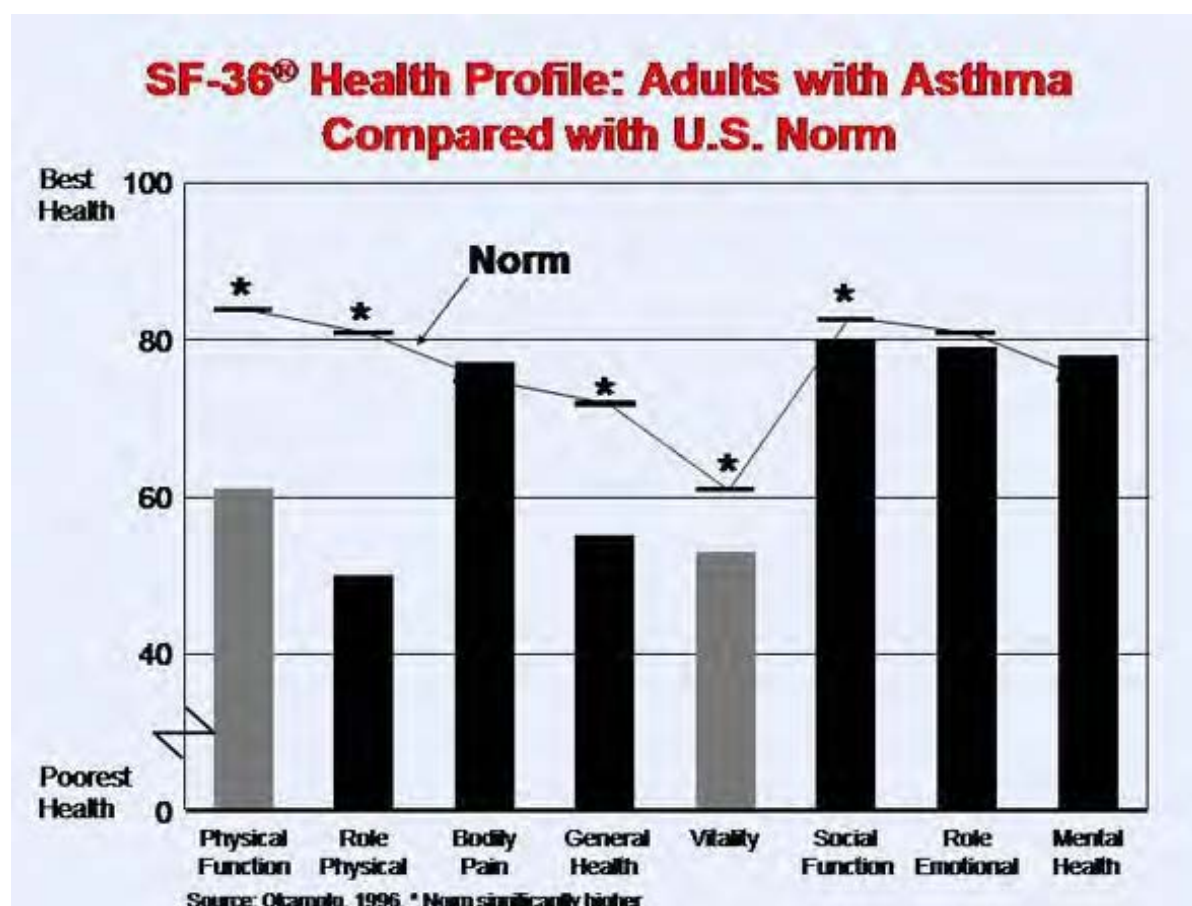


Figure 2: SF-36 health profile of asthma sufferers and US normal; adopted from Okamoto (227)

The SF-36 short form, established as a measure of asthma-related health compromise, is demonstrated in the above graph against a normal healthy population. See Figure 2.

Soft and hard measures in research

Patient-centred questionnaires such as the SF-36 short form are, for clinical research purposes, considered 'soft measures'. This means that if there is any conflict with the results of the 'hard measures' of clinical research (biological or laboratory-based indicators of physiological change), the results of patient-centred questionnaires such as the SF-36 are not definitive research findings (224).

The SF-36 may be combined with a disease-specific questionnaire in a 'moderate asthma' population (asthma sufferers maintaining daily medication use with no limitation of activity)

to monitor the self-reported impact of a ‘series of chiropractic treatments’ on their experience of asthma (228, 229). As a ‘soft measure’ of research, this is pivotal to a patient-centred clinical trial, but is best combined with laboratory-based research outcomes of a biological nature showing any physiological changes occurring in the clinical trial.

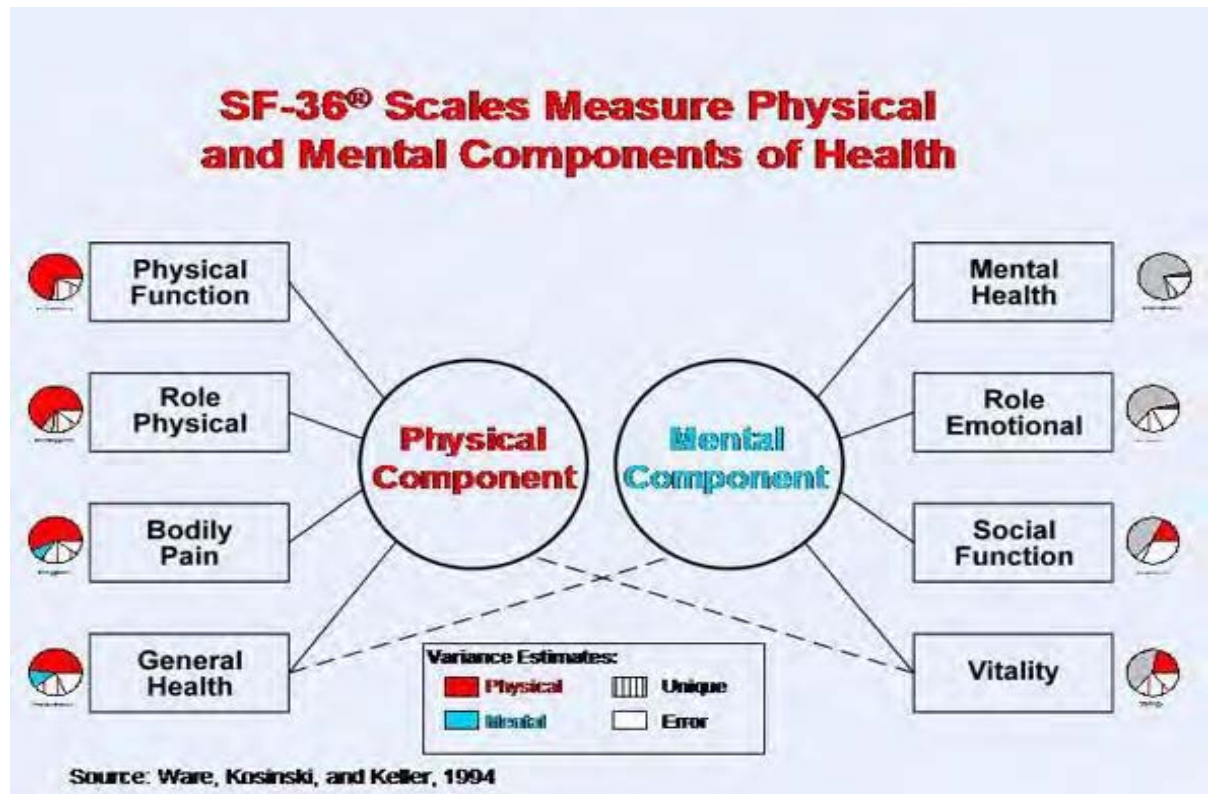


Figure 3: SF-36 short form is a measure of the physical and mental components of health; adopted from Ware (230)

The SF-36 short form includes one multi-item scale that assesses the following eight health concepts (230):

1. Limitations in physical activities because of health problems
2. Limitations in social activities because of physical or emotional problems
3. Limitations in usual role activities because of physical health problems
4. Bodily pain
5. General mental health (psychological distress and wellbeing)
6. Limitations in usual role activities because of emotional problems

7. Vitality (energy and fatigue)

8. General health perception.

2.2.4 Depression Anxiety and Stress Scales (DASS)

The Depression Anxiety and Stress Scales (DASS) is a psychometric tool developed on the premise that no difference, except in degree, exists between anxiety and depression. This was determined after an observation that the relative performance of ‘psychometric items’ in both clinical and non-clinical subject groups was the same. A fundamental mechanism of emotional disturbance was observed to exist to a lesser degree in ‘non-clinical’ subjects. The severity or degree, not a categorisation of pathology, was a differential diagnosis of anxiety and depression.

The DASS was developed from ‘non-clinical’ sample groups and correlations, outside the established self-reporting scales of depression and anxiety. (The DASS was validated by ‘clinical subject’ sampling groups).

The self-scoring of depression and anxiety

The three factors of the DASS share a moderate correlation with other self-scoring scales of depression and anxiety; the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) (231). The BDI has been in use since the 1960s. It focused on a high correlation, with clinical samples, of subjects with depression and anxiety. The BDI specifies, as does the DASS, that each question in the questionnaire is considered only over the previous seven days. This will anchor an individual’s emotional state during self-administration as an experience. The DASS measures differences in the degree of a person’s experience of depression, anxiety and stress. ‘Anxiety’, as expressed in the DASS, was found to reveal the individual’s physical and social concerns. ‘Depression’ and ‘stress’ are only associated with social concerns and not physical concerns.

Depression, according to the DASS, is a 'loss of self-esteem' and low perception of any sense of control regarding future personal outcomes being faced. It is more a reflection of the individual's sense of self-value or worth than a conventional sense of 'sadness and loss'.

Anxiety, according to the DASS, involves prolonged anticipation of a threat, which may be physical, but is usually psychological. Consequently, the ability to cope, to perform as expected and avoid failure, is threatened in a state of anxiety.

Stress according to DASS

Stress, according to the DASS, is a separate dimension of ill health. This negative emotion evolved during the development of the DASS scales. It is described as a more persistent state of over-arousal. Despite overlapping terms such as 'nervous tension', it is a dimension of an individual expressing continuing difficulty in meeting the demands of their daily life with lowered tolerance and heightened frustration as a result of this negative emotion.

Asthma and emotion

Monitoring the three negative emotional states of depression, anxiety and stress in asthma may be of research value in a clinical trial. Depression and anxiety are associated with asthma, with each of these negative emotions reported as present in asthma hospitalisations and asthma morbidity (106). Assessment of emotional wellbeing is an increasing individual focus of healthcare management and improved self-monitoring of these three negative emotional states may be of benefit to an asthma sufferer. This impact in asthma pathophysiology is little understood. Any role they have in the pathophysiology of asthma, particularly functions of the autonomic nervous system, may contribute to asthma research and understanding. It has been suggested asthma patients be routinely screened for depression and anxiety during both hospital and primary care management (106, 232-234).

Emotional breathing

Normal breathing is a healthy function of the body with an active and passive phase. There is a relaxed emotional feeling of release during 'breathing out', as exhalation is passive in quiet

breathing. There is normally a passive release of the whole upper torso on exhalation due to the natural elastic recoil after inspiration. The inhalation phase of breathing is physically felt as an expansion, as the excursion of the ribcage moves it out and a feeling of pressure laterally is the diaphragm contracting. This diaphragm movement is just a one centimetre excursion in normal tidal breathing, but during abnormal patterns of breathing this can increase by up to ten centimetres when there is forced inspiration and expiration (42).

A 'locus of negative emotion' is associated with disturbed patterns of breathing. Poor health, with feelings of anxiety and depression can cause a disturbance in an individual's respiratory rate (235). Hyperventilation is seen as a sub-type of panic disorders, resulting in a metabolic excess of carbon dioxide if hyperventilation persists. Shallow breathing or erratic patterns of respiration can become a poor health habit, resulting in the accessory muscles of respiration (neck and shoulder area) becoming involved in chronic lung dysfunction (99).

The sense of wellbeing that accompanies the good lung function of well-managed asthma is noted by individual asthma sufferers. In well-managed asthma, there is a less abnormal pattern of breathing for the individual asthma sufferer that self-confirms their sense of control in asthma. This critical feeling of 'being in control' is important for the asthma sufferer and fosters normal respiratory function (235).

Triggers

Two classifications of asthma are intrinsic and extrinsic asthma. Intrinsic asthma is triggered by factors of the internal environment and extrinsic asthma is due to triggers of the external environment.

An individual asthma sufferer will have a number of factors that are known to them as their triggers. Then, there are some factors that are of an unknown origin; the nature of these is often complex and can trigger asthma episodes without any warning.

The extrinsic factors are related to the external environment and include allergic factors. The inflammatory nature of allergic responses or ‘allergy-type’ asthma is a focus of current asthma medical management.

Less understood are factors such as anticipation, anxiety and stress that may trigger an episode of asthma. These ‘intrinsic’ triggers of asthma are important considerations in the management of the individual with asthma (236, 237). Both the intrinsic and/or the extrinsic triggers of asthma may result in the onset of the paroxysmal episodes of compromised breathing. This airway dysfunction is the hallmark of asthma. The pathway of asthma pathophysiology is dependent on the nature and type of trigger, extrinsic or intrinsic, and is different for individual asthma sufferers. The inflammatory aspect of the airway compromise is currently managed well with asthma medications to reduce the inflammatory pathophysiology.

The AMP focuses on the education of the asthma sufferer, specific medication requirements, Peak Flow self-monitoring and responsible awareness of asthma triggers. The existence of a persistent negative emotional state in an individual asthma sufferer has an impact on the effectiveness of an AMP (238, 239).

Chronic multi-factorial illness

Depression is a feeling of helplessness and of general hopelessness. At the extreme, it can manifest clinically with real thoughts of death. Depression is associated with low self-esteem and a lack of control. There is an associated depression of actual physiological wellbeing, less fitful sleep and a reduced respiratory vigour (240). The negative emotional state, an associated physical compromise of poor health combined with a concurrent psychosocial issue, is linked to severe asthma attacks (241, 242). An asthma sufferer’s AMP may benefit from including this self-monitoring tool of any negative locus of emotion in asthma.

A 'locus of negative emotion' is associated with chronic asthma. A level of perpetual chronic strain may result. Though not well understood, a self-perpetuating cycle of neuro-endocrine change within the hypothalamic-pituitary-adrenal (HPA) axis may occur with this chronic strain (243). This state, for the asthma sufferer, is a 'stress' disorder of the ANS. The out-of-control HPA axis fuelled by the chronic 'locus of negative emotion' or cycle of depression can be an intrinsic factor in asthma. Chronic multi-factorial ill health such as asthma has associated factors of depression and anxiety and functional disorders of the ANS. In the profile of an asthma sufferer, the existence of a negative locus of emotion is known to affect quality of life (232).

The DASS allows a connectedness of three dimensions of negative emotions to exist, as part of the experience of chronic multi-factorial illness. The DASS is a valid health monitoring tool; it is not a tool for the diagnosis of clinical depression. It is used for measuring and monitoring the negative emotional locus of depression, anxiety and stress associated with the health experience of the asthma sufferer (244-247).

2.2.5 Self-monitoring of lung function in asthma: Peak Expiratory Flow Meter

The Peak Flow Meter (PFM) is a hand-held instrument used to measure and monitor lung function. The PFM provides a self-monitoring system to record Peak Expiratory Flow (PEF) or personal lung function by the asthma sufferer.

Pfms have been used in the management of asthma since the 1950s. The original PFMs were developed by Dr Wright and were cumbersome metal instruments. They recorded airflow as it passed through the 'Wright scale'. Subsequent plastic modelling and further development led to the very por 'mini Wright' Peak Flow device. It has been the standard on which all Peak Flow meters have been based (248).

The PFM offers an easy to understand method for the purpose of consistent, self-recorded data. The PFM warns of asthma signs and symptoms worsening in an individual and provides confidence and awareness as part of an active AMP (249).

An AMP is developed around the individual. The responsible and accurate use of regular lung function monitoring devices forms the foundation of an effective AMP whether written, symptom-based and/or PFM-based. The PFM is accepted as the most appropriate method within an AMP for self-monitoring lung function (14). AMPs formally refer to the best PEF recording as a benchmark reference for each asthma sufferer. This is the 'previous best' PEF, being the best of three readings (not an average). A consistent time of day, and preferably morning and early evening recordings, are to be charted daily. A range of acceptable normal readings are expressed as a percentage of the 'previous best' reading. As a general rule, if the average reading is frequently one-third below the 'previous best', it may mean that the asthma is not controlled (250).

The PFM has a degree of variability considered as acceptable for use by individuals self-monitoring lung function at home. The more sophisticated readings of the spirometer are used to test pulmonary function in a laboratory or clinical setting. Spirometry is mentioned here in reference to its valid use in monitoring the progress of chronic lung dysfunction such as asthma.

Spirometer readings measure air moving in and out of the lungs during various prescribed lung and respiratory manoeuvres. They show how much air can be inhaled and exhaled and how fast. Spirometer readings are used to show the effectiveness of a pharmaceutical agent, and monitor potentially toxic effects of ingested chemicals and gradual lung tissue changes in chronic lung conditions (42).

PFMs are used to measure Peak Expiratory Flow (PEF) in litres per second. PEF is the greatest expiratory flow achieved with a maximum forced effort after maximum inspiration.

Traditionally, in asthma management, a best PEF score is determined by the asthma sufferer and this is then used for that individual against which all other PEF performances are then rated.

The readings of the PFM are dependent on airway calibre, the lung's elastic recoil properties as well as the patient's effort. Asthma sufferers usually require advice on how to consistently use the PFM for their self-directed application and to achieve consistent readings.

The PFM is an integral part of the co-management activities of the AMP. The greatest value of a PFM to an asthma sufferer is the relative change they may see in their PEF readings. For example, PEF readings will usually have reduced for a period of time before any signs of an impending acute asthma episode are apparent. Similarly, PEF readings will increase if a program of asthma management is showing benefit for the individual asthma sufferer.

A 'personal best' is established by each asthma sufferer. This is a lung function recording as a reference point for that individual asthma sufferer's PFM recordings. A new-found confidence for the asthma sufferer is achieved with the AMP in relation to any treatment regimen or new therapy, enabling the individual to respond confidently to changes in PFM readings, asthma signs and symptoms.

Current AMPs recommend the same PFM is used consistently by that individual for the purpose of monitoring their PEF readings (251). In a clinical or emergency setting, a different PFM to the one in use at home may be used in the assessment. The patient will usually be quoting their 'personal best' according to their own PFM in use at home. This is to be noted so the medical provider is not confused in making changes to AMP medications.

Reviewing repeated use of the PFM to obtain 'personal best' PEF readings shows a fatigue factor influences the readings. A phenomenon of Manoeuvre-Induced Bronchospasm (MIB) occurs where repeated attempts by an asthma sufferer to produce three consecutive PEF

scores can reduce the readings dramatically from the first attempt to the third (due to MIB) (252, 253).

For the purposes of this asthma clinical trial, the PFM was to be used as a research tool and a new mini-Wright Peak Flow Meter was given to each asthma participant. The repeated attempts of second or third PEF readings per session were likely to discourage participants and may have reduced participant compliance. Another concern was also the need to avoid any MIB that may have artificially driven the overall group performance down.

2.2.6 Physiological markers of change in health in asthma

For this research trial, a set of laboratory-based physiological markers was used. Markers were developed to examine evidence of the efficacy of chiropractic treatment. The choice of biomarkers is discussed as a research tool for the assessment of asthma as a multi-factorial condition, with some underlying dysfunction of the ANS, the hypothalamic-pituitary-adrenal (HPA) axis and the immune system. These biomarkers are reviewed with background on their role in the health of the body. Markers of physiological change in the state of the ANS are also examined as to whether they may contribute to the evidence of any efficacy of chiropractic treatment. Any changes in ANS function in the asthma sufferer may help the understanding of some plausible mechanisms that may help explain the benefits of chiropractic treatment for asthma.

2.2.7 Immune response in asthma (IgA)

IgA is one of the five types of immunoglobulin or antibodies in the body (IgG, IgA, IgM, IgD, IgE). Immunoglobulins provide a defence against pathogenic invasions and allergenic exposures in the body. IgA is the most abundant immunoglobulin in body secretions. It is synthesised in mucosal tissues and has a specific role in respiratory conditions such as asthma, COPD and chronic bronchitis. There is more IgA produced than all the other immunoglobulin combined.

Respiratory surfaces

The respiratory surfaces have a defensive layer; the epithelial layer with its tight cell junctions. This constitutes a physical barrier, and the epithelial cells are covered by the electro, negatively charged glycocalix. Bronchial secretions are produced by sub-mucosal glands and goblet cells with some surfactant from the Clara cells. This gel layer of the epithelium is made up of mucus, mucins and free proteins. IgA may also improve the viscoelastic properties of the airway secretions, implicating IgA in the clearance mechanisms of inhaled particles. IgA is also known as a protective immune protein scavenger in the mucosal secretions. The breakdown of the lung defensive mechanisms is a focus of asthma pathophysiology. Reduced mucociliary motility is a hallmark of compromised airways. This induces the cough mechanism for clearing the airways and the onset of the restrictions and 'mucous plugs' associated with asthma (254-256).

Though the function of IgA is still being researched, there is good evidence that immunity to infection at a mucosal level is IgA-mediated (257).

IgA and immunity

Immunoglobulin circulates via the blood system providing an immune response through the body. Several hundred square metres of mucosal surfaces come into contact with the environment. This includes the length of the intestinal tract and the mouth, nose, eyes, genitalia and lungs. The genetic tendency in asthma is for allergic reactions to occur in the respiratory surfaces of the asthma sufferer (99).

The broader role played by IgA in mucosal homeostasis is of increasing research interest in understanding the causes of asthma. It is possible that an altered or prolonged state of persistent immune-inflammatory processes within the lung epithelium promotes hypertrophy and the pathological remodelling of bronchial smooth muscle as seen in atopic individuals (258, 259).

Allergy-type asthma and mucosal immune response

Asthma is classified as 'extrinsic' asthma when the asthma episodes are precipitated by external triggers or allergenic-type exposures (airborne allergens, animal hair, paint fumes, air pollution, perfumes, industrial chemicals, wood dust, grasses, pollens, moulds, house dust mites, foods, temperature changes, cigarette smoke, some medicines such as aspirin).

IgA is associated with the allergy-type response. The immune response in asthma is triggered by such allergenic-type exposures and this is usually via the nose, mouth or lungs. A mucosal IgA response has been shown in the nasal mucosa of patients with allergic rhinitis, after an allergen challenge. A specific IgA response has been documented in the nasal and bronchial mucosa of patients with atopic asthma and/or rhinitis sensitised to house dust mites (260).

IgA is the most abundant of secretory immunoglobulin and the predominant immunoglobulin isotype produced in the human body. IgA dominates humoral mucosal immunity. IgA provides a highly specialised immune response that will re-establish and maintain local homeostasis in the event of innocuous antigens, infection and exogenous invasion of the mucosal surfaces of the body (261, 262).

An increase in the presence of IgA produces an increased immune response to pathogenic invasion of the respiratory epithelium. There are antibacterial proteins and peptides including large amounts of secretory IgA that complement the complex immune barrier of the lung epithelium (99).

IgA plays a role in the body/host's defence against infections and in all inflammatory processes. In the lungs, this is achieved in part by the ability of IgA to inhibit the adherence of micro-organisms or viruses to the mucosal surface. In addition, IgA may facilitate the removal of antigens from the sub-mucosa in transporting them through the epithelial layer. Furthermore, the binding of IgA to particles facilitates their phagocytosis (262).

IgA and asthma research

A study of younger asthma sufferers showed they had lower IgA levels than those of the healthy control group. There may be some compromised immune development involved in these findings of low levels of IgA in young asthma sufferers, as opposed to non-asthma subjects (263, 264).

For research purposes, the clinical impact of altered levels of IgA levels in asthma may be further understood by examining the severe deficiency of IgA known as ‘Selective IgA Deficiency IgAD’. IgAD is the most common of the primary immunodeficiency syndromes. It is associated with an increased prevalence of atopic conditions, food sensitisation, recurrent infections, and neoplastic and auto-immune disorders. All other serum immunoglobulin is present at normal or increased levels in IgAD. There is just a profound deficiency of IgA (265).

Current asthma management focuses on allergenic and inflammatory aspects of asthma pathophysiology. Asthma medication regimens address the underlying inflammatory processes of the respiratory surfaces of the asthma condition (3).

IgA has been found to be at lower levels in severe asthma subjects than normal subjects; this may indicate IgA plays some role in the compromised immune response found in the asthma sufferer (266). This research may contribute to understanding any IgA link between asthma and the role of IgA levels in effective immune responsiveness to allergens in the asthma sufferer (254, 267, 268).

2.2.8 Stress response in asthma (cortisol)

The work of Hans Selye in the 1950s showed that the stress response in the body, co-ordinated by the nervous system, acts as a ‘signal’ of pathogenic invasion or a stress factor. A neuro-endocrine occurs in response to a stressor and the hypothalamic-pituitary-adrenocortical (HPA) axis is triggered. The body response adapts and re-establishes the equilibrium of body function and homeostasis returns (269). The neuro-endocrine and the

immune systems appear to be in direct communication during this cycling, acting as systemic communicators. Cytokines act as endocrine factors, triggering feedback between the HPA axis and the immune system (270, 271).

As the circulating cortisol persists in a cycle of unrelenting stress, internal mechanisms of homeostasis are disturbed. Without an effective feedback control at the pituitary, hypothalamus and higher brain centres, the prolonged higher levels of glucocorticoids circulating may also cause atrophy of the lymphatic system. This results in decreased levels of circulating lymphocytes and a reduction of antibody production. A persistent immune-compromise leaves the body more susceptible to pathogenic invasion (272).

Research scientists are able to build on the Hans Selye's original understanding of this cycle of defence and health maintenance. Finding new ways to measure and monitor body functions with developments of the science of psycho neuro-endocrinology, the far-reaching systemic effects of chronic stress are being understood (273).

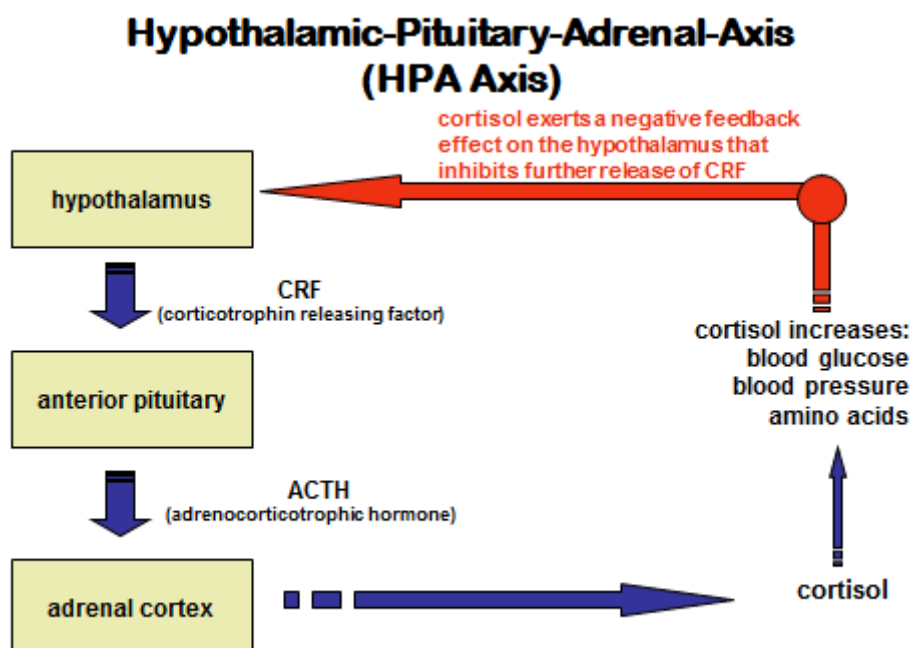


Figure 4: HPA axis demonstrating the cycle of stress response

Asthma and stress

Each asthma sufferer has a unique set of triggers or factors that are associated with their asthma. This milieu of factors contributes to the onset of the underlying pathophysiological mechanisms of asthma. Whether the trigger is extrinsic or intrinsic in origin, the stressor causes a physiological stress response in the body. The nature of the stress response in an individual asthma sufferer may form an important aspect of their asthma profile. The physiological stress response to triggers or stressors is a measure of the level of the body in its healthy resilience; in the asthma sufferer this contributes to the state of their asthma.

The stress response of a body is therefore both reflective of the severity and nature of the stressor or stimuli, the duration of this stressful stimuli and the level of physiological susceptibility that is part of the individual's health profile (274).

Stress response

Cortisol is produced in response to stress. A neurogenic response to any type of stress, physical, chemical or emotional, will cause adrenocorticotrophic hormone (ACTH) to be released from the anterior pituitary gland. Within minutes there will be a release of cortisol into the circulatory system of the body (99). Sudden stress and physical distress is associated with the increased secretion of cortisol. If the stressor is prolonged or becomes chronic, this cycle of circulating cortisol causes a prolonged increase in circulating cortisol which will then suppress immune function (99).

Mind-body medicine

The nervous system participates in the immediate humoral response or modulating of immune function. With health research developments, some 20 years later, the psychoneurophysiological understanding of this cycle of the HPA in the stress response has developed into the mind-body medicine of psychoneuroimmunology and psychoneuro-endocrine physiology (177). This altered activity of the sympathetic nervous system may

occur when the human survival mechanism of ‘fight or flight’ is aggravated by autonomic dysfunction (275).

Sympatheticotonia is a condition of autonomic dysfunction with abnormal tonicity of the sympathetic nervous system creating ill health (276, 277). This is little understood and involves the stress response of the body. A condition of sympatheticotonia is said to be the cause of abnormal vascular responses such as unexplained, increased blood pressure and odd signs such as ‘goose bumps’. It may also be that sympatheticotonia is responsible for abnormal autonomic reflex activity such as gastric upset (278).

Asthma and cortisol

Stress, depression and anxiety and the dysregulation of the HPA axis are all seen in chronic asthma (279). Patients with chronic illness suffer prolonged or persistent stress as part of their condition. This may cause an over-activation of the HPA axis with a neuro-endocrine cascade of physiological changes, resulting in severe immunosuppression and an altered stress response (270). These altered immune and stress responses in the body are either part of the genetic tendency for asthma to develop, or part of the effects of chronic asthma.

Many diseases are treated with pharmaceutically synthesised cortisols such as cortisone, prednisolone, and other synthetic corticosteroids. Asthma is one condition treated with these synthetic corticosteroids. The medical management of asthma successfully uses a range of sympathomimetic pharmaceuticals to treat the underlying pathophysiology of asthma.

Levels of cortisol

This clinical trial examined changes in cortisol concentrations to observe whether changes in the level of cortisol circulating were associated with any changes in the health and sense of wellbeing in asthma participants.

2.2.9 Three preliminary studies in research design

Three preliminary studies were conducted. Two were preliminary clinical studies offering a forum for decision-making regarding the research design of this clinical trial. These are

introduced as aspects of the research design selection process and only a brief description of findings discussed.

2.2.10 Preliminary study - the circadian rhythm and cortisol in asthma

For the purposes of this clinical trial, preliminary laboratory investigations were undertaken to examine cortisol as a reliable and reproducible research measure. Non-asthma and asthma participant salivary samples were collected for laboratory-based cortisol analysis. This was performed at the laboratories of the Department of Biological Sciences under the direction of Dr Sinan Ali.

Background to testing cortisol levels in asthma

Cortisol exists in the body in two forms; one which is bound to corticosteroid-binding globulin (CBG) and the other which is unbound and freely circulating.

Typically, up to 90% of circulating cortisol is bound to the CBG. Serum cortisol assays are often designed to measure total cortisol concentrations and the clinical significance of total cortisol measurement is highly debated. It is the free cortisol concentration which is clinically most informative about various health conditions and disease states such as Cushing's disease. Free serum cortisol is largely measured 'in-house' for comparative and other research purposes, often with small numbers of subjects due to technical complexities and the associated costs involved.

Cortisol measurements

There is considerable variability in any reported reference range intervals, not only for total plasma cortisol but also for free cortisol and cortisol bound to CBG. Normally, free unbound cortisol is less than 10% of total cortisol but as the total cortisol exceeds saturation of CBG, the percentage of free cortisol increases.

An alternative to measuring free cortisol in serum is to measure cortisol in unstimulated saliva. Cortisol in saliva reflects the free concentration seen in serum with a five minute lag-time. The percentage of free cortisol within an individual can fluctuate due to both

endogenous and exogenous factors, such as illness, stress and trauma. There are fluctuations in free, unbound cortisol as part of the pathophysiological responses of the body to prolonged or abnormal levels of stress.

Physical, mental and emotional stress and cortisol

Levels of physical pain will elicit a response via the brainstem and the hypothalamus, leading to large quantities of corticotrophin-releasing factor (CRF). Within minutes, large quantities of cortisol are circulating in the blood. The CRF released from the hypothalamus controls the secretory rate of ACTH from the anterior pituitary, which then controls the secretion of cortisol. Severe mental or emotional stress will cause an equally strong response and release of cortisol via the limbic system and then the hypothalamus and anterior pituitary (99).

In recognising the prevalence of elevated cortisol levels in illness, it is necessary to also recognise the variations in cortisol concentrations in the body throughout the day as a result of the circadian rhythms.

The circadian rhythm

Figure 5 demonstrates the circadian rhythm of humans. The circadian rhythm observes the 24-hour cycle of cortisol which is normal. There is a high level of CRF, ACTH and cortisol in the early morning before rising and a low level in the late evening around midnight. This demonstrates 24-hour cyclical alteration in the hypothalamus signals. Of note, is that the 24-hour cycle changes when the person changes their sleeping habits. For research purposes, the time of the measurement of cortisol is important.

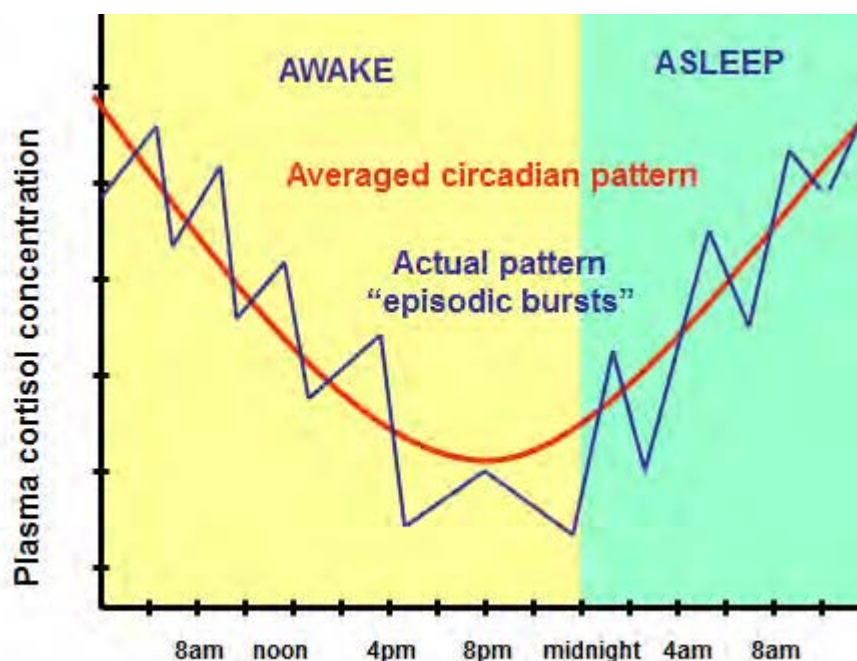


Figure 5: The averaged circadian rhythm.

Typically cortisol levels start to rise early in the morning, with cortisol reaching a peak upon waking and declining throughout the day so that the level obtained at 8pm is around 20% of the value obtained at 8am. In this study, salivary sampling was chosen as a way to measure cortisol for the duration of this trial, as it was easy for participants to handle. For a number of reasons, including the use of self-monitoring research measures, it was desirable for this study to employ an assay which did not involve invasive procedures. The participants were to produce the salivary sample at home and also an invasive procedure would possibly be stressful and influence levels of free circulating cortisol.

Preliminary studies of the asthma participants demonstrated that the median 30-minute post-awakening cortisol levels in salivary samples of asthma individuals differed significantly by the type and amount of inhaled steroid (glucocorticoids) used. A reduction was also observed in cortisol after the 30-minute post-awakening, while glucocorticoids were then observed to have little to no impact on cortisol levels in salivary samples 12 hours after awakening.

These observations were important for analysing changes in cortisol levels in chronic asthma. It was recognised that the population sample for the clinical trial was a population of asthma sufferers actively participating in an AMP. The AMP had a medication regimen with self-medication strategies including glucocorticoid inhaler therapy. While it may be argued that free circulating cortisol levels may be influenced by the daily use of glucocorticoids therapy, this preliminary study demonstrated that it did decrease ‘awakening’ cortisol levels. However, the daily use of glucocorticoids had no impact on the 12-hour post-awakening result. The research team for the asthma project decided that morning and evening salivary samples would be collected for three days of each week during the trial. Any time change in the salivary collection, and any unexpected use of medication, was to be noted by the asthma participant.

Pattern of Cortisol Levels over 1 week

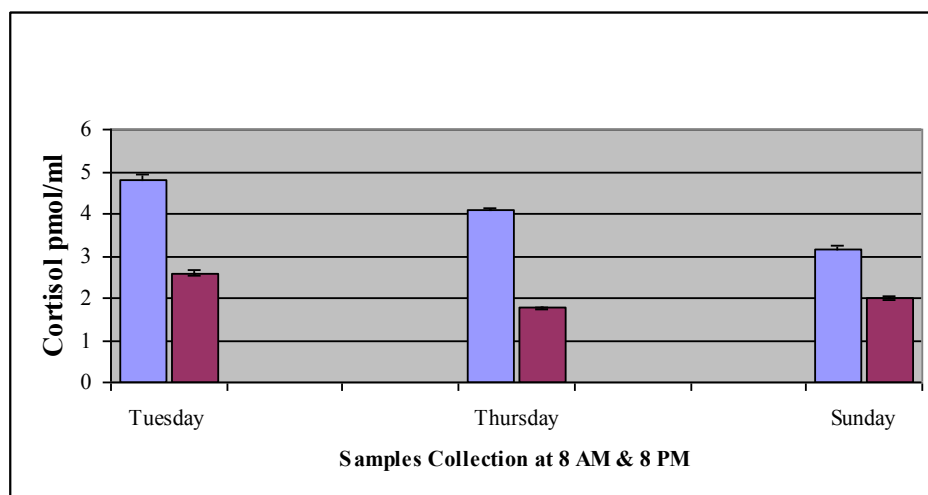


Figure 6: Asthma participants and cortisol levels higher in the am salivary collections

2.2.11 Preliminary study - Asthma/non-asthma spinal findings

This preliminary study is briefly presented here in its role for the selection of an appropriate research tool for the purpose of investigating the clinical recordings of chiropractors without the use of any one chiropractic clinical technique. A one day study was conducted to examine whether the examination of the spine and the treatment of asthma by ‘typical’ chiropractors in ‘typical’ practices could be appropriately recorded for research purposes. A clinical recording sheet was developed and used to identify levels of the spine without the use of chiropractic clinical technique terms.

It did not involve treatment. The participating chiropractors were asked to examine the spine and note their findings of levels of spinal dysfunction. This was conducted as a randomised, one-day clinical trial involving 50 young participants (30 asthmatic and 20 non-asthmatic controls) and four chiropractors using four ‘mainstream’ clinical techniques of spinal dysfunction.

Fifty participants were invited from advertisements in the newsletters of schools and asthma support groups around Macquarie University. The participants were required to be between over two and under 18-years-of-age. To be included, participants had to be under the care of a medical practitioner for their asthma and on a current regimen of asthma medication. They were not to have consulted a chiropractor or any physical therapist for the two months prior to the study. Participants were excluded if they experienced symptoms of their asthma or if they knew any of the chiropractors on the day of the study. The median age was eight years, with an equal number of boys and girls. Each participant had a signed parental consent and was accompanied by a parent.

Four participating chiropractors were selected from a focused mailing to 20 chiropractors practising around the Macquarie University area of Sydney. They were selected on the basis of their daily practice of one of four identified chiropractic clinical techniques. The

chiropractic clinical techniques considered as within the scope of ‘typical’ practice were the Activator Method, Gonstead Technique, Motion Palpation/Diversified and Sacro-Occipital Technique. The chiropractors were blinded as to which participants were asthma sufferers and which were ‘non-asthma’ participants (the control group).

The chiropractors were each positioned at one of four ‘clinic’ stations for the day of the trial and did not move from that clinic station. The chiropractors were informed that each of the participants would attend each of the four stations during the course of the day. The attendance order was randomly determined prior to the commencement of the clinical trial by randomised computer ordering. The attendance was then checked off the attendance sheet as their allocated number, as each participant attended each clinic station. Each participant was able to move around the four stations in a self-determined order. This was preferred to investigator-based ordering to minimise order effects or any possible cumulative changes impacting both the asthma participants and chiropractors.

The participating chiropractors were instructed to assess the spine and related articulations and structures according to their clinical technique. The simple clinical recording sheet was used for this research purpose. This recording sheet was a schematic pencil drawing of the spine and related structures developed. The use of clinical technique jargon was discouraged in recording findings of spinal levels, though an allowance for recording clinical technique was made. Each chiropractor was asked to use a simple ‘x’ to mark the spinal level(s) detected as being a level of spinal dysfunction. Each participant was examined only - no treatment was given.

The finding of levels of spinal dysfunction

The finding of levels of spinal dysfunction according to clinical technique was indicated on the clinical recording sheet. The results of use of the clinical recording sheet of spinal findings showed they had been marked in a way that allowed easy identification of specific spinal

segments. The prevalence of spinal levels of dysfunction was assessed for research purposes. Prevalence was determined by the percentages of findings of specific spinal levels, measured over the full number of possible specific spinal levels.

Notes from this preliminary study:

Chi-square analysis was used to establish any prevalent findings in the asthma sufferers' spines not found in the non-asthma controls: There were three levels determined more than any others: C1, (C1, $p < 0.001$), T4, (T4, $p < 0.001$) and the level of sacro-iliac joint of the pelvis, (SI, $p < 0.001$).

At the T4 spinal level, 30.8% of asthmatics had recordings of spinal dysfunction, while only 13.1% of non-asthmatics were found to have recordings of spinal dysfunction at the same level.

Results

The Spinal levels of prevalence in 30 asthma participants' spines were: C1: 39.1. %, T4: 30.8%, S1: 56.6%.

The Spinal levels of prevalence in 19 non-asthma participants' spines: C1: 28.9%, T4: 13.1%, S1: 40.7%.

Percentage difference between non-asthma and asthma spinal markings at certain spinal levels: C1: 10.2%, T4: 17.7%, S1: 15.9% with a magnitude of difference found at three levels: C1: 1.4, T4: 2.4, S1: 1.4.

Comments on research design selection

The use of the 'clinical recording sheet' was considered practical. Participating chiropractors demonstrated that they could co-operate with appropriate clinical recordings within the prescribed schematic drawing. This study confirmed chiropractors identified spinal levels of dysfunction with their clinical techniques and that a research tool for clinical research could be used. The research into chiropractors in a contextual setting of a typical practice would use

a clinical recording sheet to examine chiropractic treatment with ‘typical’ chiropractic clinical techniques.

2.2.12 Preliminary study - A six-week crossover

A six-week single-blind crossover study was conducted to review the use of physiological markers as research tools. The sham or ‘no treatment’ option of control of the chiropractic treatment was assessed. The options of lung function testing methods were also assessed as to their usefulness in a multi-site, clinical trial of asthma sufferers.

An advertising campaign of media articles advertisements and direct contact with asthma support groups was conducted. They all responded to an advertisement campaign in the local newspaper in the area of Macquarie University asked: ‘Do you want to help other asthma sufferers?’ Thirty-seven subjects were selected who had been on a medically managed regimen of asthma medications for at least 12 months. They were all provided X-rays of the spine and were experiencing only mild symptoms of asthma at the time of the study. The exclusion criteria included having had any treatment from a chiropractor or a physical therapist during the two months preceding the trial and any acute asthma symptoms during the preceding six-week period. Three subjects dropped out during the trial as their asthma became acute and two changed their mind about attending.

All were under the care of a medical practitioner and a current regimen of asthma medications (45% female and 55% male; average age, 48-years-old). They were told that they would be receiving a ‘program of chiropractic treatments’ during the research but were blinded as to when during the six-week period they would receive the treatments, how many they would receive and what they were to expect as treatment. They were required to attend a treatment and outcomes assessment room set up in the university, three times per week for the duration of the trial.

The PhD candidate administered the assessment and treatment of spinal levels of dysfunction, as a 10-year experienced chiropractor in private practice. The method of salivary collection for the practical acquisition of salivary samples (1-2mls) was tested. Peak Flow Meters were used and lung function was tested by a spirometer unit. The participants were randomised into two groups (randomised computer ordering). Only the chiropractor knew into which of the groups they were allocated. One group received treatment of the levels of spinal dysfunction and the other received 'no treatment'.

'No treatment'

The 'no treatment' was exactly the same in the preamble of meet-and-greet, and the subject would lie face down or up as instructed by the chiropractor. A series of health questions and home care advice was exchanged; the chiropractor did not touch the body in the 'no treatment' group. The research model of the crossover design and the 'no treatment' control group was considered. The participants were quite relaxed and stated that they were not concerned whether they received treatment knowing it would be occurring at some point during the 6 weeks or at the completion of the trial. After three weeks, the treatment group was crossed over with the 'no treatment' group. Thus, each subject received nine adjustments during a three-week treatment period and then attended and received 'no treatment' for a three-week no-treatment period.

Research tools used in this research

Stress questionnaires, bioassays and lung function testing were conducted at specific points during the six weeks of the trial.

A self-reporting questionnaire, the Depression, Anxiety and Stress Scales (DASS) was included as an instrument to measure emotional changes before and after each three-week period (three times).

Peak Flow and spirometer readings of vital lung capacity (FEV1) were obtained before and after each attendance for chiropractic care (18 times).

Cortisol levels were determined in salivary samples collected. Bioassay of cortisol levels before and 15 minutes after each chiropractic ‘treatment’ was completed. Salivary samples were collected before and 15 minutes after each chiropractic treatment (18 x 32 samples: laboratory testing by the Department of Biological Sciences, Macquarie University; using Amerlex Cortisol Radioimmunity (RIA) from Amersham) frozen on the day of collection at -20°C and thawed on the day of analysis.

Comments on research design selection

The DASS was used as a patient-centred questionnaire to register any experience of a locus of negative emotion in the asthma participants that was not a separate clinical morbidity.

It appears that anxiety caused a greater manifestation of a physiological response than depression and stress. This may be due to the prolonged nature of anxiety as opposed to stress. This would be examined further in the large multi-site trial.

Cortisol levels were seen to remain high for the group receiving ‘no treatment’ in weeks one to three (18.5pmol/ml). This finding reduced after the crossover in the research design when they received treatment in week four to six (14.4pmol/ml levels). Cortisol levels decreased for the group receiving treatment in weeks one to three (13pmol/ml). This then was notably maintained throughout week four to six (no treatment received) and significantly decreased for the group in their no treatment post-three-week period. It may be that increased cortisol levels led to generalised immune suppression. A test for immune response would be helpful as an associated physiological marker in the multi-site trial.

The use of spirometer testing (only FEV1) before and after treatment and before and after no treatment showed no statistical difference for the duration of the six weeks. The PFM readings showed no statistical difference before and after treatment, and before and after no treatment for the duration of the six weeks. PFMs are an integral part of every AMP. The asthma sufferers were involved in PFM self-monitoring with an AMP already. The PFM was considered as the research tool most appropriate for clinical research where self-monitoring of lung function was required by the trial participants.

2.3 Aims and objectives

For the purposes of this trial a ‘program of chiropractic care’ is defined as a ‘series of 18 chiropractic treatments’.

2.3.1 Aims

The aims of the clinical trial were:

1. To determine whether a ‘program of chiropractic care’ produces any therapeutic benefit in the condition of asthma.
2. To examine whether ‘a program of chiropractic care’ may have any beneficial effects on the health of the individual asthma sufferer within the context of their asthma
3. To contribute to healthcare research and understanding of the pathophysiological mechanisms underlying the asthma condition
4. To examine whether ‘a program of chiropractic care’ may have any role in the management of asthma within an asthma management plan.

2.3.2 Objectives

In the context of these broader aims, the clinical trial had the following specific objectives:

1. To use a series of patient-centred questionnaires to involve the individual asthma sufferer in actively monitoring their health changes within their asthma management plan

2. To use a 'series of research tools' (objective and subjective) to quantify any therapeutic benefits for asthma from 'a program of chiropractic care' (a set of biomarkers of physiological change, being the objective or 'hard' measures alongside a patient-centered set of questionnaires, being the subjective or 'soft' measures).
3. To examine the findings of the following series of research measurement tools separately and collectively:
 - A. Patient-centred questionnaires:
 - Initial profiling of asthma individual
 - Depression and Anxiety Stress Scales (DASS)
 - Disease-specific asthma questionnaire
 - SF-36 (health-related quality of life assessment) (HQoL)
 - B. Self-monitoring measurement:
 - Lung function with the use of the Peak Flow Meter (PFM)
 - C. Laboratory-based analysis of two 'biomarkers' of health change:
 - IgA (immune response)
 - Cortisol (stress response).

Chapter 3 – Methods

In preparation for this study, all described methodologies used in the trial were approved. The human ethics approval reference number for the trial is Macquarie University 26MAY2000-RO42 and HE26SEP2003-RO2633. The clinical trial was registered with the Australian Clinical Trial Registry Number: ACTR 00081909. The ethics documentation is included in the appendix.

3.1 Research design of the asthma study

This was a 14-week research study design of four randomised groups; three asthma participant groups and one non-asthma participant control group. The Fleming's procedure was used to determine the sample size for this study of chiropractic treatment for asthma (280, 281). Based on preliminary study results, that demonstrated a difference in free circulating cortisol concentration ($p < 0.05$) between two asthma participant groups after chiropractic treatment, a power analysis was performed. This was used to demonstrate a meaningful sample size for this study, where significance is set at 0.05 (one-sided test) with proportion 1 set at 0.05 and proportion 2 set at 0.01. *A priori* sample size was determined as 105 participants per group (420 trial participants).

Multi-site, single-blinded

The research design examined chiropractic treatment with a 'no treatment' control group. All asthma participants were told they would receive chiropractic treatment and were blinded as to when their treatment would start during the 14-week study. This clinical trial was conducted in the actual clinics of 19 practising chiropractors. The participating chiropractors were not blinded. They were aware of which participant group was to receive chiropractic treatments. The front desk and administrative staff in the participating chiropractors' clinics were also blinded as to which of those asthma participants who attended their clinic were part of the group receiving treatment; they presumed all were receiving treatment as required by the study.

Typical practice setting

The research model had individual asthma participants experiencing treatment in the contextual setting of an actual chiropractic clinical encounter. For the purposes of this research trial, the treatment was not a specific chiropractic clinical technique and there was no sham control of a chiropractic clinical technique. The treatment group received chiropractic treatment as provided by that chiropractor routinely in a ‘typical’ clinical setting of a chiropractic practice. The ‘no treatment’ group that attended the clinic were privy to the usual routine of that typical chiropractic practice, including ‘professional time’ with the chiropractor, but were not touched by the practitioner.

The clinical trial examined chiropractic as a ‘program of care,’ defined for the purposes of this research as a series of 18 chiropractic treatments delivered three times every week over a six-week period by practising chiropractors working with typical clinical techniques in their daily routines.

Participant groups

There were three groups of asthma sufferers in the study (there was a fourth age-matched control group). Group A of asthma participants attended the participating chiropractic clinics and received 18 chiropractic treatments over six weeks. A second group, group B, attended the participating chiropractic clinics, but did not receive treatment. These two groups were designed to examine any tendency for improvements to occur due to the therapeutic benefits of the clinical encounter of a ‘typical’ practice setting. The third group, group C did not attend the participating chiropractic clinics and were monitored from home. Group C was designed to act as a control for any tendency for improvements to occur spontaneously whether any treatment was administered or not.

The ‘typical’ practice setting of the research design required participating chiropractors to treat each asthma participant in their clinic, using their normal routines and usual clinical techniques. These chiropractors were in private practice and had provided chiropractic

treatments to the public via their practice, for at least five years. Four nominated chiropractic clinical techniques were identified, for the purposes of this research, as mainstream or ‘typical’ of general chiropractic practice. Participating chiropractors confirmed daily use of the nominated chiropractic clinical techniques in their normal clinical routines of chiropractic treatment.

The trial examined ‘typical’ chiropractic treatments used in the clinics of the practising chiropractors.

The research design included a ‘clinical recording sheet’ as a research tool to allow for a quantifiable factor of chiropractic treatment to be developed and examined. The levels of the spine that were treated in the asthma participants by participating chiropractors were recorded on this sheet.

Patient-centred trial

This was a patient-centred trial. The self-awareness and self-monitoring by the asthma sufferer as a part of their active asthma management plan (AMP) was considered. As part of the research model, a series of patient-centred questionnaires was used to encourage the same self-responsibility and interactive approach as the participant’s AMP.

Self-monitoring lung function with home-based Peak Expiratory Flow Meters (PFMs) measured lung function changes in this clinical trial.

The research aimed to examine the efficacy of chiropractic treatment. The laboratory-based research tools were used with the ‘softer measure’ of patient-centred questionnaires. The study examined biomarkers of IgA (immunoglobulin A) as a component of immune responsiveness and cortisol levels as an indicator of stress response in the asthma participants. Biomarkers were used in the clinical trial to observe for indications of a plausible biological mechanism that may be involved in any therapeutic benefits from the chiropractic treatment for asthma.

Research tools

A series of research tools was used. A number of objective physiological changes were measured. A set of baseline measurements was collected prior to the treatment, during weeks one to three. A second data collection occurred immediately following the ‘treatment’ phase in week seven and data was collected again at six weeks after the ‘treatment’ phase had finished, in week 14. This data set at six weeks after ‘treatment’ phase had finished, was designed to allow for a ‘time lag’ measurement for any sustained therapeutic benefits from the chiropractic treatment to be observed.

3.2 The clinical trial process

3.2.1 Administrative protocols

The multi-disciplinary research team set up an asthma project administration office for coordinating activities, holding meetings and all administrative procedures. The office monitored research standards and procedures involving asthma participants and participating chiropractors. The office co-ordinated contacts for the flow of the clinical trial, all correspondence, attended to the office work and data collation as required. The study required regular phone contact for quality control checking, data collection processes, trial commencement and completion advice and other formal contact with asthma participants, participating chiropractors and their staff throughout the study.

For research purposes it is to be noted there was a high level of contact required for the success of this large multi-site clinical trial. The phone roster covered seven days; all requests needed an answer immediately. The asthma participants were self-monitoring and making data collections several times a day. The trial required home-based data collection and clinic attendances by the asthma participants. Their chiropractic treatment was scheduled over 6 days according to each participating clinic’s varied opening hours.

Asthma study: 14 weeks flow diagram

Below in Figure 7 is the flow of the asthma study, asthma participants, and the three phases of the 14 weeks study.

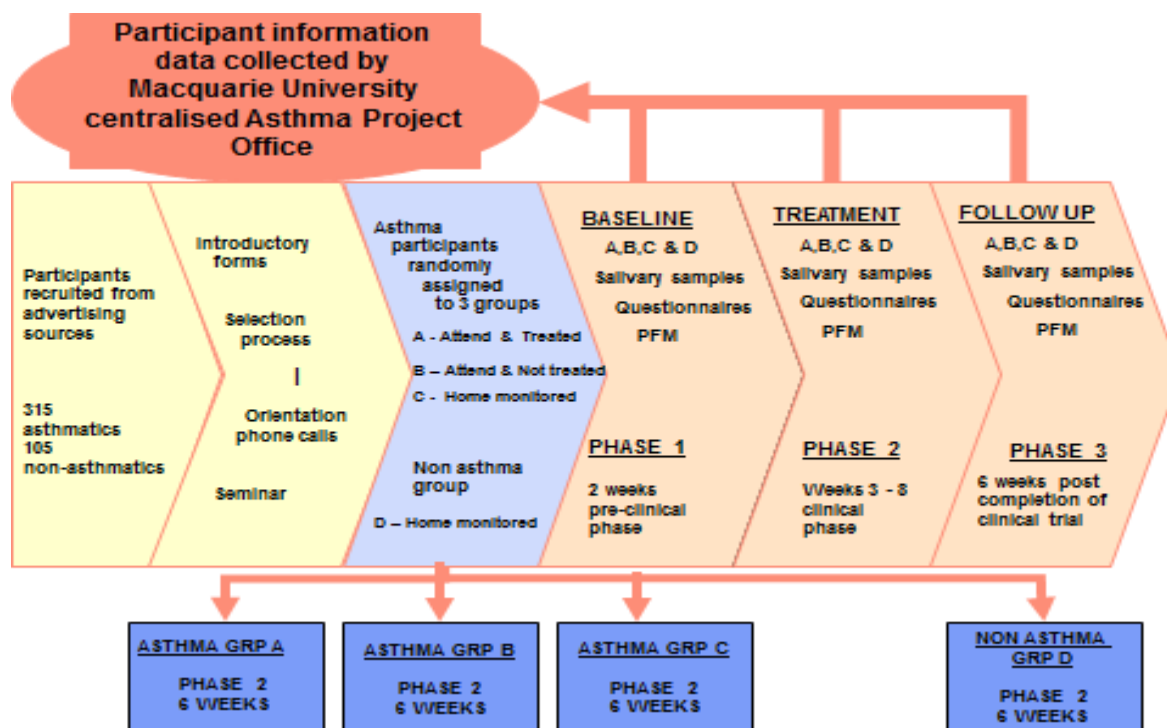


Figure 7: Participant flow diagram of asthma study (14 weeks)

3.2.2 Trial participants - advertising

Over a period of 12 months prior to the study, a campaign of newspaper advertising, radio presentations and media interviews was developed to promote the clinical trial. It was administered from the asthma project office. Asthma interest groups were identified and contacted, and appropriate articles, interviews, presentations, promotional stalls and advertisements were arranged. Groups that assisted in these initial promotions included the Asthma Foundation of NSW, as well as various schools, parents, citizen groups and community-based groups.

The asthma project office created flyers for distribution throughout university campuses and local shopping areas in Sydney, and advertisements were placed in suburban newspapers.

Macquarie University issued a press release and the principal investigator and other research team members were involved in radio interviews and presentations regarding the clinical trial.

There was a range of word of mouth contacts but the majority of initial advertising can be grouped by percentage into media areas of use; 42% metropolitan papers 29% local and university papers 16 % asthma groups and 13% TV/radio.

Allowing for the participant capture rate of the first 12 months, it was decided that in order to capture the sample size of 105 per group the study needed to capture the interest of over 1200 people through all forms of advertising. This included asthma and non-asthma participants.

An advertising campaign saw 657 phone calls received by the project office; 60 of those who called were not interested and 597 requested forms be posted regarding their participation. 60% then dropped out following the receipt of correspondence explaining the detailed nature of the trial. 150 attended the seminar and commenced involvement in the trial. 148 started the trial. 142 completed the trial in full with all data collection requirements. 6 participants (4%) did not complete the trial.

This was a demanding trial for asthma participants, in terms of the 14-week time commitment, the rigour of clinic attendances and the precise nature of all data collection required. A focused consultative process of education and understanding of all these aspects of their involvement was given to each potential participant prior to their agreement to participate in the trial. This may have contributed to the small number who dropped out after commencing their involvement in the trial. Only four per cent of asthma participants left the trial and did not complete the full requirements of the study.

3.2.3 Asthma participants - selection criteria

Each potential asthma participant was asked to telephone the asthma project office for an initial interview. There was a requirement for the asthma participant to be a moderate asthma

sufferer with an active AMP. They were to be in a state of 'well-managed asthma' as defined within their AMP, self-aware of their responsibility to monitor their asthma with a Peak Flow Meter and under concurrent care with their medical provider. Chronic asthma sufferers with moderate asthma were selected on the basis of a current medical diagnosis of asthma for at least 6 months with a daily medication regimen. Each asthma participant was asked to advise his or her medical physician and have confirmed their current AMP confirmed. A medical liaison officer on the research team was available for this process of confirmation when required. Due to the rigour of self-monitoring required in the study, especially the saliva collection, only asthma participants over 8 years of age were invited to take part.

The nature of the clinical trial, including the time commitment required, was fully explained to each asthma participant during the initial phone call enquiries. They were informed they would need to attend a participating chiropractic clinic three times each week over a six-week period, and that there would receive 18 chiropractic treatments. They were told that they would be required to attend research clinics throughout Sydney for the clinical trial period of six weeks. Participants were advised that the research model of the asthma trial had the participants receiving treatment at differing times during the 14 weeks. They were to be comfortable in not knowing when the treatment would commence. The research design would decide at which stage of the clinical trial they would receive treatment and while they would attend the chiropractic clinics for appointments, they would not be aware at which stage the treatment would start.

Questionnaires about the participant's own asthma and health were introduced. The purpose of collecting salivary samples with the rigour of salivary collection was explained. The importance of their lung function and its self-monitoring according to their asthma management plan was reinforced.

Each participant confirmed that they were comfortable with these requirements.

3.2.4 Asthma participants – exclusion criteria

There were a number of criteria excluding potential asthma participants from taking part in the trial. Any acute presentation of asthma was reason for exclusion. Any indication of the participant not active in their AMP was reason for exclusion. Any manipulative therapy received during the previous three-month period was reason for exclusion. Any health condition or other physical complications that contraindicated manipulative therapy, such as osteopenia or osteoporosis, were reasons for exclusion. These clinical areas of exclusion were discussed on the first and second phone calls ensuring potential participants, the medical officer on the team and their personal medical practitioners were all in contact as required during this preliminary contact.

These pre-trial screening phone calls were followed by a mailing of an introductory form and clinical assessment questionnaire. This correspondence assisted in the selection process and helped identify reasons for exclusion. The return correspondence was followed up by the PhD candidate. Other exclusions were degenerative neurological conditions, cardiovascular comorbidities present with their asthma and pregnancy-related issues. Also included as exclusion criteria were any involvement in current litigation for health insurance or other insurance claim and non-compliance with the pre-trial clinical requirement of an X-ray screening.

3.2.5 Introductory seminar for asthma participants

After the initial phone contact with the asthma participants, a series of advice forms was sent confirming details of the clinical trial, and also the initial clinical assessment forms. An invitation was included to all potential participants to an open seminar with an informal afternoon tea. This gave the clinical research team the opportunity to discuss eligibility and introduce the asthma study. Each asthma participant who could not attend this introductory seminar was briefed by telephone.

The introductory seminar explained all aspects of the trial. The chiropractic treatments and X-ray services were explained as being offered free of charge. Attendance at participating chiropractic clinics was discussed. In addition, the introductory seminar detailed all the data collection methods, again confirming participant willingness to comply with all instructions during the study. The method of salivary sample production was demonstrated and the storage method and bag identification procedures for the sputum to be placed in the freezer were fully explained. The use of a new Peak Expiratory Flow Meters for the study was demonstrated and all requirements of the self-recording procedures were explained.

Also communicated in the introductory seminar, was the system of study for sending and receiving all sets of questionnaires and data collections; diarised forms, completion dates, return post instructions and emergency numbers were verbally explained and given in written form.

The participants were informed that their program of '18 chiropractic treatments' would not necessarily improve their asthma and there was no published proof of chiropractic being of any benefit to their condition. They were informed that the chiropractic 'treatment' used in the clinical trial was considered normal or mainstream chiropractic treatments, and it was the sort of treatment that other asthma sufferers may have received when attending chiropractors for help with their asthma.

Asthma participants were asked to not receive any other treatment during the trial except their ongoing medical management and to maintain their pharmaceutical regime as required by their consulting medical practitioner in relation to their asthma.

All asthma participants were informed that they would be randomised to one of three groups of asthma sufferers, and that the groups were all then to be in different stages of treatment during the clinical phase of the 14-week study. The asthma participants were told that the study design required chiropractic treatment for the different groups to occur at a certain times

during the 14 weeks. When attending the chiropractic clinics, they would not be aware at which appointment 'treatment' would commence.

The research design ensured asthma participants understood that they were randomly allocated as to their 'treatment period' and that this would start at any one of their 18 appointments, over the length of the clinical trial. All asthma participants were personally assured that if they ended up being in the group of asthma participants who would not receive any chiropractic treatment during the whole study of 14 weeks, they would receive their full entitlement of the 18 chiropractic treatment at the conclusion of the trial.

During the introductory orientation seminar for asthma participants, each was told that the research study asked them to maintain normal daily routines and lifestyle during the trial. The participants were asked that their clinic attendances and data collection be thought through so as to have these routines arranged within their own daily and weekly schedule. This focused discussion was designed to avoid the subject participants having sudden surprise at the rigour of the trial once they had commenced. It was decided if well prepared before the trial, participants would be more likely to maintain all the requirements and complete their involvement of 14 weeks. Each participant was required to attest to a full understanding of the study data collection and recording methods and the details of their 14-week involvements and clinic attendances. Each participant was to confirm verbally their understanding of the study requirements, the nature of the treatment and their agreed involvement. All participants were issued with a number for their own reference and correspondence purposes with the clinical research investigator and the asthma project office for the duration of their involvement in the study.

3.2.6 Consent forms

Asthma participants were supplied with information, along with consent forms to verify their agreement to participate in the clinical trial. (See appendix 3.2.5 consent forms)

The consent forms outlined the nature of chiropractic treatment involved in the clinical trial, including the risks of chiropractic as a healthcare intervention as it involves spinal manipulation and the possibility of some temporary soreness following some manipulative procedures.

A second consent form for participation in the clinical trial specified the release of confidential clinical information from the participating clinicians during the study's treatment phase. Consent to a pre-trial X-ray screening was also required of asthma participants.

3.2.7 Newsletters and regular contact

Asthma participants were encouraged to have contact with the asthma project office, and the project coordinator also contacted them regularly. In addition, the asthma project office distributed asthma study newsletters to support general morale and a team spirit for asthma participants and the participating clinics. Both were also invited to social occasions at the university during the course of the study.

3.2.8 Information packs

Information packs were sent to all asthma participants about data collection and for general reference throughout the weeks of the clinical trial.

The pack contained a detailed, written guide to their practical participation in the 14-week study, with information explaining data collection and recording procedures. A personalised and dated timeline of the 14 weeks of the clinical trial was included for their reference.

Each participant also received an asthma study 'names and numbers' fridge magnet with the phone number of the asthma project office. A fun asthma project team T-shirt ('I spit for asthma') and an asthma study tote bag were included, contributing to a focus on pride in being part of a large university-based group all involved in studying asthma.

Each information pack also included a new Peak Expiratory Flow Meter with Peak Expiratory Flow charts developed for the asthma research trial. In addition, the pack contained a number

of polypropylene saliva collection vials, packaged with instructions for saliva sample collection and storage, and self-reporting questionnaires with self-addressed envelopes. Options to collect and store saliva at the participating clinics or have this collected by the university couriers were all available during the 14-week study period.

Questionnaires (groups A, B and C asthma participants)

Week 1 Questionnaire:

In a self-addressed envelope: asthma trial questionnaire (pink); including initial profile and asthma disease-specific DASS questionnaire (blue); and general health questionnaire SF-36 (green); university X-ray clinic referral form and phone number for X-ray screening appointment at the university clinic.

Week 7 Questionnaire:

In a self-addressed envelope: asthma-specific questionnaire (white); DASS questionnaire (blue); and general health questionnaire SF-36 (green).

Week 14 Questionnaire:

In the self-addressed envelope: asthma-specific questionnaire (white); DASS questionnaire (blue); and general health questionnaire SF-36 (green).

Questionnaires (group D, non-asthma participants)

Group D was the non-asthma participant group. This group did receive Peak Flow meters and monitoring charts with instructions on their use for the purposes of the asthma research trial.

Week 1 Questionnaire:

In a self-addressed envelope: asthma trial questionnaire (pink); DASS questionnaire (blue); and general health questionnaire SF-36 (green).

Week 7 Questionnaire:

In a self-addressed envelope: DASS questionnaire (blue); and general health questionnaire SF-36 (green).

Week 14 Questionnaire:

In the self-addressed envelope: DASS questionnaire (blue); and general health questionnaire SF-36 (green).

3.2.9 Clinic attendance

The project office sent an introductory mail-out to the staff in each participating clinic to familiarise them with the nature of the trial. This correspondence outlined the intended clients and their dates of attendance at their clinic for the six-week clinical phase of chiropractic treatment.

Instructions were for the clinics to manage the asthma participants as they did all their clients. For example, there would be contact for any missed appointments, educational materials with all usual daily routines, greetings and procedures as per their practice protocols.

Appointment schedule

The asthma project office first contacted the study's participating chiropractors to confirm their available dates for taking appointments for the asthma participants. This required 18 appointments during the six-week period of the clinical phase of the study. These dates and scheduling of regular appointments were discussed and contact between the clinics and the asthma participant arranged. The clinic desk staff called the asthma participants to introduce themselves and make the series of appointments.

Each asthma participant then completed their baseline documentation and data collection two weeks prior to attending one of the participating clinics.

Asthma participants

A letter was sent to each asthma participant with the name of the clinic they were to attend, the participating chiropractor's name and the name of the clinic's desk staff member, along with confirmation that they could expect to hear from the clinic staff soon. To confirm these next steps for their clinic attendance, the project office coordinator also phoned the asthma participants.

3.2.10 X-ray review

Asthma participants were informed during their introductory seminar that an X-ray would be required prior to their involvement in the clinical trial. Each was subsequently contacted by the Macquarie University outpatients' clinic and an appointment for an X-ray of their full spine was requested.

The Macquarie University outpatients' clinic resident chiropractic radiologist, DR Peter Bull reviewed all films for any contraindications for spinal manipulation. These X-rays were taken after an initial clinical assessment. There were no asthma participants excluded for these reasons.

3.2.11 Randomisation

A computer-generated number randomisation was used to allocate asthma participants into one of three groups (A, B and C). The variables of the chronic condition of asthma were not analysed. All asthma participants were identified for the duration of the trial in all data collection, analysis and display of results by a study identification number.

Group	Total Number	Average Age	Male	Female	Average Years of asthma
A	41	41.2	16	25	27.8
B	40	47.8	27	13	34.9
C	39	39	11	28	24.7
TOTAL	120	42.7	54	66	29.1

Table 1: The three parallel groups of asthma participants after randomization process

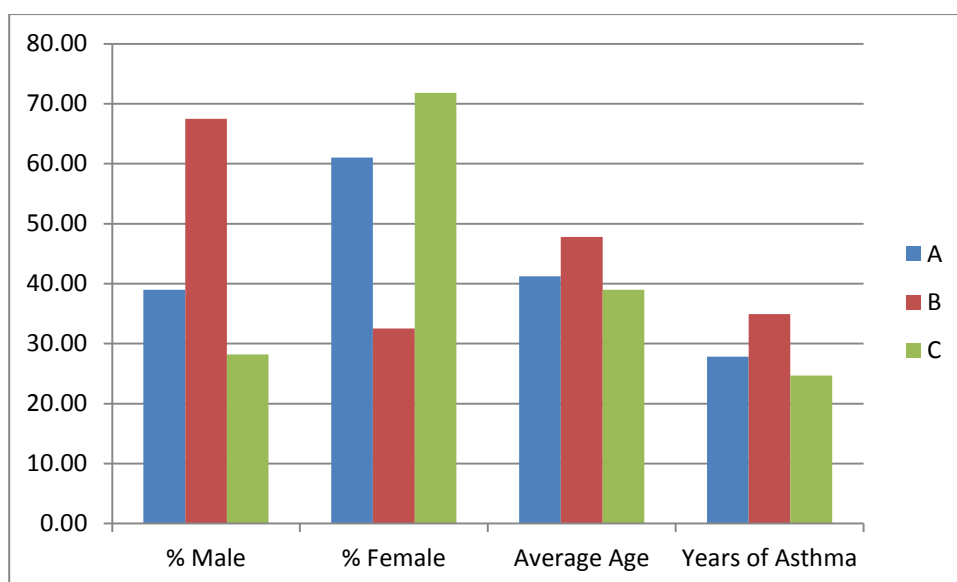


Figure 8: The three parallel groups of asthma participants after randomization process

3.3 Participating chiropractors

Information about the asthma research project was mailed to 100 chiropractors in the Sydney region in Australia, taken from the Sydney ‘Yellow Pages’ telephone directory. Sixty phone calls were received from chiropractors. The PhD candidate explained the trial and sent invitations to the orientation seminar. Forty-two attended the orientation seminar. Twenty-three were not interested in participating in the research and did not proceed following the seminar.

Nineteen participating chiropractors and their clinics were involved in the clinical phase of the asthma trial. One participating chiropractor did withdraw after commencement of the study, citing that they had given too much time to asthma participants for ‘no financial benefit’. Another participating chiropractor dropped out without any reason before the participants began attending any appointments at his clinic. During the 18 months of the clinical trial, three new chiropractors and clinics were selected as participants.

3.3.1 Invitation to participate in the research

Practising chiropractors interested in participating in this research and able to offer their clinics’ involvement were invited to respond by phone, allowing for any questions to be

answered. Their intentions to participate in university-led clinical research that would require their full co-operation were clarified at this point. The trial's objective was to establish, from the outset, each participating chiropractor's research interest and professional willingness to abide by standards set by the asthma project office throughout the clinical phase of the research study.

3.3.2 Selection criteria

The participating chiropractors and clinics involved in this study were to be seen as representative of typical or mainstream chiropractic practice in Australia. As such, all chiropractors participating in the treatment phase of this study needed to meet certain criteria. They were to be in private practice with an established routine use of at least one of four clinical techniques selected for the purposes of this clinical trial. The specific criteria used in selecting chiropractors to be involved were as follows:

- An established private practice of at least five years
- Member of one professional chiropractic association in Australia
- Two colleagues attesting on clinical technique proficiency
- Daily use of at least one of four identified mainstream clinical techniques (Activator, Gonstead, Sacro-Occipital Technique and Motion Palpation/Diversified)
- An active professional commitment to postgraduate seminars and studies
- An ongoing interest in the future and development of chiropractic within the broader Australian healthcare system
- A willingness to commit to involvement in a clinical trial of up to 12 months duration
- A willingness to commit to the research protocols of a university-led clinical trial;
- A willingness to use a standardised record sheet for the purpose of research
- A commitment to avoid using adjunctive therapies or supplements during the trial;

- The capacity to offer professional time, premises and administrative staff for a clinical trial of up to 12 months duration
- Clinic staff willing to abide by university-led research standards
- Full cooperation with all procedures and protocols of the research trial as instructed
- Encouragement and understanding of asthma participants' active AMPs
- Sufficient and secure filing and computer facilities for all paperwork and correspondence
- A demonstrated high regard for ongoing contact with the project office for the quality control of their clinic's participation.

3.3.3 Introductory seminar for chiropractors

An introductory seminar was held for chiropractors interested in participating in the clinical research trial. This commenced with an overview of the asthma study and the more practical aspects of their involvement as a participating clinic.

First session: introduction and individual forms

During the first session of the seminar, all chiropractors were handed a 'participating chiropractic clinic' form to be completed during the first session and handed back to the PhD student for review before the second session. This form requested details of their years in clinical practice, undergraduate and postgraduate education and any other relevant qualifications and clinical preferences of health areas of interest and clinical techniques. Also obtained was information on areas of chiropractic interest, the physical nature of the practice administration (computer and/or paper recording systems), as well as details of staff (by name) who would be involved with the chiropractor's participation in the trial.

Chiropractors were also asked to describe their clinic's procedures and protocols for clients, their education and management processes and how the front desk delivered these to their clients. Finally, the form asked for the name of a clinic staff member who would be making liaison phone calls with the asthma participants as needed during the trial.

Second session: an interactive Q&A session

Following the first session, this interactive part of the seminar allowed chiropractors to express their own research ideas and hear about the research standards of the university-led study during its clinical trial phase.

During this session, the nature of the research was outlined, the clinical phase of the trial was described and the rationale as to the reasons for it occurring in ‘real’ clinical practice settings was explained. The chiropractors participating in the research study were to be seen as ‘typical’ of mainstream chiropractic practice. For the purposes of the research, a ‘typical’ chiropractor would be delivering ‘typical’ chiropractic treatment in a ‘typical’ chiropractic clinical setting.

Four mainstream clinical techniques

The four clinical techniques selected for the purposes of this research were introduced at the interactive session, and feedback on this selection was requested. The mainstream clinical techniques were Gonstead, Activator, Sacro-Occipital Technique and Motion Palpation/Diversified.

The clinical phase of the study

The chiropractors interested in participating in the study were then informed that their whole clinic and staff would be part of the clinical phase of this asthma research study. The clinical phase would see them involved for a six-week period and their clinic would provide a clinical setting for the research. During this time, their staff would need to assist with all appointments, coordinate with the asthma project office, and maintain all contact with both the participants and the research investigators. The clinical trial required the participating chiropractors to assess the asthma participants in their own clinic settings for 18 appointments, three times a week for the six weeks of the clinical phase. The asthma participants were to attend their clinics at no charge. The participating chiropractors were

informed no payment would be made for their own participation and that of their clinic in the research study.

Some attending chiropractors stated clearly that they wanted their style of practice to be researched and were not interested in the ‘research standards’ of the university-led research trial required of all participating clinics.

Chiropractors who did request to be involved in the trial but failed to fulfil the selection criteria, were informed by telephone. They were told why they were not sui for this particular clinical trial and that their inclusion in future clinical trials would be a possibility.

3.3.4 Background of clinical techniques for participating chiropractors

A basic profile or understanding of chiropractic clinical techniques was answered by each chiropractor who attended the introductory research seminar. They were first asked to detail those techniques they were taught in their undergraduate program and the percentage of their inclusion of these techniques in their clinical routines. Then they were asked to list the postgraduate techniques they had learnt and now use in daily practice and the percentage of their inclusion of these techniques in their clinical routines.

The answers to these questions did indicate some chiropractors were singular in their choice of chiropractic clinical technique and other chiropractors combined ‘clinical approaches and techniques’ from both undergraduate and postgraduate studies.

Results are displayed in 3 tables

(See Tables 1, 2 and 3)

The clinical techniques were discussed with input from the chiropractors as to the importance of their clinical technique and their attitude to techniques with which they were not familiar. The orientation seminar discussion confirmed that there was a divisiveness that requires further understanding for the chiropractic profession to grow as a self-critical discipline. The technique profiles were outlined by 14 participating chiropractors during their orientation

seminar in response to the questions about their use of techniques in their practices. These chiropractors and their participating clinics were all in the Sydney metropolitan region, located in: Artarmon, Bondi Junction, Camden, Concord, Dee Why, Drummoyne, Eastlakes, Fairlight, Lane Cove, Liverpool, Surry Hills, Wentworthville and Westleigh.

Techniques taught in undergraduate programs of chiropractic	Number of chiropractors who stated they had been taught the clinical technique	% this undergraduate clinical technique used in daily practice
Diversified	10	71
Drop-Piece	3	21.4
Gonstead	3	21.4
Activator Method	2	14.3
Toggle (hole in one)	1	7.1
Atlas Specific	1	7.1
SOT (Sacro-Occipital Technique)	1	7.1
Thompson Technique	1	7.1
Biomechanical Blocking	1	7.1
Motion Palpation	1	7.1

Table 2: Undergraduate techniques used in daily clinical routines

Postgraduate education about clinical techniques	Number of chiropractors who stated they studied the technique after graduation	% of treatment that uses the postgraduate clinical technique in daily practice
Gonstead	3	21.4
SOT(Sacro-Occipital Technique)	4	28.6
Activator Method	8	57.1
BEST	1	7.1
NET (Neuro-Emotional Technique)	1	7.1
Diversified	3	21.4
Atlas Specific	1	7.1
Cranial Work	1	7.1
Thompson Technique	1	7.1
Upper Cervical Toggle	1	7.1
Recoil Adjusting Instrument	1	7.1

Table 3: Postgraduate techniques used in daily clinical routines

Clinical techniques used daily in practice	Number of chiropractors who stated they use this clinical technique	% this clinical technique is used in their daily practice
Activator	8	57.1
X-ray Analysis	8	57.1
Motion Palpation	6	42.7
Diversified	6	42.7
Nutrition	6	42.7
SOT	5	35.7
Thompson	4	28.6
Technique/Drop-Piece	4	28.6
Gonstead	3	21.4
Applied Kinesiology	2	14.3
Thermography	2	14.3
Surface EMG (Electromyography)	2	14.3
Dermathermograph	2	14.3
Acupuncture	1	7.1
C1 Specific Approach	1	7.1

Table 4: Clinical techniques (undergraduate and postgraduate) used in daily clinical routines

3.3.5 Orientation for chiropractors

Initial orientation centred on an interactive discussion with the participating chiropractors to ensure as many concerns as to their involvement could be addressed before the research trial commenced. All the forms to be used and data collection arrangements were reviewed. These discussions covered practical requirements of the clinical phase of the study. The chiropractors were required to confirm they were 100% satisfied they could use the ‘clinical techniques’ identified as a normal part of their routine clinical practice, and that they were 100% confident they could fulfil all professional obligations in treating the asthma participants during the clinical phase.

Clinical treatment

It was explained to the participating chiropractors that the term ‘subluxation’ would not be used for the purpose of this research, but its use in their normal practice routines could be maintained. All other clinical technique terms, clinical SOAP notes and other observations were to still be recorded for their own professional reasons.

The chiropractors were told that for the purposes of this research, the term ‘spinal dysfunction’ would replace any other chiropractic clinical technique-based terminology or any subluxation description of what they were treating.

Identifying level of ‘spinal dysfunction’

The chiropractors were asked to confirm they did identify levels of spinal dysfunction when using their clinical techniques for treating patients in their chiropractic practice. All participating chiropractors were informed again, that for the purposes of the research trial, their chiropractic clinical technique was not being examined and that any identified level of ‘spinal dysfunction’ they found was deemed to exist on the merits of the clinical technique by which it was determined.

A clinical recording sheet

The research trial required participating chiropractors to mark any level of ‘spinal dysfunction’ treated on a clinical recording sheet (see Appendix). This sheet included a simple drawing of the spine with the spinal vertebrae clearly shown schematically, from occiput to sacral base. This clinical recording sheet was explained as a common language clinical research system. The chiropractors were to mark the spinal level of treatment with a simple ‘x’. They were shown where to make other clinical comments and technical notes outside the spinal schematic drawing, as may be required by their professional obligations.

Asthma participants

It was also explained to the chiropractors that there were four groups of asthma participants in this research study, and that those in groups A and B would attend participating chiropractic clinics for 18 appointments for six weeks of the clinical phase of the study. The asthma participants were equally allocated across participating clinics for the clinical phase of attendance.

The participating chiropractors were not blinded as to the group of asthma participants to be receiving treatment. Participating chiropractors only, not the clinic administrative staff, were

aware that the colour of the participant's file was significant. The colour of the plastic file indicated which group the asthma participant belonged to. Green files were for the treatment group and red files were for the 'no treatment' group. The asthma participants were also blinded as to this protocol.

Group A 'treatment'

These asthma participants attended a participating clinic as a patient for 18 appointments for the six weeks of the clinical trial. The participating clinic staffs were to form the normal relationship with each participant as per the typical procedures used with all of their patients. Attendance at the clinic included all normal educational and customer service as practised by that clinic. So, when the staff or the participating chiropractor greeted the asthma participant, they would be greeted as per the normal procedure at the clinic or invited to read and/or watch educational materials. When invited into the treatment room area, the chiropractor would ask all their usual health-related questions as per normal practice, including those about posture, diet, exercise routines and then specifically regarding their asthma. The participating chiropractor was instructed to assess and treat the asthma participant as per their usual clinical technique routine, making a treatment record on the clinical recording sheet of any levels of spinal dysfunction treated.

Group B 'no treatment'

These asthma participants attended a participating clinic as a patient for 18 appointments for the six weeks of the clinical trial. It was explained to the participating clinic staff that they were to receive participants as per normal procedures used for all clients. Their attendance was for a chiropractic program of care and the clinic was to include all normal educational and customer service as practised by their clinic. So, when the staff or the participating chiropractor greeted the asthma participant, they would be greeted as per the normal procedure at the clinic or invited to read and/or watch educational materials. When invited into the treatment room area, the chiropractor would ask all their usual health-related

questions as per normal practice, including those about posture, diet and exercise routines. The asthma participants would then be asked a few questions specifically regarding their asthma signs and symptoms, and the state of their asthma according to their AMP.

However, participants in this group were not physically touched. The participating chiropractors were to ask the asthma participants to lie down, relax and focus on their breathing for a few minutes. They were then asked to get up and confirm their next appointment as they were leaving the clinic.

3.3.6 Chiropractic clinical techniques

These clinical techniques were considered as mainstream for the purposes of the trial. Each technique is explained in similar terms in the Glossary. Here, the techniques are referenced.

Activator Method

The Activator Method is a system of chiropractic assessment and management which seeks to determine the precise area of subluxation (an alteration of the normal dynamics, anatomical or physiological relationships of contiguous articular structures). The areas of subluxation are determined by specific, orderly isolation tests of prone leg length analysis. A mechanical hand-held device is used to deliver treatment of a specific joint identified as showing dysfunction (282, 283).

Gonstead Technique

The Gonstead Technique is a method of chiropractic assessment and management which seeks to determine each component of the subluxation complex, emphasising the difference between the subluxation and areas of spinal compensation. The method involves visualisation, radiograph analysis, nervoscope testing and static and motion palpation. There is a precise method of manual adjustment to the level of the spine determined as showing the primary dysfunction (284, 285).

Diversified/Motion Palpation

Diversified/Motion Palpation is a method of chiropractic assessment and management which seeks to determine aberrant motion, especially joint dysfunction. This method is centred on

the active and passive palpation of joint motion. This technique emphasises this joint dysfunction as the component that perpetuates the subluxation. Diversified Technique uses many procedures to introduce motion into the spinal segment identified as the level of dysfunction (286, 287).

Sacro-Occipital Technique

The Sacro-Occipital Technique focuses on the cerebro-spinal fluid (CSF) and its flow within the spinal column. The SOT chiropractor uses triangular-shaped wedges or 'blocks' in its treatments, as well as manual treatments of specific dysfunction in the spine and related areas. It identifies the level of spinal dysfunction via palpatory and observational diagnostic procedures. (288,289).

3.3.7 Clinical recordings of treatment

A schematic outline of the spine was developed for the purpose of chiropractic clinical research known for the objectives of this trial as the 'clinical recording sheet'. The clinical recording sheet was a pencil line drawing comprising separate 'block' segments (square shapes) representing C1 to L5. There was a clearly drawn pelvis at one end and the base of the skull at the other. Each segment was intentionally separated from the segment above and below to minimise confusion and marking errors. The marking system was developed as a research tool for use across different chiropractic clinical techniques in clinical practice research. It was intended to allow the common practice of treating levels of spinal dysfunction in chiropractic practice to be developed for research purposes.

The spinal levels of dysfunction treated

Each participating chiropractor was shown how to identify on the clinical recording sheet the spinal level(s) of dysfunction they treated. Where a vertebral level of the spine was identified, or particular vertebrae were indicated for treatment by their clinical routines, the participating chiropractor marked that level on the schematic outline of the spine. A simple cross was decided on as having a common meaning for recording purposes. This simple 'X' was applied

to the whole square, representing that one spinal segment or part thereof, depending on the participating chiropractor's clinical decision. However, for the purpose of data collection, a mark on all or part of a spinal segment 'square' indicated that segment was to be included as 'marked'.

18 separate clinical recording sheets

The 18 clinical recording sheets to be used in treating the asthma participants were distributed to each participating chiropractor; with written instructions attached. A new clinical recording sheet was required for each appointment. Each participant file contained 18 separate clinical recording sheets to be used three times each week during the clinical phase of six weeks.

3.3.8 Orientation for participating clinics and staff

There were 19 participating chiropractic clinics involved through the study with locations that included the inner city area of Sydney, the eastern suburbs, northern suburbs, north-western suburbs, the western suburbs and the northern beaches.

Phone calls

The asthma project office made introductory phone calls to all participating clinics. The participating chiropractor and each of their administrative clinic staff were encouraged to contact the project office if any issues or confusion occurred during the trial. They were informed that a research investigator would always be available, with diversion to mobile/cell phones when the project office was unattended.

The participating clinics all agreed to maintain a close liaison with the project office and understood the necessity of the asthma participants attending all 18 appointments; agreeing to notify the project office of any participant who missed two of their scheduled appointments.

Clinic correspondence

Administrative staff was informed of all correspondence they were to expect from the project office. The participants' files and introductory forms were mailed to clinics one week before the asthma participants' 'clinical phase' of 18 appointments commenced. The participating

clinics were asked to let the asthma project office know when these documents arrived and to call the project office if they did not arrive the week before a participant's first appointment.

The participant's file contained clinical notes, X-rays and a confidential information release form. The confidential release form was to be signed by the asthma participant, along with any of the clinic's own requirements and forms.

Data storage

The participating clinics were educated in assisting with some data collection during the clinical phase and in the six-week post-trial data collection period. They were required to confirm they had a refrigerator to store the hygienically sealed and pre-labelled salivary samples. Clinic administrative staff were then asked to assist the study by providing storage in a refrigerator/freezer for the thrice-weekly collection of these samples (to be picked up by the research office courier).

Clinic administration file

Each participating clinic had an administration file established by the project office. All details of the participating clinic's location, days and hours of practice, staff names, details of the desk staff duties, nominated contacts at the front desk for the clinical phase of the trial, and how many asthma participants were attending or had attended their clinic was maintained in this clinic administration file. All relevant clinic staff details, professional details and personal contact details were kept on file in the project office.

3.4 Asthma study groups: A, B, C and D

Group A

This group consisted of 41 asthma participants who attended 18 appointments and received chiropractic treatment three times every week during the six-week treatment phase of the 14-week study.

Group B

This group consisted of 40 asthma participants who attended 18 appointments and did not receive chiropractic treatment in the six-week clinical phase of the 14-week study.

Group C

This group consisted of 39 asthma participants who did not attend the participating clinics and did not receive chiropractic treatment during the entire 14-week study.

Group D

This group consisted of 22 non-asthma participants who did not attend participating clinics and did not receive chiropractic treatment during the entire 14-week study.

Note that group D (a control group of non-asthma sufferers) participated in all areas of data collection except the disease-specific asthma profiling, during the 14-week period. They participated from home and formed a normal population sample.

3.5 Asthma study: phases 1, 2 and 3

There were three groups of asthma participants and one group of non-asthma controls (in total 142 participants) involved in the clinical trial.

There were three phases, with three points of data collection at each of these phases. The data collection started before the commencement of the clinical trial and the final data collection point occurred when the study concluded at 14 weeks. See Table 4 below.

First, a pre-trial baseline data collection point occurred in the two-week period prior to any clinical attendance; 0-3 weeks (phase 1).

Second, a treatment phase data collection point occurred at the completion of the clinical phase, 3-8 weeks (phase 2).

Third, a post-treatment phase data collection point occurred six weeks post-treatment after the completion of the clinical phase, 8-14 weeks (phase 3).

Phase 1	Phase 2	Phase 3
Baseline	Post-treatment clinical phase	6-wks post-clinical
data* (0-3 weeks)	data*(8 weeks)	data*(14 weeks)
Group A	Asthma sufferers, receiving treatment, attend centres	All subjects provided salivary samples as
Group B	Asthma sufferers, receiving no treatment, attend centres	well as questionnaires at three data*
Group C	Asthma sufferers, receiving no treatment monitored from home	collection points of the three phases during the
Group D	Non-asthma sufferers, age-matched controls monitored from home	asthma study
Two weeks pre- treatment	Six-week program of 18 chiropractic treatments (clinical treatment phase)	Six weeks post-treatment

Table 5: The four parallel groups showing the data* collection points through phases 1, 2 and 3 of the randomized 14-week study

3.5.1 Data collection in phase 1

The baseline data collection of initial questionnaires/samples of saliva/Peak Flow readings occurred two weeks prior to the ‘treatment’ phase (Table 4).

All participants were required to monitor their Peak Expiratory Flow (PEF) outcomes with an 8am and an 8pm PEF reading.

All participants were required to give these saliva samples at 8am and at 8pm for three days of the week: Tuesday, Thursday and Sunday.

All participants were required to complete all questionnaires, including the initial asthma background profile questionnaire.

3.5.2 Data collection in phase 2

The ‘phase 2’ data collection of patient-centered questionnaires/samples of saliva/Peak Flow readings occurred at eight weeks following the ‘treatment’ or clinical phase (Table 4).

Groups A and B

All participants from groups A and B were required to attend their agreed participating chiropractic clinic. The program of chiropractic care (defined as a series of 18 chiropractic treatments) was delivered three times each week for a six-week period. Appointment times were made as close as possible to the same time of day for each attendance to minimise potential variants in body measurements (cortical and immune status data for the trial). The participants' attendance involved the regular routine of the participating clinics, including any chiropractic educational practices. The participants were aware that they were attending for an 18-visit program of chiropractic care and understood they would not know when their treatment commenced. At every clinic appointment, each asthma participant in group A received treatment from the participating chiropractor. Each participating chiropractor recorded the levels of the spine treated on the clinical recording sheet. Group B participants attended their 18 appointments with the chiropractor at the participating clinic. They also took part in all normal practice routines except that there was a clinical discussion with the chiropractor but no physical contact in that clinical encounter. All groups completed their data collection, questionnaires, samples and PEF recordings as required by the study for phase 2. Questionnaires, PEF scores and salivary samples, as required by the study, were able to be stored at the participating clinic for the university courier to collect.

3.5.3 Data collection in phase 3

The 'phase 3' data collection of patient-centered questionnaires/samples of saliva/Peak Flow readings occurred at 14 weeks, six weeks after the completion of treatment or the clinical phase (Table 4).

Participants of all groups were required to complete the follow-up or post-trial data collection at 14 weeks (six weeks post-treatment). All participants from groups A and B were able to leave the samples and questionnaires at the agreed participating chiropractic clinic or call the project office for a courier collection. Asthma participants in group C provided salivary

samples and questionnaires, dropping them at a nearby participating clinic or calling the project office for a courier collection.

3.6 Salivary samples and laboratory methods

3.6.1 Asthma participants

All asthma participants were educated in how to use devices (labelled vials) to collect saliva for the purposes of this research, and how their samples would be stored and subsequently transported. Subjects provided between 3 and 5 mls of saliva in each collection tube. Each asthma participant confirmed that this procedure was manageable for them personally.

Salivary collection process

This salivary collection occurred two weeks prior to the trial, during the clinical trial and six weeks post-completion of the clinical phase of the study. Collection days were Tuesdays, Thursdays and Sundays (i.e. three times a week) each week.

All collection tubes were pre-labelled with each patient's identification code and the times and dates of salivary collection. The asthma participants were then given the collection tubes in a specific order for ease of use. This was to help avoid any mix-up of the collection tubes during the course of the study.

Salivary samples were collected by asthma participants at 8am and 8pm (daily circadian rhythm of cortisol levels). It was explained to the asthma participants that both collection times were important. The asthma participants were requested to collect their salivary samples before taking any oral corticosteroid pharmaceutical (if part of their AMP).

They were also instructed not to miss the collection time and that any error in collection time was to be recorded if it was not 8am or 8pm.

Saliva storage and transport

The collection tubes containing the saliva were then put in the sealed plastic bags provided.

Samples were collected in two large mouth-stoppered tubes and were then to be placed on ice until they were frozen or placed in the freezer immediately.

Alternatively, asthma participants were able to leave their samples at participating clinics for storage in their freezers. The asthma project office couriers picked up the bagged samples from each participating clinic or organised for the frozen samples to be freighted at the end of every two-week period. The samples were then stored in the Department of Biological Sciences' laboratory freezers.

3.6.2 Laboratory analysis

All participants provided salivary samples for the duration of the trial which were processed for concentration levels. A total of 23,856 salivary samples were analysed for the 142 participants over the 14-week trial period. Every salivary sample was tested independently, twice, for cortisol concentration. Baseline cortisol levels for each group were captured during the first two weeks of the trial. It was the 'am' sample of saliva that was used for the analysis of IgA.

Immunoassay procedures

Most immunoassay procedures for total serum cortisol have been applied to measure urinary total free cortisol. This requires extracting and removing large numbers of cortisol metabolites and conjugates that may cross-react with the cortisol antibody in the assay so that total free unbound cortisol is measured. Urinary assays offer the advantage of avoiding blood sampling and there is also an integrative effect since the amount of cortisol metabolite accumulates over time and the variability of its secretion can be averaged out. High performance liquid chromatography (HPLC) methods are more specific than current immunoassays for urine cortisol measurements and are an attractive alternative.

Laboratory analysis of all samples was within the Department of Biological Sciences at Macquarie University using a combination of commercially sourced kits and in-house testing procedures.

Laboratory kits

In this study, commercially available kits were used with laboratory methods of modifications made to testing due to salivary samples being used as biomarkers in this trial.

DSL-2000 cortisol DA RIA kit

Purchased from Diagnostic Systems Laboratories Inc., the radioimmunoassay kit (DSL-2000 Cortisol DA RIA kit) was developed for use with serum. For the purposes of this research, laboratory procedures altered the amounts of reagents for it to work with saliva. Each salivary sample was assayed in duplicate twice for each research measurement, including cortisol, osmolality, creatinine and albumin. In order to validate the cortisol results and discount the possibility that they may reflect serum contamination of saliva during sampling and/or reflect various clinical conditions, osmolality, creatinine and albumin were measured. Samples which showed unusual levels in these measures were omitted from statistical analysis. Osmolality was measured using a vapour pressure osmometer (Wescor, United States of America) while both creatinine and albumin were measured by end-point colourimetric assays.

The enzyme-linked immunosorbent assay (ELISA)

ELISA is a useful and powerful method in estimating ng/ml to pg/ml ordered materials in the solution, such as serum, urine, sperm and culture supernatant (290).

The basic principle of an ELISA is to use an enzyme to detect the binding of (Ag) antibody (Ab). The enzyme converts a colourless substrate (chromogen) to a coloured product, indicating the presence of Ag:Ab binding. An ELISA can be used to detect either the presence of Ags or Abs in a sample, depending on how the test is designed. ELISA has been widely used in life science research (290). ELISA has also proven a very useful method for the

detection of IgA in many respiratory conditions. Detection of IgG and IgA against A60 antigen was carried out by enzyme-linked immunosorbent assay (291).

Data completeness

All patient-centred questionnaire results were reviewed for completeness. Questionnaires, Peak Flow Meter, cortisol and IgA laboratory data results were reviewed and sorted for compliance. Complete data collection was reported allowing for a few salivary samples not received. The clinical recording sheets were reviewed for the markings on the spinal vertebrae; all sheets were marked adequately for accurate data collation. All data was presented in spread sheets for statistical analysis.

3.7 Statistical analysis

All data collected from the prescribed questionnaires across all primary research measurements as outlined in the study flow chart of data collection (see Table 4), was migrated into pre-prepared spread sheets for basic as well as detailed statistical manipulation. Specifically, each data point was addressed with specific statistical tools that related to the nature of the data acquisition processes of the research trial. Data analysis software programs were used during the trial. SPSS (Statistical Package for the Social Sciences) used with SAS (Statistical Analysis System) for statistical analysis of data during the trial including one-way analysis of variance (ANOVA) two-way ANOVA, generalised estimation equation (GEE) and GEE longitudinal analysis. There was ongoing statistical advice and input from Macquarie University statisticians in consultation with the principal investigator during this process of statistical manipulation and detailed analysis of the data. Presented is the various approaches used for the data from the different research tools in their statistical management.

3.7.1 Asthma disease-specific (symptoms data)

The SAS and SPSS programs were used for analysis of the disease-specific questionnaires profiling of the asthma participants. The data from the two questions of asthma profiling

questionnaire; night/daytime symptoms and the use of reliever medications were computed with the SAS and SPSS computer programs.

3.7.2 SF-36 wellness questionnaire (SF-36 data)

A program that generates SAS code for scoring the SF36 was used, so that the lowest and highest possible scores are set at 0 and 100. Then transforms 0-100 scales to have a mean of 50 and a standard deviation of 10 in the general Australia population (norm based scale scores NBS).

To measure the changes in health, the health outcome measure 2 weeks before treatment was subtracted from these outcomes at the end of treatment and six weeks later. One-way analysis of variance (ANOVA) was used to compare the changes in health with respect to treatment groups. A confidence interval (C.I) of the changes in health was also calculated at 95% C.I (292).

3.7.3 Depression Anxiety and Stress Scales (DASS data)

In order to investigate the changes in DASS over the study period and the differences in DASS between groups, odds ratio based on ordinal logistic regression were calculated. But the score test indicated a violation of the proportional odds assumption. Given the distribution of the DASS scales, an odds ratio suggested by McNeil was found to be the best approach for this study. In this method, Pearson's test for independence is used to assess statistical significance, and odds ratios are used to measure the strength of the associations between the specified category for each variable and other categories combined (293) .

3.7.4 Peak Expiratory Flow (PEF data)

Group average readings and group performance

PEF parameters of interest were functions of overall group average reading as well as reviewing group performance for their morning and evening across for the three difference phases of the trial. Diurnal variation, as measured by daily amplitude, is the difference

between morning and evening PEF scores. This was a feature of the three phases within the trial rather than that of a single best score of the day.

One-way analysis of variance (ANOVA)

One-way analysis of variance (ANOVA) was used to compare lung capacity with respect to four participant groups by phase (three separate phases of the clinical trial). Since the changes in lung capacity vary between patients a two-way ANOVA was also used to compare the lung capacity between sessions by group after adjusting for patient ID.

Generalised estimation equation (GEE) and GEE longitudinal analysis

Generalised estimation equation (GEE) was used to analyse the repeated measurements in the longitudinal design with exchangeable working correlation. This assumed that the correlation was constant between any two observations times. All analysis was either performed on SAS statistical program or SPSS. PEF readings over the 14 weeks for all 4 groups were analysed using the GEE longitudinal analysis with generalised linear models for the line of best fit. This facilitated for repeated measures in this longitudinal study and the patterns observed for average PEF scores between groups A, B and C across the 14-week trial as time periods.

3.7.5 Laboratory-based biomarkers (salivary sample data)

Generalised estimated equations (GEE)

The repeated outcomes were analysed using generalised estimated equations (GEE). The treatment effects for all GEE models were examined after adjusting for the salivary sample collection day (Tuesday, Thursday and Sunday) and time effects for cortisol analysis (am or pm). Linear quadratic and interaction time effects were included in all GEE models. Quadratic time effects were included in the models to allow for the possibility that continuous outcome measures may decrease (or increase) during anytime of the trial. Further analysis of the data using the GEE models have demonstrated that linear time effects, linear interaction time effects, quadratic time effects and quadratic interaction time effects were not significant (5% level). These observations further suggest that earlier findings in group concentration were viable.

Cortisol statistical analysis

Continuous repeated outcomes were analysed using generalized estimated equations (GEE) to account within subject correlation. The treatment effects for all GEE models are examined after adjusting for the day (Tuesday, Thursday and Sunday) and time effect (am or pm). Diurnal variation, as measured by daily amplitude which is the difference between morning and evening cortisol concentration was a feature of the three phases within the trial rather than that of a single best score for that subject.

One-way analysis of variance (ANOVA)

One-way analysis of variance (ANOVA) was used with respect to the four participating groups in the three separate phases of the clinical trial. In examining changes in cortisol from baseline to week 8 and from baseline to week 14 between groups one-way ANOVA was used. Subject effects were adjusted using two-way ANOVA but were not significant.

A two-way ANOVA

Since the changes in cortisol vary between patients a two-way ANOVA was also used to compare cortisol changes between sessions by group after adjusting for patient ID. Linear, quadratic and interaction time effects were included in all GEE models as the correlation is constant between any two observations times. Quadratic time effects were included in the models to allow for the possibility that continuous outcome measures might decrease (or increase) during anytime of the trial. Data grouped by linear and quadratic time interactions allows for these patterns to be identified and for magnitude of difference in groups to be seen. To reduce skew effects cortisol was transformed using the natural log. All analysis was either performed on SAS statistical program or SPSS.

Further analysis of the data using the GEE models have demonstrated that linear time effects, linear interaction time effects, quadratic time effects and quadratic interaction time effects were not significant (5% level) (294, 295). These observations further suggest that findings in group cortisol concentration were viable.

3.7.6 Clinical recording sheets (spinal findings data)

The chi-square test was used in this statistical analysis of the markings of levels of spinal dysfunction of the 756 chiropractic treatments during this clinical trial of asthma and chiropractic treatments.

The findings were analysed with a statistical test for overall fit of a logistic regression model and the Hosmer and Lemeshow test, also called the chi-square test (296). The study data was reviewed in line with the logistic regression model; having covariates and a sample size that may be considered small, the chi-square statistical analysis was then chosen as appropriate. Chi squared goodness-of-fit test was conducted to test if the proportions of spinal dysfunction prevalence are equal across all regions. In order to obtain adequate sample size, the spinal levels were aggregated into 15 regions.

Chapter 4 – Results

This chapter presents the results of the clinical trial. The results are followed by specific comments. The questionnaires, and clinical recording sheet used are included in the Appendix. There were three phases in the trial at which point there was data collection of the SF-36, DASS and disease specific questionnaires:

- At two weeks pre-treatment, baseline reading at 0-3 weeks (phase 1).
- Post-treatment (completion of clinic attendance) at week 8 (phase 2).
- Six weeks post-completion of clinical attendance, at week 14 (phase 3).

4.1 Patient-centred questionnaires

A copy of each questionnaire may be viewed in the Appendix.

4.1.1 Disease-specific questionnaire: asthma

Asthma symptom index; composite variable represented the frequency with which individuals awaken during the night and in the morning with asthma symptoms.

Asthma medication use; composite variable represented the mean number and frequency of asthma related medication used.

Disease-specific questionnaire: asthma (symptoms)

The responses of the asthma participants at the three data collection points of the trial in regards to their asthma symptoms are displayed in the Figure 9.

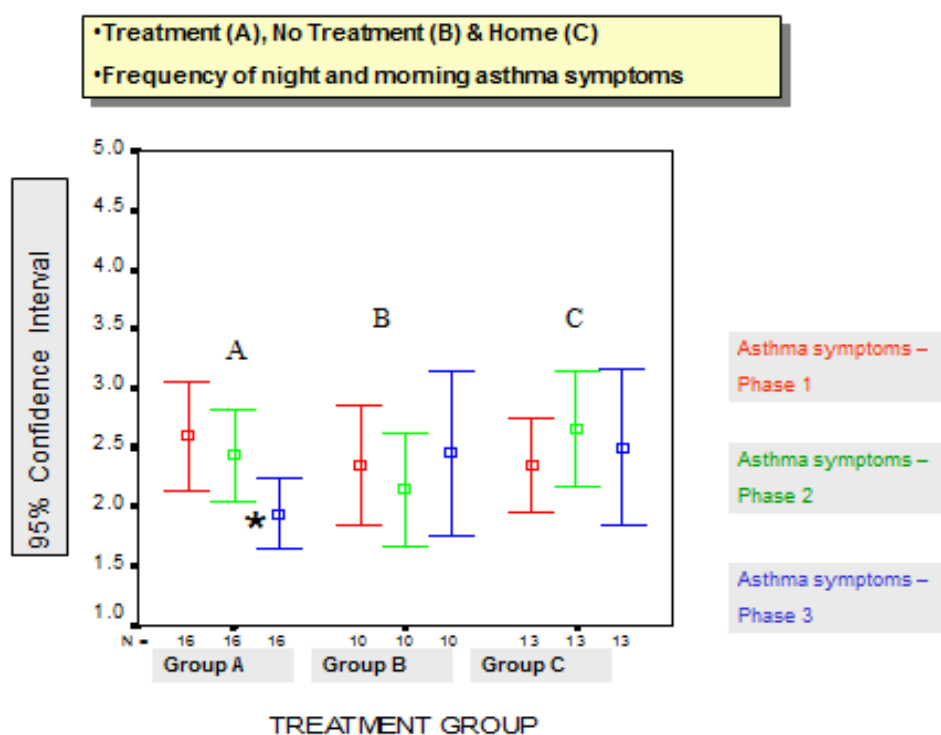


Figure 9: Groups A, B and C: asthma symptoms.

Notes for Figure 9:

- * Note there was a decrease in the asthma symptoms following the chiropractic treatments and this decrease in morning and night symptoms were most notable at six weeks after the treatment phase had finished (phase 3).

Group A demonstrated symptomatic improvements after the treatment, phase 2 (week 8). Results recorded by the asthma participants at the post-treatment period of six weeks showed a continuing improvement in reported changes in self-reported asthma symptoms.

A 95% confidence interval was observed in the improvement trend from the baseline response indication of asthma symptoms experienced at night and in the morning, over the three data collection points of the 14-week study. The greatest improvement was noted in group A at the final data collection point (phase 3). This reported decrease in symptoms for the asthma participants was statistically significant ($P < 0.05$).

Disease-specific questionnaire: asthma (medication use)

A decreased use of 'reliever' asthma medication was reported in group A, post-treatment (phase 2). At the completion of the trial, there was a further decrease in the self-reported need to use asthma reliever medication that was statistically significant ($P < 0.05$).

The observation is indicated in Figure 10.

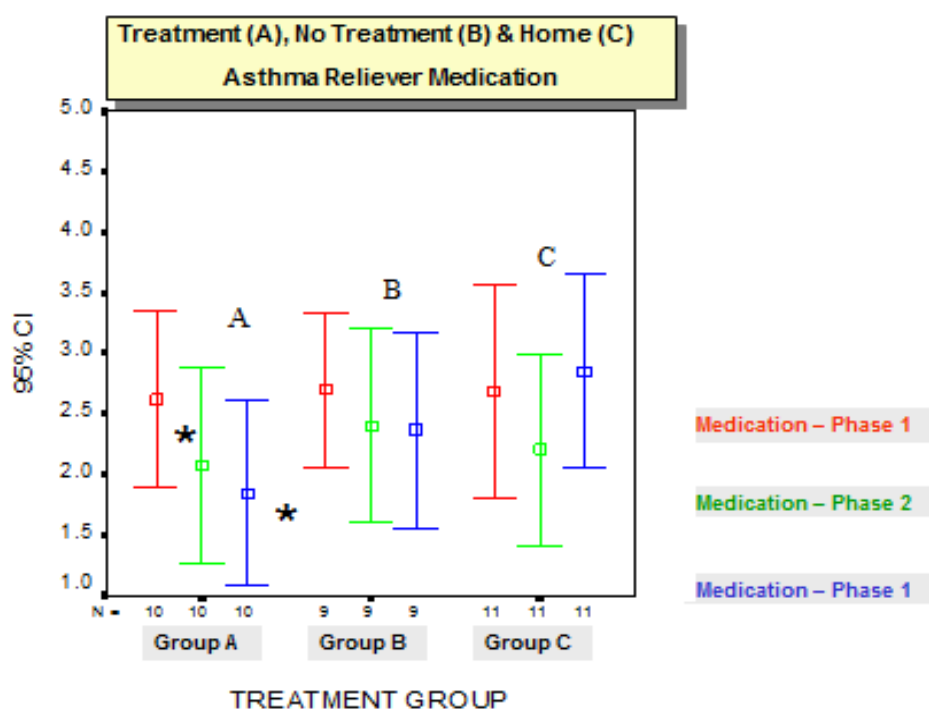


Figure 10: Groups A, B and C: use of reliever asthma medication

Notes for Figure 10:

- * Note there was a significant decrease in the asthma participants' use of reliever medication six weeks after the treatment phase had finished (phase 3).

4.1.2 SF-36 patient-centred questionnaire: Health Quality of Life (HqoL)

The SF-36 Quality of Life (HqoL) was used over three data collection points during the 14-week study. The SF-36 was used to measure physical and mental aspects of health in the asthma participants at two weeks pre-treatment baseline reading (phase 1); post-treatment (completion of clinic attendance) at week 8 (phase 2) and six weeks post-completion of clinical attendance at week 14 (phase 3).

The 95% confidence interval is reported for the changes in health for each group of asthma participants as presented in Table 6.

		A	95% C.I	B	95% C.I	C	95% C.I
PF	S2-S1	0.58	(-1.44,2.59)	-0.65	(-2.36,1.05)	-0.10	(-3.90,3.70)
	S3-S1	1.36	(-0.26,2.98)	-0.64	(-2.34,1.06)	-1.24	(-4.19,1.71)
RP	S2-S1	-0.71	(-3.87,2.44)	4.90'	(0.73,9.07)	-1.53	(-7.94,4.88)
	S3-S1	1.73	(-1.05,4.51)	2.19	(-5.12,9.50)	0.95	(-4.48,6.38)
BP	S2-S1	0.11	(-2.57,2.79)	3.23	(-0.72,7.17)	-2.20	(-6.33,1.93)
	S3-S1	0.46	(-2.02,2.95)	7.75'	(2.78,2.72)	0.80	(-2.97,4.57)
GH	S2-S1	2.72' *	(0.47,4.97)	1.20	(-2.21,4.62)	-3.87'	(-7.28,-0.46)
	S3-S1	1.82	(-0.27,3.91)	-0.42	(-3.84,3.00)	1.48	(-1.03,3.98)
EN	S2-S1	4.68'	(1.75,7.61)	3.63	(-0.01,7.27)	-0.36	(-4.34,3.62)
	S3-S1	2.92	(-0.19,6.03)	1.94	(-4.15,8.03)	-1.01	(-5.69,3.67)
SF	S2-S1	2.03	(-1.53,5.59)	2.78	(-1.44,6.99)	0.40	(-6.30,7.10)
	S3-S1	1.46	(-1.58,4.45)	-2.14	(-7.99,3.72)	2.22	(-2.74,7.18)
RE	S2-S1	3.52	(-0.69,7.74)	1.29	(-5.59,8.17)	0.00	(-7.35,7.35)
	S3-S1	2.17	(-2.02,6.36)	-2.38	(-10.03,5.27)	6.19'	(1.04,11.34)
EM	S2-S1	4.88	(2.67,7.09)	2.94	(0.01,5.87)	2.52	(-0.48,5.52)
	S3-S1	3.00	(0.14,5.87)	2.35	(-1.19,5.89)	2.98'	(0.99,4.97)
Physical	S2-S1	-0.99	(-3.46,1.48)	1.95	(-1.08,4.98)	-2.81	(-6.29,0.67)
	S3-S1	1.16	(-0.74,3.05)	2.86	(-0.88,6.61)	-1.46	(-4.57,1.65)
Mental	S2-S1	5.23'	(1.85,8.61)	2.80	(-2.34,7.95)	1.73	(-3.20,6.67)
	S3-S1	2.23	(-0.77,5.23)	-0.88	(-6.75,5.00)	4.56'	(0.51,8.61)

Table 6: SF-36 data by group and domains

Statistically significant results in bold italics;

'Denotes significantly different from baseline;

* Denotes significantly different from group C;

Physical functioning (PF); Role physical (RF); Bodily pain (BP); General health score (GH); Energy (EN); Social functioning (SF); Role emotional (RE); Emotional wellbeing (EM); Physical health; Mental health.

SF-36 mental and physical health: group A

Physical and mental aspects of health as recorded by the asthma subjects within group A are displayed in Figure 11.

Group A: Mental & Physical Outcomes

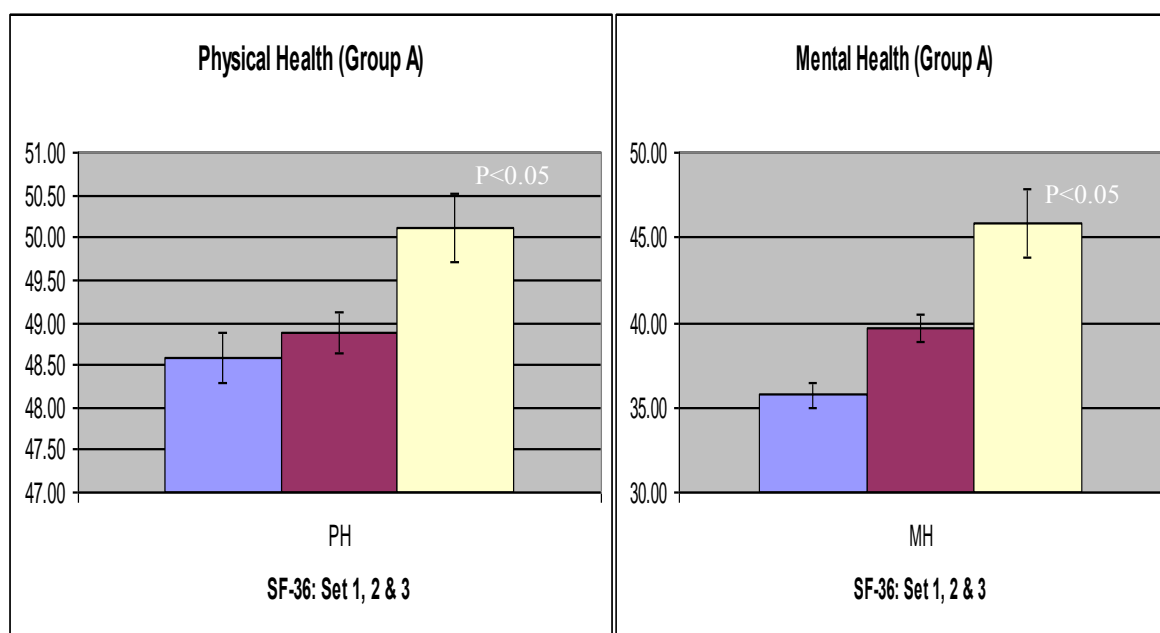


Figure 11: Group A: mental and physical health SF-36 responses

Legend: Y axis represents the scores of responses and the X axis shows the three phases of the trial; blue on the left (phase 1), purple in the middle (phase 2) and cream on the right (phase 3).

Notes for Figure 11:

There were significant improvements following chiropractic treatment and these were most notable at the final point of data collection, six weeks after the treatment phase had finished.

An improvement in self-reported physical health domains was demonstrated at the post-active treatment phase of the trial and six weeks post-completion of the data collection at 14 weeks (phase 3). The findings of physical and mental improvements as measured with the use of the SF-36 was statistically significant ($P < 0.05$).

An improvement in self-reported mental health domains was demonstrated in the post-active treatment phase of the trial and observed at six weeks post-completion treatment data collection at 14 weeks (phase 3). The findings of physical and mental improvements as measured with the use of the SF-36 was of significance ($P < 0.05$).

SF-36 mental and physical health: group B

Physical and mental aspects of health as recorded by the asthma subjects within group B are displayed in the Figure 12.

Group B: Mental & Physical Outcomes

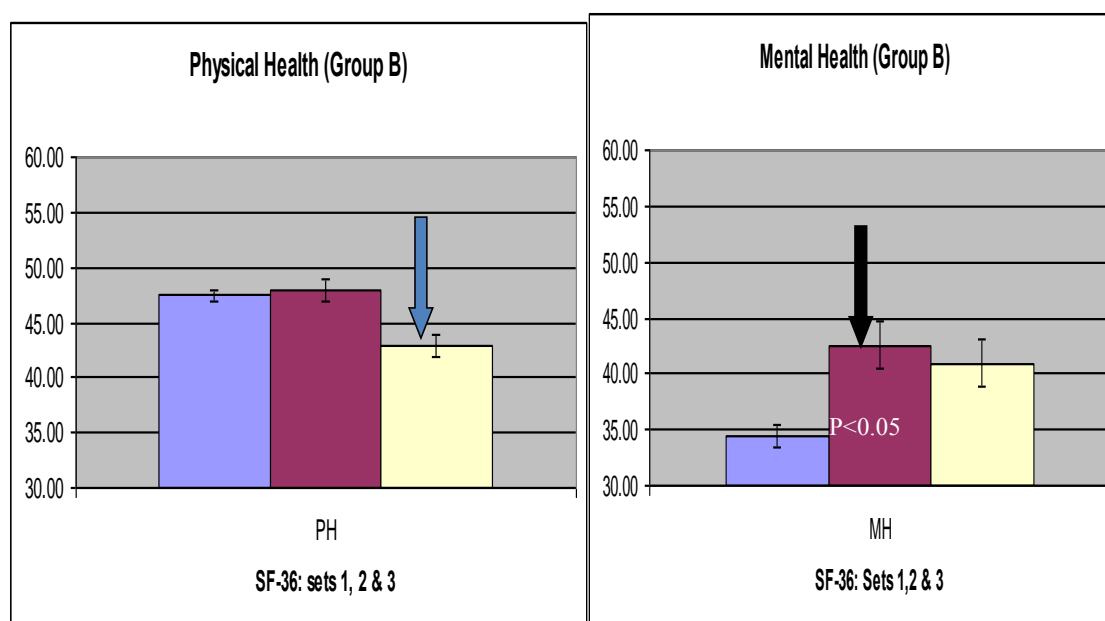


Figure 12: Group B: mental and physical health SF-36 responses

Legend: The graph on the left shows group B's physical health domain responses from the use of the SF-36 questionnaire over the three data collection points during the 14-week clinical trial, with the first at the baseline reading two weeks prior to the commencement of the active treatment (phase 1); the second at eight weeks, at-the post active treatment (phase 2) and the third at the six-week post-completion data collection, at 14 weeks (phase 3).

The graph on the right shows group B's mental health domain responses from the use of the SF-36 questionnaire over the three data collection points during the 14-week clinical trial, with the first at the baseline reading two weeks prior to the commencement of the active treatment (phase 1); the second at eight weeks, at-the post active treatment (phase 2) and the third at the six-week post-completion data collection, at 14 weeks (phase 3).

Group B demonstrated a minor improvement in self-reported physical health domain responses at the second data collection at eight weeks, at the post-active treatment (phase 2).

Group B demonstrated a decrease in the self-reported physical health domain responses at the six-week post-completion of active treatment data collection at 14 weeks (indicated in Figure 12 by a blue arrow).

Group B demonstrated improvements in self-reported mental health domain responses at the second data collection at eight weeks, at the post-active treatment (phase 2).

The finding of improved mental health domain responses, as measured with the use of the SF-36, was of significance ($P < 0.05$) in group B at the second data collection at eight weeks post-treatment (phase 2) (indicated in the graph on the right by the black arrow).

Group B demonstrated a decrease in the self-reported mental health domain responses at the six-week post-completion data collection at 14 weeks (phase 3).

The improvement of self-reported mental health was statistically significant ($P < 0.05$) following the treatment phase 2 in group B. This finding of health improvement in the group that attended the clinic but did *not* receive treatment, may indicate that there was a clinical or therapeutic encounter effect, or a Hawthorne effect, occurring for this group. Therapeutic benefits from their participation during the clinical phase may have been demonstrated in the improvements noted in the mental domains of the SF-36 in this group. Notably, at the final data collection phase 3, 14 weeks, the reported mental improvements by group B were not sustained.

SF-36 mental and physical health: group C

The SF-36 was used to measure physical and mental aspects of health as recorded by the asthma subjects in group C. The results are displayed in Figure 13.

Group C: Mental & Physical Outcomes

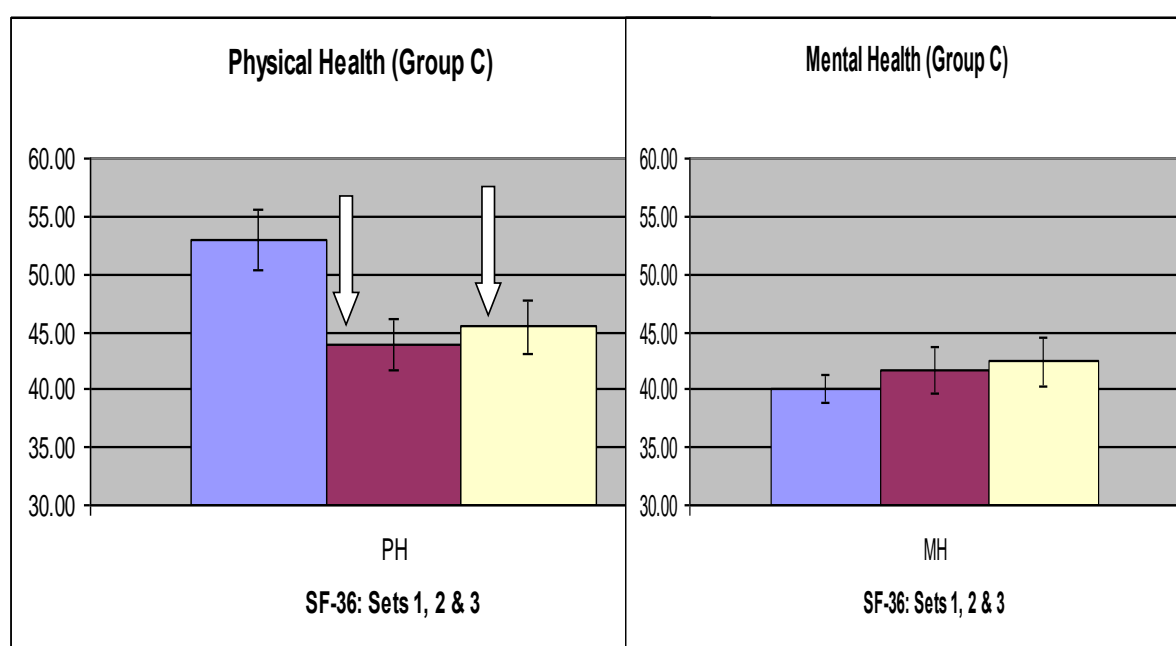


Figure 13: Group C: physical and mental health SF-36 responses

Legend: The graph on the left shows group C's physical health domain responses and the graph on the right shows group C's mental health domain responses from the use of the SF-36 questionnaire over the three data collection points during the 14-week clinical trial, with the first bar on the left in both graphs being the baseline reading two weeks prior to the commencement of the active treatment (phase 1). The second bar in both graphs refers to the data collection at eight weeks, at post-active treatment (phase 2). The third bar in both graphs represents the data collection at the six-week post-completion data collection at 14 weeks (phase 3).

Group C demonstrated a decrease in self-reported physical health domain responses at eight weeks, at the post treatment (phase 2). (See white arrows in Figure 13).

Group C then demonstrated some minor improvement again in self-reported physical health domain responses recorded at the six-week post-completion of active treatment data collection at 14 weeks (the end of the trial). (See white arrows in Figure 13).

The finding of a decrease in the self-reported physical health domain responses at the second data collection at eight weeks (phase 2) and then slight improvement at six weeks post-active treatment (phase 3) poses a question. Does the knowledge of being excluded from the active treatment phase have a physical effect? It may indicate that anticipating a treatment program, as seen in group B, may have an effect.

Group C demonstrated some improvement in their self-reported mental health domain responses at post treatment (phase 2). Group C then demonstrated a further minor improvement in mental health domain responses at the six-week post-completion of active treatment data collection at 14 weeks (phase 3).

This group was randomly allocated to be at home and were not to receive treatment until after the 14-week study was completed. There may have been a psychological effect from the randomisation as seen in group B, who did not know when their treatment would commence. The difference for group C was that they knew they were not attending the clinics. A possibility is that there was no mental anticipation occurring in this group during the 14 weeks. This may be a contributing factor in their mental domain responses then improving as the trial ended and they were aware they were to receive their promised 18 chiropractic treatments.

4.1.3 Depression Anxiety and Stress Scales: DASS

DASS: groups A, B and C

Depression, Anxiety and Stress Scales (DASS) were applied over three data collection points during the 14-week study. DASS were used to measure a locus of negative emotions in the asthma participants at two weeks pre-treatment baseline reading (phase 1); post-treatment (completion of clinic attendance) at week eight (phase 2) and at six weeks post-completion of clinical attendance at week 14 (phase 3).

Weeks	Group	0 (%)	1 (%)	2 (%)	3 (%)
0-2 weeks	A	458 (74)	127 (21)	24 (4)	7 (1)
	B	141 (72)	45 (23)	7 (4)	2 (1)
	C	151 (77)	30 (15)	6 (3)	8 (4)
3-8 weeks	A	458 (78)	107 (18)	20 (3)	2 (0)
	B	148 (71)	40 (19)	9 (4)	11(5)
	C	147 (76)	32 (16)	11 (6)	4 (2)
9-14 weeks	A	435 (78)	93 (17)	19 (3)	11(2)
	B	142 (69)	45 (22)	12 (6)	7 (3)
	C	165 (75)	38 (17)	13 (6)	5 (2)

Table 7: Distribution of anxiety by groups and phases 1, 2, 3

Weeks	Group	0 (%)	1 (%)	2 (%)	3 (%)
0-2 weeks	A	397 (71)	119 (21)	34 (6)	8 (1)
	B	150 (67)	47 (21)	17 (8)	9 (4)
	C	151 (64)	65 (27)	16 (7)	5 (2)
3-8 weeks	A	414 (70)	142 (24)	27 (5)	5 (1)
	B	161 (73)	30 (14)	17 (8)	14 (6)
	C	138 (66)	63 (30)	8 (4)	1 (0)
9-14 weeks	A	393 (64)	179 (29)	34 (6)	9 (1)
	B	147 (70)	39 (19)	18 (9)	5 (2)
	C	145 (69)	50 (24)	15 (7)	0 (0)

Table 8: Distribution of depression by groups and phases 1, 2, 3

Weeks	Group	0 (%)	1 (%)	2 (%)	3 (%)
2 weeks	A	260 (42)	277 (45)	59 (10)	18 (3)
	B	99 (44)	83 (37)	26 (12)	15 (7)
	C	123 (52)	72 (30)	32 (13)	11 (5)
3-8 weeks	A	297 (52)	218 (38)	51 (9)	6 (1)
	B	118 (53)	71 (32)	18 (8)	16 (7)
	C	105 (50)	87 (41)	14 (7)	4 (2)
9-14 weeks	A	279 (49)	217 (38)	57 (10)	21 (4)
	B	117 (56)	67 (32)	15 (7)	11 (5)
	C	113 (54)	74 (35)	21 (10)	2 (1)

Table 9: Distribution of stress by groups and phases 1, 2, 3

Notes for Tables 7-9:

Tables 6-8 show the distribution of the DASS scales for each treatment and session. The ordinal scale is skewed toward lower scale ($y=0, 1$).

Anxiety

There was no significant difference in anxiety level between groups A and B and the baseline as shown in Table 7. However, group C has significantly higher proportion of very bad response ($y=3$) compared to group A.

In the second session (3-8 weeks), proportions of very bad response ($y=3$) are significantly higher among group B and C compared to group A.

Despite the fact that the proportions of very good response ($y=0$) among group A compare to groups B and C are not significant, it may be noted that the proportions of 'very good response' are higher among group A at the second session. In the third session, this proportion is significantly lower among group B.

In addition, the proportion of 'bad response ($y=2$)' is lower among group A after second session, whereas it is higher at the baseline.

From baseline to the third session, it seems that the proportion of patients with anxiety problems decreased among group A.

Depression

There was no significant difference in depression level between groups A and B, and A and C at baseline as shown in Table 8.

In the second session, proportion of good response ($y=1$) is significantly higher among group A compared to group B. For the proportion of very bad response, group A is significantly lower than group B.

In the third session, the proportion of good response is still significantly higher among group A than group B.

It seems that the proportion of patients with depression problems increased among group B after second session, with lesser extent in the third session.

For group C, no trend can be seen.

Stress

As shown in Table 9, there was significant differences in stress level between groups A and B, and A and C at baseline, with higher proportion of very bad response among group B compared to group A. For group C, lower proportion of good response and higher proportion of very good response compared to group A.

In the second session, the proportion of very bad response among group B is still higher compare to group A, with more extent compare to the baseline.

For group C, no trend can be seen.

Figure 14 looks at the scaling responses of asthma groups A, B and C to DASS. This graph shows the baseline readings at two weeks (phase 1) and at six weeks post-completion of treatment at 14 weeks (phase 3) of groups A, B and C.

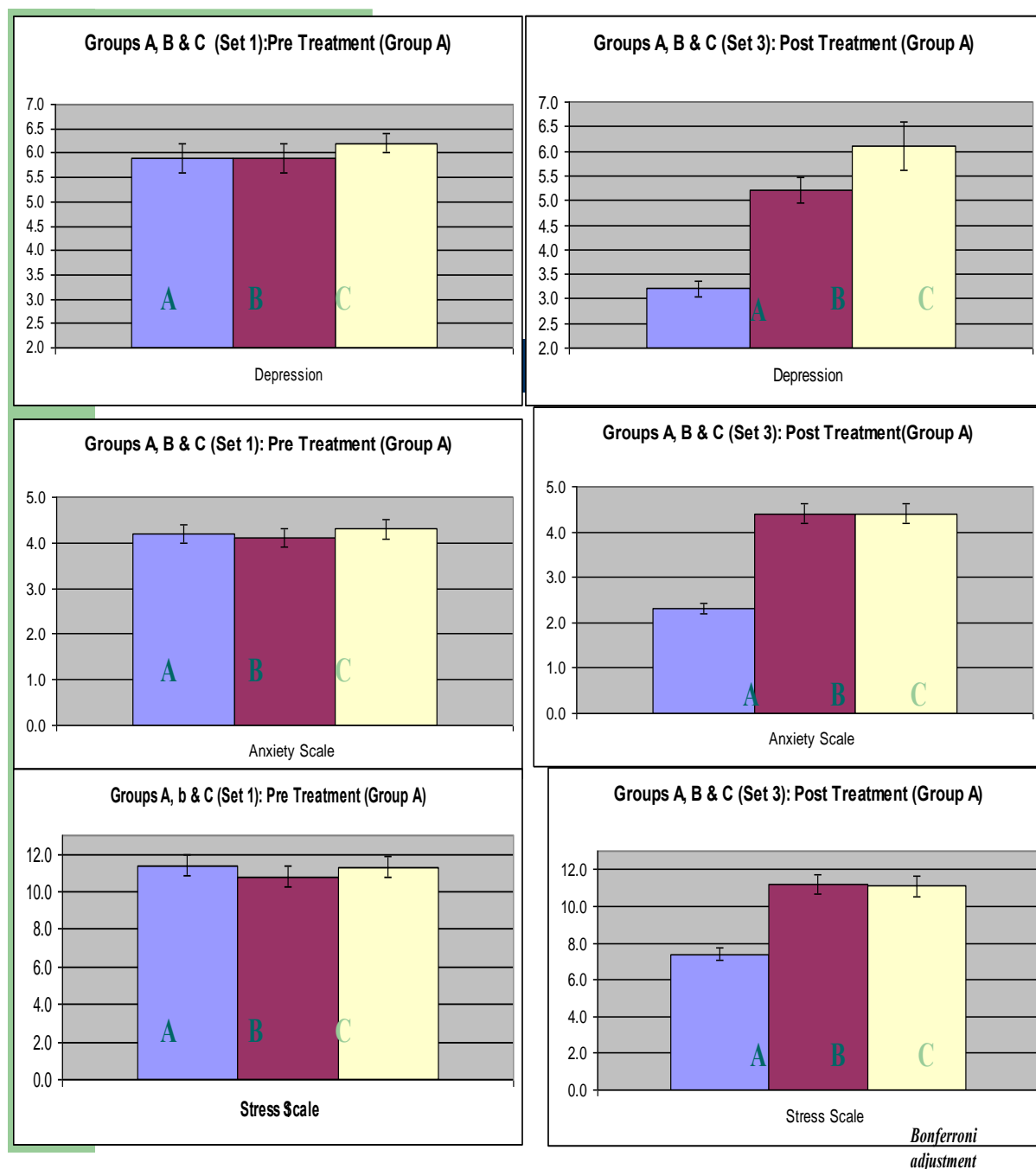


Figure14: DASS three groups

Legend: Graphs in Figure 14 are to be viewed as the three scales of emotions. Top to bottom are Depression, Anxiety and Stress.

Left graph shows A (blue) B (purple) and C (cream) at the baseline.

Right graph shows A (blue) B (purple) and C (cream) at six weeks post-treatment data collection at 14 weeks.

Notes for Figure 14:

These six graphs show the results of the DASS scales of depression, anxiety and stress across the three asthma participant groups. There was a significant improvement in these three negative emotions for the asthma participants following the chiropractic treatments and that this was most notable at the final point of data collection, 6 weeks after the treatment phase had finished.

Group A demonstrated a decrease in the self-reported scaling of the negative emotion of depression at the conclusion of the trial, at six weeks post-completion of treatment. This group also demonstrated a decrease in self-reported scaling of the negative emotions of anxiety and stress at the final data collection of the trial.

Group B demonstrated a decrease in self-reported scaling of the negative emotion of depression at the conclusion of the trial, at six weeks post-completion of treatment. This group also demonstrated a small increase in their self-reported scaling of the negative emotion of anxiety at the conclusion of the trial, at six weeks post-completion of treatment.

Group B did not demonstrate any change in their self-reported scaling of the negative emotion of stress at the conclusion of the trial, at six weeks post-completion of treatment.

Group C demonstrated no change in their self-reported scaling of the emotions of depression, anxiety and stress at the conclusion of the trial, at six weeks post-completion of treatment.

It is to be noted that in group B, the depression scale decreased at the conclusion of the trial, observed at the six weeks post-completion data collection point of 14 weeks. This may be due to some beneficial placebo effect of no longer anticipating treatment. In group B, there was no change observed in all the three scales of DASS, as a locus of negative emotion, so it is not clear what this finding may mean for the asthma participants who attended the clinics but did not receive treatment. Why the depression scale was noted separately as having improved is unclear.

The asthma subjects in group A showed improvements in the DASS scaling as a locus of negative emotion during the clinical trial. The changes in group A across the three negative emotions indicate that a therapeutic benefit was occurring in their experience of negative emotion with the series of 18 chiropractic treatments.

DASS demonstrated that participants in group A, at the end of the 14-week trial had received a therapeutic benefit from a series of 18 chiropractic treatments. This benefit was clinically significant as measured by changes of the locus of negative emotions known to be associated with asthma. Figure 15 shows the overall changes across the three scales of DASS that were statistically significant ($P < 0.05$).

4.2 Peak Expiratory Flow (PEF) monitoring

Peak Expiratory Flow scores from each asthma participant were collated and tabled for that individual. Scores were also pooled together by group to demonstrate group performance (groups A, B, C and D).

4.2.1 PEF scores for groups A, B and C (phase 1)

Baseline scores for groups A, B and C were determined in the first two weeks of the trial (phase 1).

The homogeneity of PEF scores from all asthma participants across the three groups at the start of the trial was assessed. Group comparisons were also determined at the baseline data collection, pre-trial, to find a pre-treatment level before the clinical phase commenced. Average PEF scores from groups A, B and C are presented. (A two-way ANOVA was performed to determine differences of mean scores across the three groups; see Table 10).

Comparison: Time

Group	Size	Mean	SE	StDev	Mean	SE	StDev
A	209	377.407	8.047	109.785	378.441	9.068	78.167
B	176	376.974	13.344	107.679	377.292	9.068	101.839
C	104	368.654	11.407	133.924	366.343	9.068	96.183

Peak flow

Adjusted for subject id

Two-way ANOVA: Residual SS: 3001606.881 r-sq: 0.43 13 missing

Factor	df	F	p-val	s	Rms	CI/2	Lev p	Bart p
Group	2/386	0.210	0.8104	116.333	8.220	31.139	0.128	0.036
Subject id+	35,351	7.414	0.0000	92.475				
Group +	2,351	0.528	0.5903	92.475	11.251	24.762	0.000	0.036

Table 10: Results of the two-way ANOVA performed at baseline collection of PEF scores (0-2 weeks) for asthma groups A, B and C

There was no difference of significance between the three groups (A, B and C) and the integrity of the data collected was assessed on a normal score plot (see Figure 16).

Confidence limits displayed on this plot are only approximate and represent the similarities in this data set observed at the start of the trial. The confidence observed in randomly allocated asthma participants of the three groups (A, B and C) was that they were all of similar score at the start of the trial.

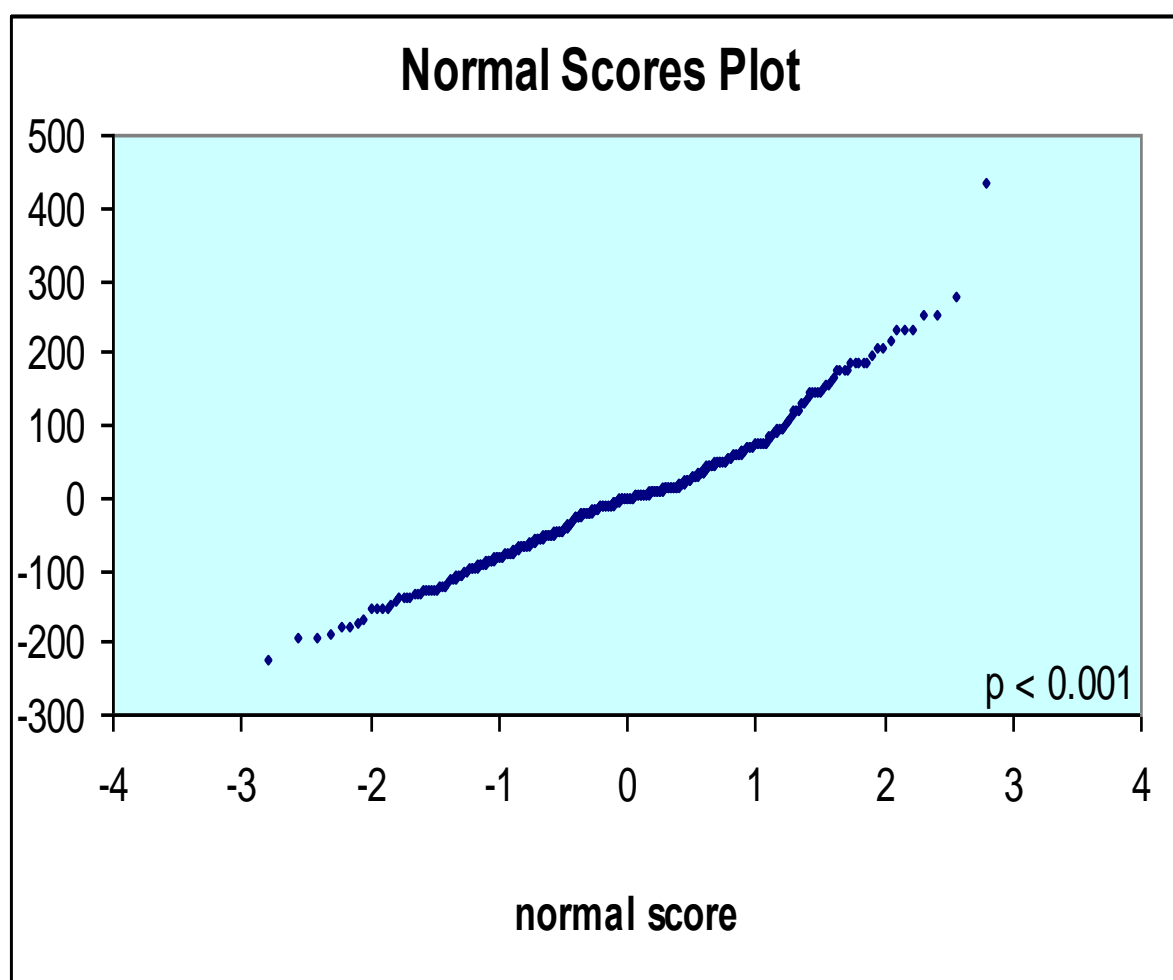


Figure 16: Normal scores plot of groups A, B and C at weeks 0-2 (baseline PEF scores)

No statistically significant differences in the PEF average scores were observed between the asthma groups at the start of the trial; observed as litres per minute (L/min) PEF readings (refer Figure 17).

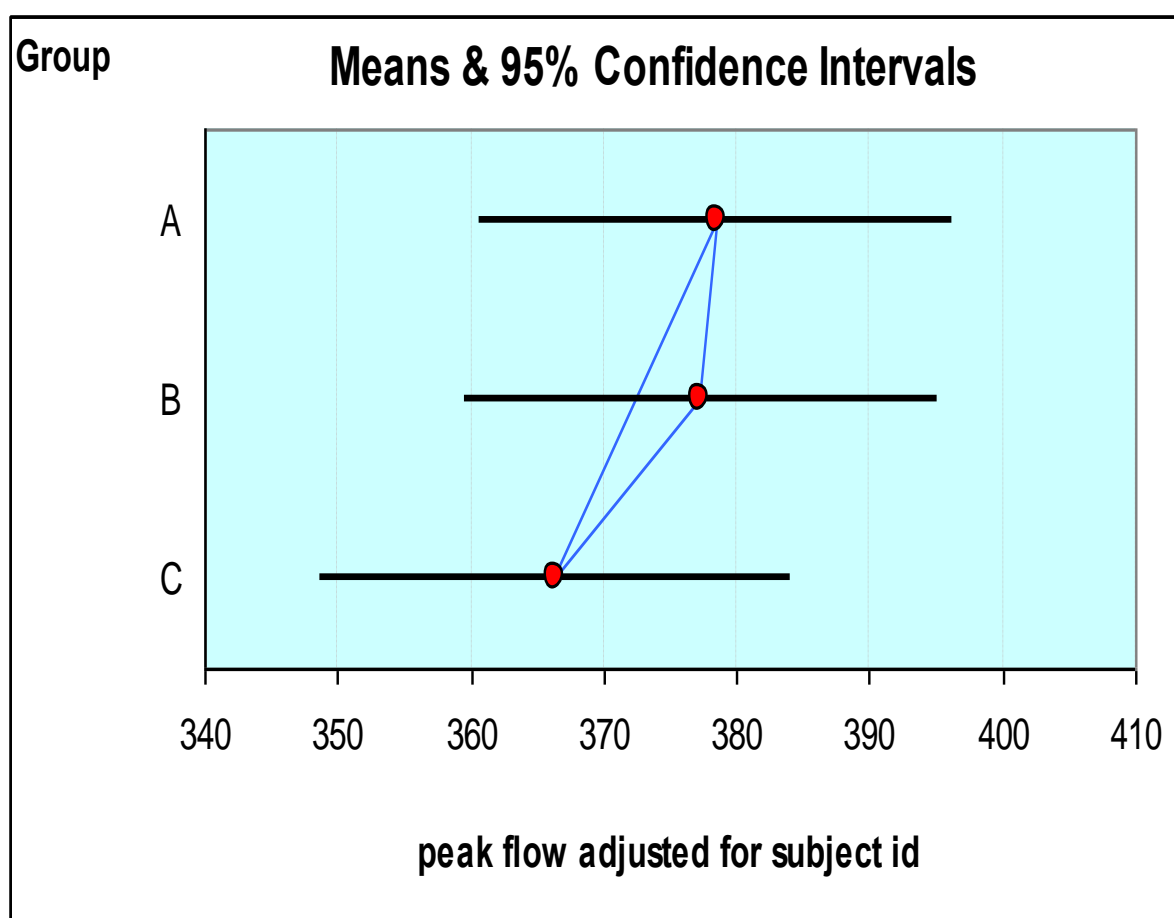


Figure 17: Baseline recordings for asthma participant groups A, B and C

Notes for Figure 17:

Baseline recordings of PEF scores (0-2 weeks) showed no significance difference between groups

4.2.2 PEF scores for groups A, B and C (phase 2)

Group comparisons were determined during phase 2 of the trial for the six weeks of treatment during weeks three to eight. Average PEF scores from groups A, B and C are presented here. A two-way ANOVA was performed to determine the differences in means across the three groups (Table 11), together with a normal scores plot (Figure 18).

Comparison: Time								
Group	Size	Mean	SE	StDev	Mean	SE	StDev	
A	629	385.184	4.549	108.249	383.622	5.214	73.275	
B	231	377.532	7.507	122.070	383.598	5.214	114.408	
C	297	381.970	6.620	119.623	380.560	5.214	94.653	
Peak flow				Adjusted for subject id				
Two-way ANOVA:				Residual SS: 9034300.394	r-sq: 0.40	49 missing		
Factor	df	F	p-val	s	rms	CI/2	Lev p	Bart p
Group	2/1154	0.391	0.1762	114.092	6.389	17.698	0.053	0.032
subject id+	351,119	21.220	0.0000	89.853				
Group +	21,119	0.085	0.9184	89.853	2.873	13.939	0.000	0.032

Table 11: Results of the two-way ANOVA for PEF scores for asthma groups A, B and C during phase 2 of the trial: 3-8 weeks

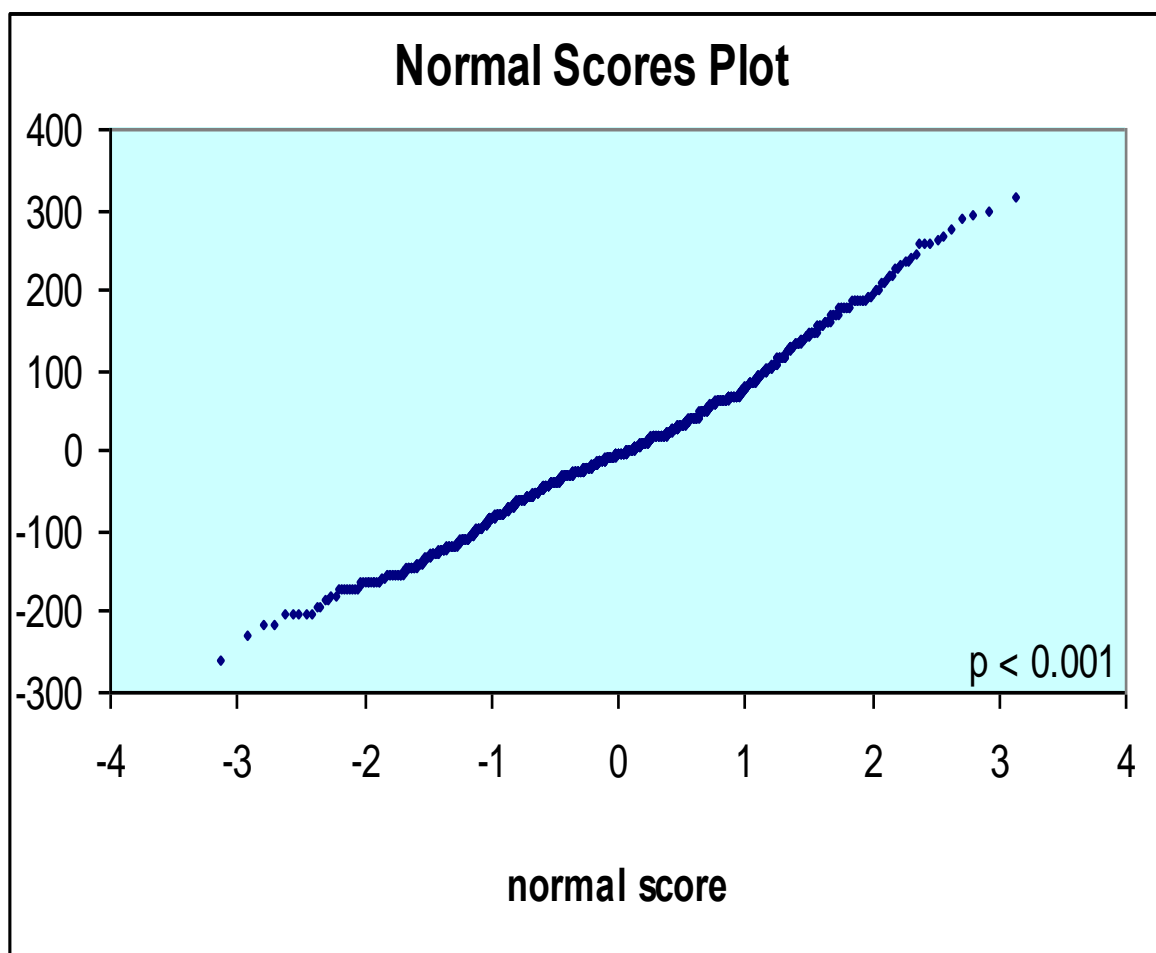


Figure 18: Normal scores plot of PEF scores for groups A, B and C at 3-8 weeks

The pattern of PEF scores observed during this period demonstrates no statistical differences between groups A and B, or A and C (Figure 19). There is no change in the pattern of PEF scores between groups after treatment or the clinical phase (weeks 3 to 8 - phase 2).

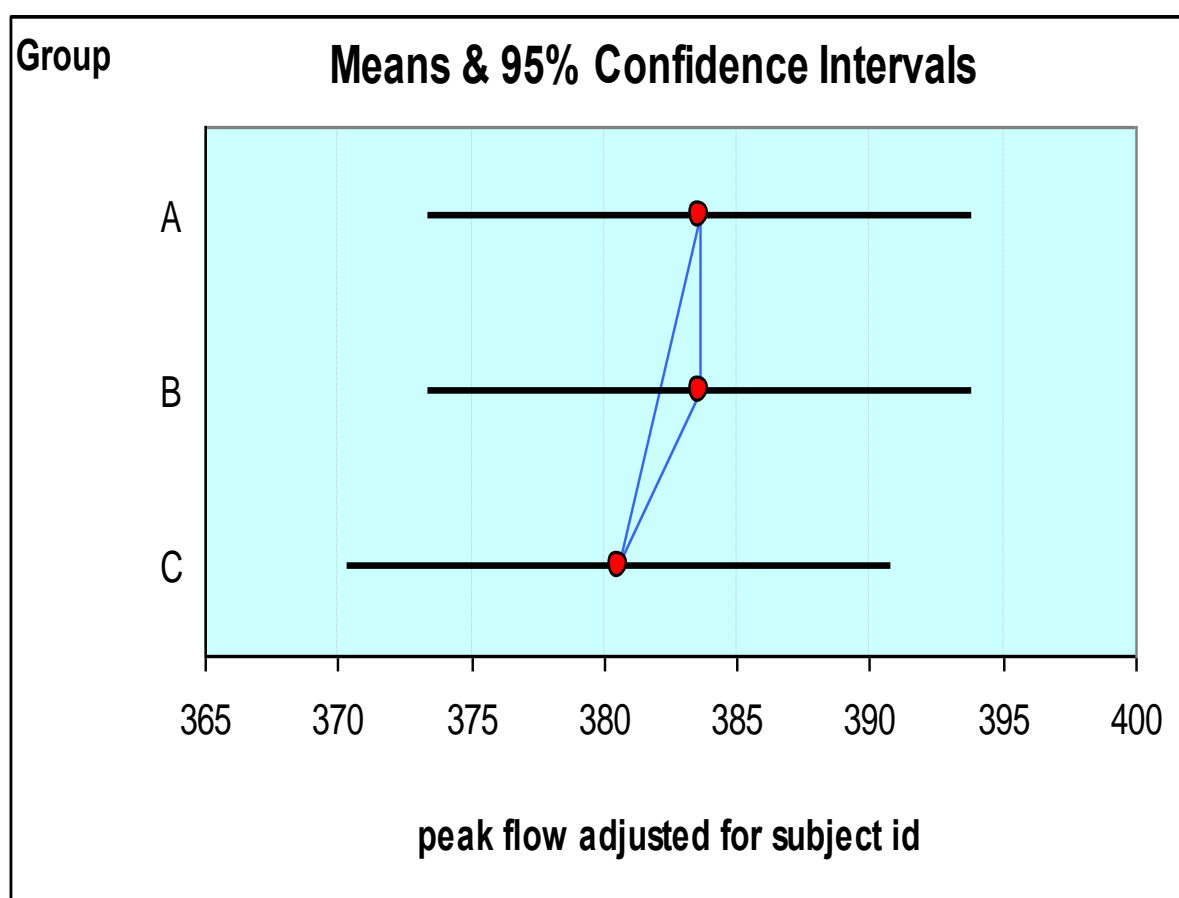


Figure 19: The mean and confidence intervals between asthma groups for PEF scores (3-8 weeks).

Note for Figure 19: No statistical difference was observed in the PEF readings at the end of the treatment phase.

4.2.3 PEF scores for groups A, B and C (phase 3)

The PEF scores for groups A, B and C were determined for the period of the study between 9-14 weeks, phase 3 of the trial. Group comparisons were determined for the six weeks of the follow-up period (phase 3). A one-way ANOVA was performed on average PEF scores for all the groups to determine differences in means across the three groups (Table 12).

Combining both am and pm average PEF scores across the 14-week period for all groups did not impact any observed patterns of the am and pm PEF scores

Comparison: PEF 9-14 weeks (-2obs)								
Group	Size	Mean	SE	StDev				
A	1092	397.047	3.724	119.801				
B	924	379.439	5.977	126.936				
C	555	381.063	5.224	126.358				
One-way Anova:			Residual SS:	31319383.82	r-sq:	0.00	41 missing	
Factor	df	F	p-val	s	rms	CI/2	Lev p	Bart p
Group	2/2068	4.767	0.0086	123.064	17.910	14.209	0.124	0.206

Table 12: Results of the one-way ANOVA for PEF scores for asthma groups A, B and C during phase 3 of the trial: 9-14 weeks of follow-up

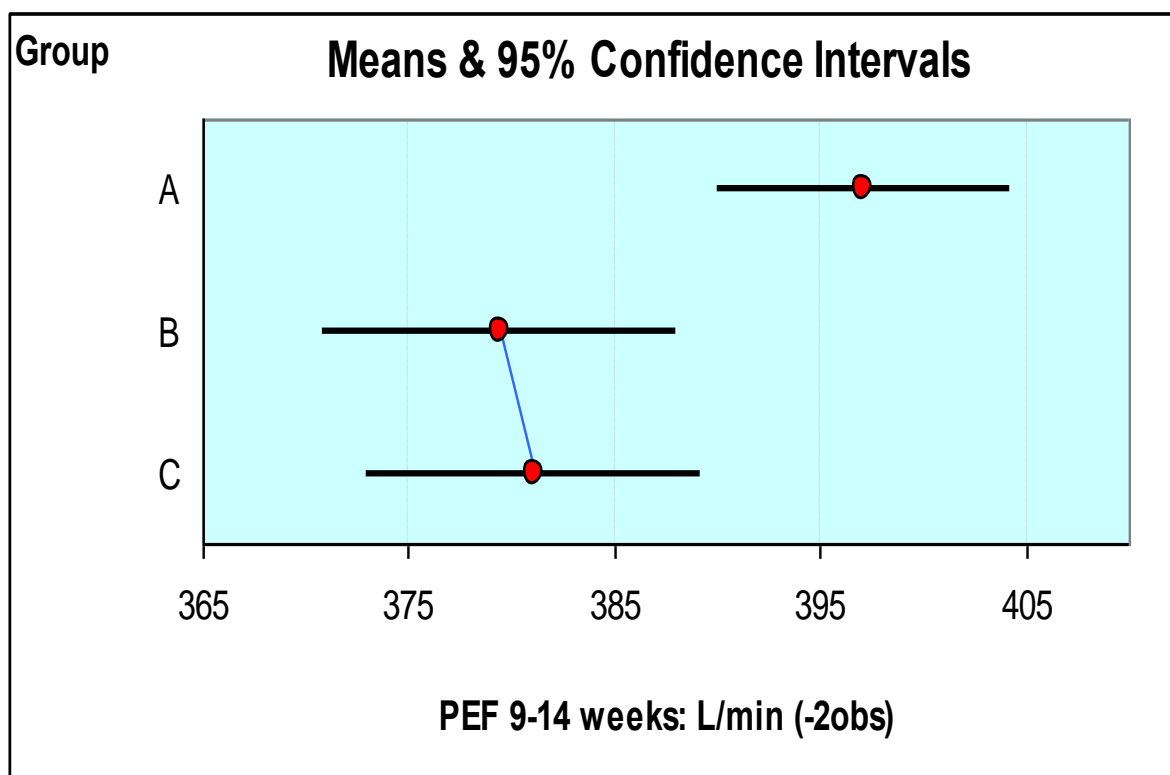


Figure 20: Mean and confidence intervals between asthma groups for their PEF scores (9-14 weeks).

Note for Figure 20: Changing PEF scores were observed at the 6 weeks post treatment data collection point; improvements in lung function for group A observed in the 6 weeks following chiropractic treatment

The overall group average performance of Peak Flow reading scores was observed to continue during the six weeks post-completion of treatment. This trend was observed as continuing at 14 weeks, the end of the trial. The pattern of overall PEF increases in group A remained significant (see Figure 20: $P < 0.008$).

The overall group average performances of both groups B and C over the full 14 weeks of study observations did not change significantly.

4.2.4 Comparison of PEF by group after fitting GEE

GEE longitudinal analysis facilitated examination of the repeated measures in the longitudinal study. PEF readings over the 14 weeks for all four groups were reviewed with GEE longitudinal analysis using generalised linear models for the line of best fit (see Figure 21).

The patterns were observed for average PEF scores, between groups A, B and C across the 14-week trial period. This pattern (see Figure 21) demonstrates an upward trend of PEF scores for asthma participants of group A, against group D performance (healthy non-asthma participant controls) in the top line of the graph as a normal range of PEF lung function. The upward trend of PEF scores by week 14 was significantly greater ($P<0.05$) in group A, than the trend of PEF scores observed for both groups B and C over the 14-week period (see Figure 21).

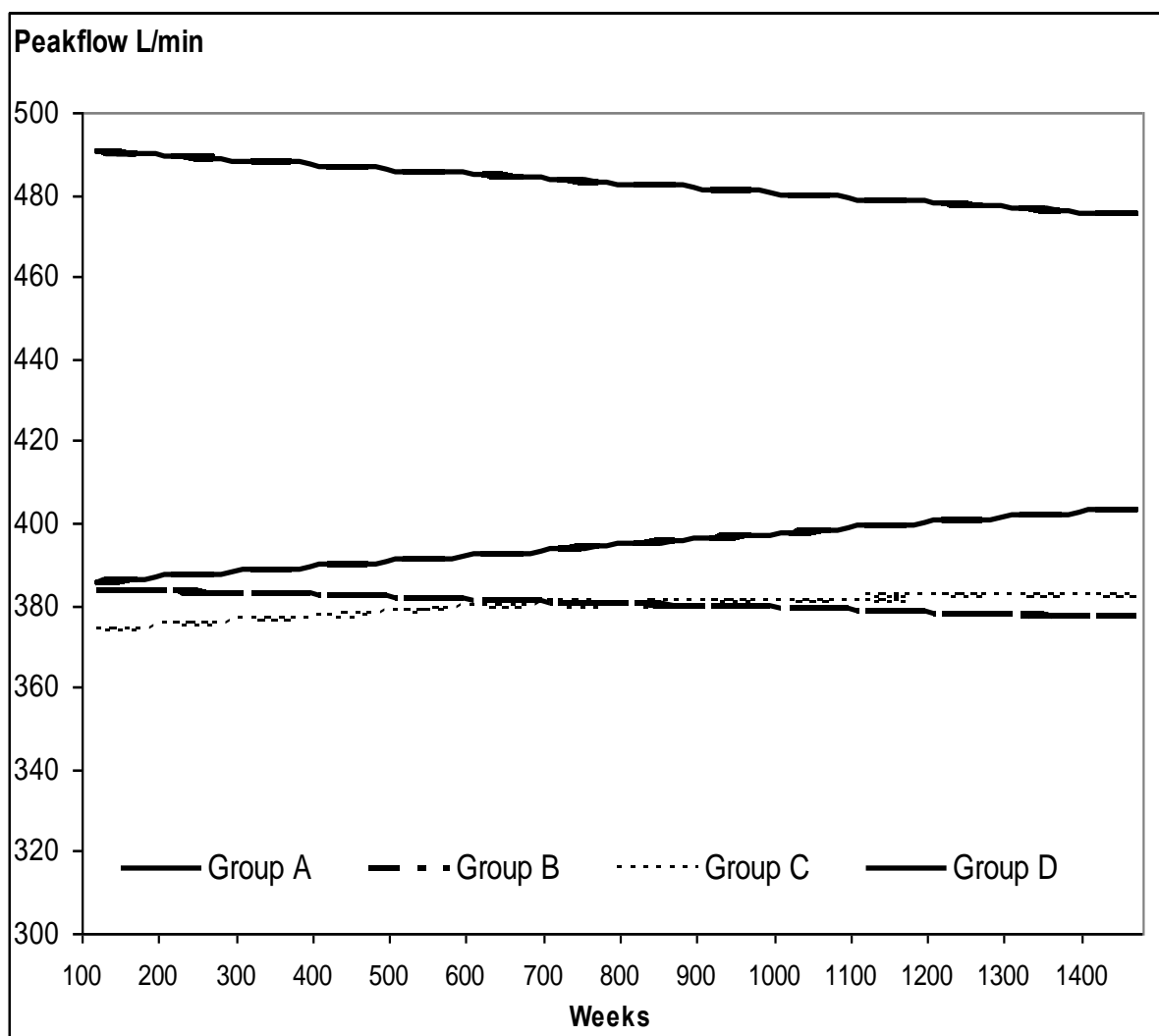


Figure 21: Comparison of PEF by group performance

Legend: x axis is the weeks of the trial represented as 100= week 1 and 1400= week 14. Y axis is the peak flow meter readings 300- 500 Litre per minute (L/min)

Note for Figure 21: Comparison of PEF by group performance, after fitting GEE. (Please note group D (non-asthma participants) is at the top of the graph and non-asthma normal PEF scores. The PEF scores of group A is represented by the solid line with an upward trend away from groups B is a semi-broken line and C is represented by a dotted line). Group A shows a trend of improvement in lung function; this is not observed in the asthma participants that did not receive chiropractic treatment.

4.2.5 PEF readings (am and pm) over 14 weeks

Am PEF scores

Average group am PEF scores were analysed for inter-group variations as well as intra-group score variations over the 14-week study. Group PEF scores were also analysed for differences in their mean across the 14-week period.

Group Average PEF scores L/min	Group A	Group B	Group C	Group D
2 weeks	377.7 (+/- 20.9)	376.996 (+/- 24.3)	371.2 (+/- 26.6)	481.9 (+/- 34.5)
3-8 weeks (phase 2)	391.3 (+/- 12.4)	379.284 (+/- 22.2)	377.2 (+/- 20.6)	482.3 (+/- 30.2)
9-14 week	405.9 (+/- 14.2)	377.632 (+/- 24.1)	383.3 (+/- 21.1)	474.1 (+/- 31.9)

Table 13 Average PEF scores for all (am readings)

Group D (the non-asthma participant group) had am readings that were approximately 100 points higher in their PEF scores than the other three asthma participant groups across the whole 14-week trial. This is an indication of a healthy range of lung function and is to be expected for the non-asthma participant group in the study.

Groups A, B and C (the asthma participant groups) had similar PEF scores at the baseline.

As compared with groups B and C, an upward trend of improved PEF scores started to emerge in group A at eight weeks. This trend continued to improve at the end of the treatment (phase 2) as well as at weeks nine to 14 for group A. This was statistically significant ($P < 0.05$) when comparing group A to groups B and C (see Table 13 for am readings).

The same upward trend of improved PEF scores can be observed when comparing intra-group performance from the baseline PEF scores at two weeks pre-trial with the 14 weeks post-trial PEF data. This improvement in lung function was significant in group A ($P < 0.05$).

The difference between the four groups is displayed below. The am PEF readings as an average of the group performance over the 14-week study clearly demonstrate the trend of peak flow and lung function improvement in group A. (See Figure 22). The data suggests a time lag of physiological activity may be occurring after the treatment phase is finished. There is a sustained improvement at 14 weeks that may indicate a period or window of measurement for this cumulative effect in the lung function as observed in these PEF readings.

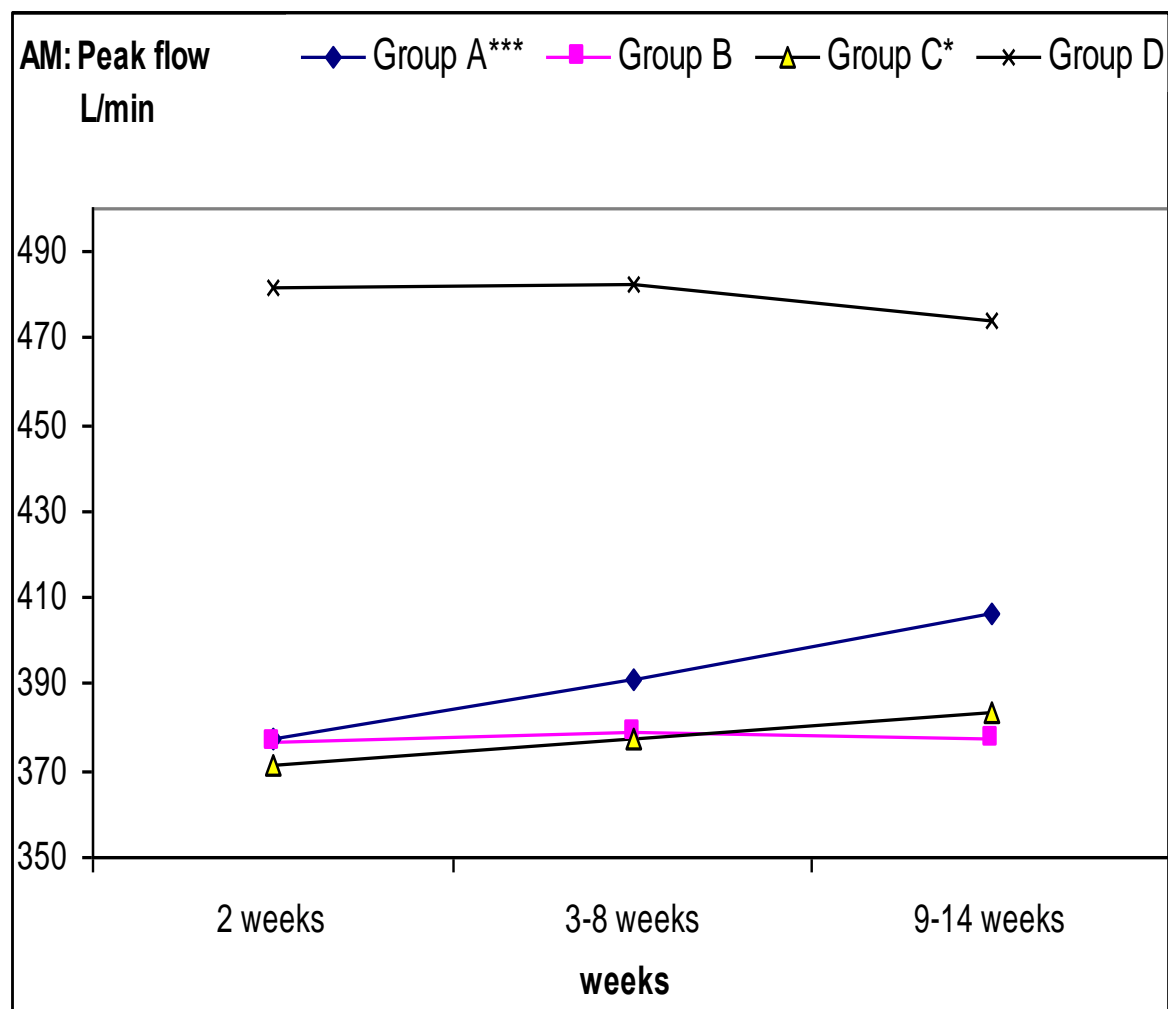


Figure 22: Am readings (average PEF in litres per minute over the 14 weeks)

Notes for Figure 2w:

Group A is represented by the blue line with the diamond shape identifier. There is a significant trend of lung function improvement observed as a continuing trend of PEF scores in group A at the completion of the 14-week study.

Pm PEF scores

Group Average pm PEF scores were analysed for inter-group variations as well as intra-group score variations over the 14-week study. Group PEF scores were also analysed for differences in their mean across the 14-week period.

Group Average PEF scores L/min	Group A	Group B	Group C	Group D
2 weeks	382.1 (+/- 21.9)	381.1 (+/- 28.2)	373.9 (+/- 32.3)	485.4 (+/- 38.3)
3-8 weeks	395.4 (+/- 18.3)	383.4 (+/- 31.9)	382.0 (+/- 29.2)	493.0 (+/- 36.1)
(phase 2)				
9-14 weeks	409.0 (+/- 14.6)	377.7 (+/- 32.4)	386.0 (+/- 31.1)	480.9 (+/- 35.2)

Table 14: pm readings in PEF scores for groups A B C and D

Group D (the non-asthma participant group) had pm readings that were approximately 100 points higher than those of the other three asthma participant groups across the whole 14-week trial. This is an indication of a healthy range of lung function and is to be expected for the non-asthma participant group in the study.

At the baseline data collection of pm PEF readings at two weeks (phase 1), all asthma groups (A, B and C) had similar PEF scores. As compared to group B and C, an upward trend of improved pm PEF scores started to emerge in group A at 8 weeks. the end of week eight (phase 2) that continued between weeks 9 to 14, during the six week post treatment period for group A when compared to group B and C. This was statistically significant ($P < 0.05$). (see Figure 23). The data suggests a time lag of physiological activity may be occurring after the treatment phase is finished. There is a sustained improvement at 14 weeks that may indicate a period or window of measurement for this cumulative effect in the lung function as observed in these PEF readings.

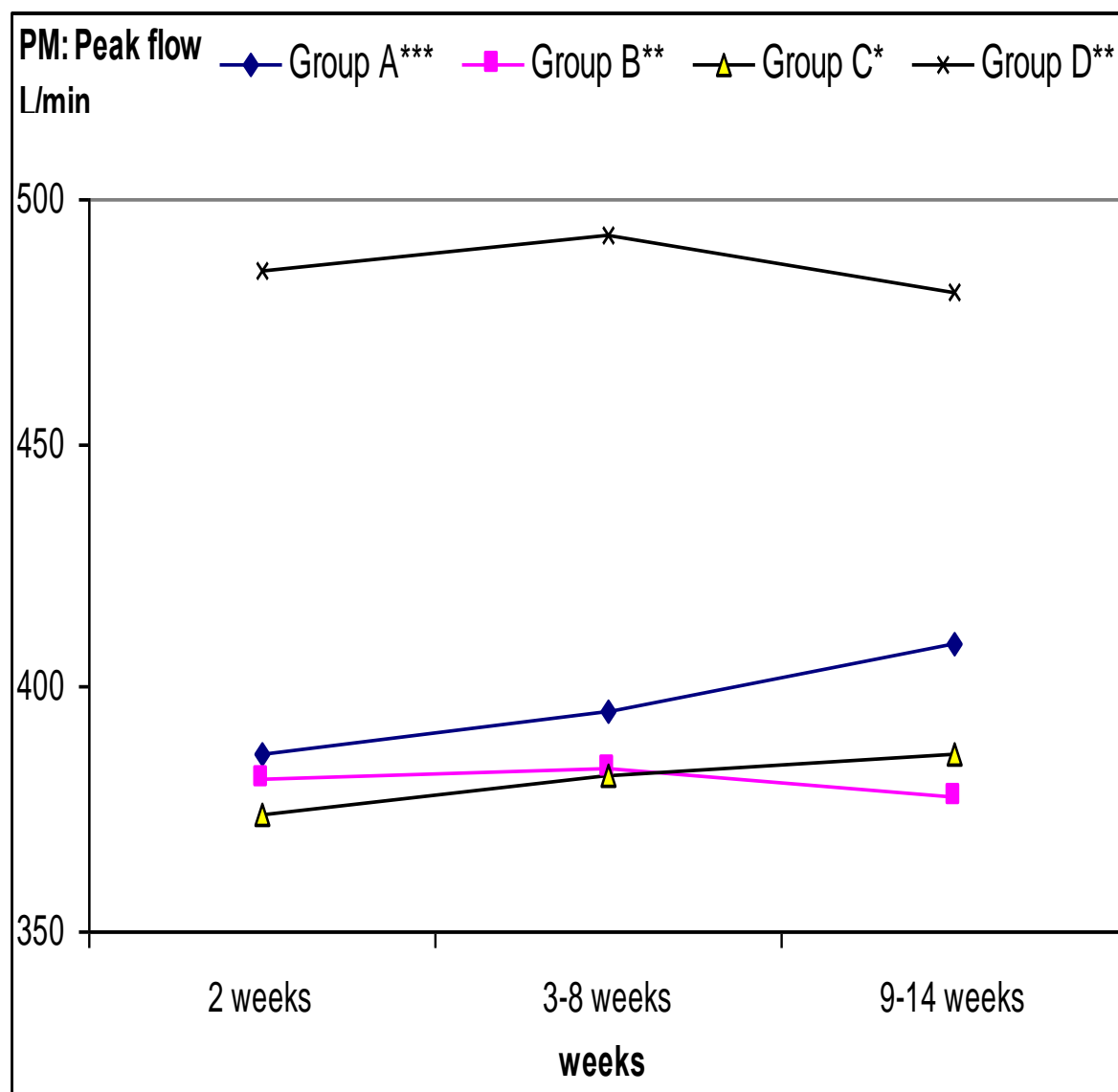


Figure 23: Pm readings (PEF average readings in L/min over the 14 weeks)

Notes for Figure 23:

Group A is represented by the blue line with the diamond shape identifier. This trend of pm readings is similar to the am readings.

4.2.6 PEF readings (averaged of am and pm scores) for groups A, B and C

The PEF readings of both am and pm scores were also averaged and analysed. These readings are displayed as a graph of the three groups of asthma participants across the 14-week study period (see Figure 24).

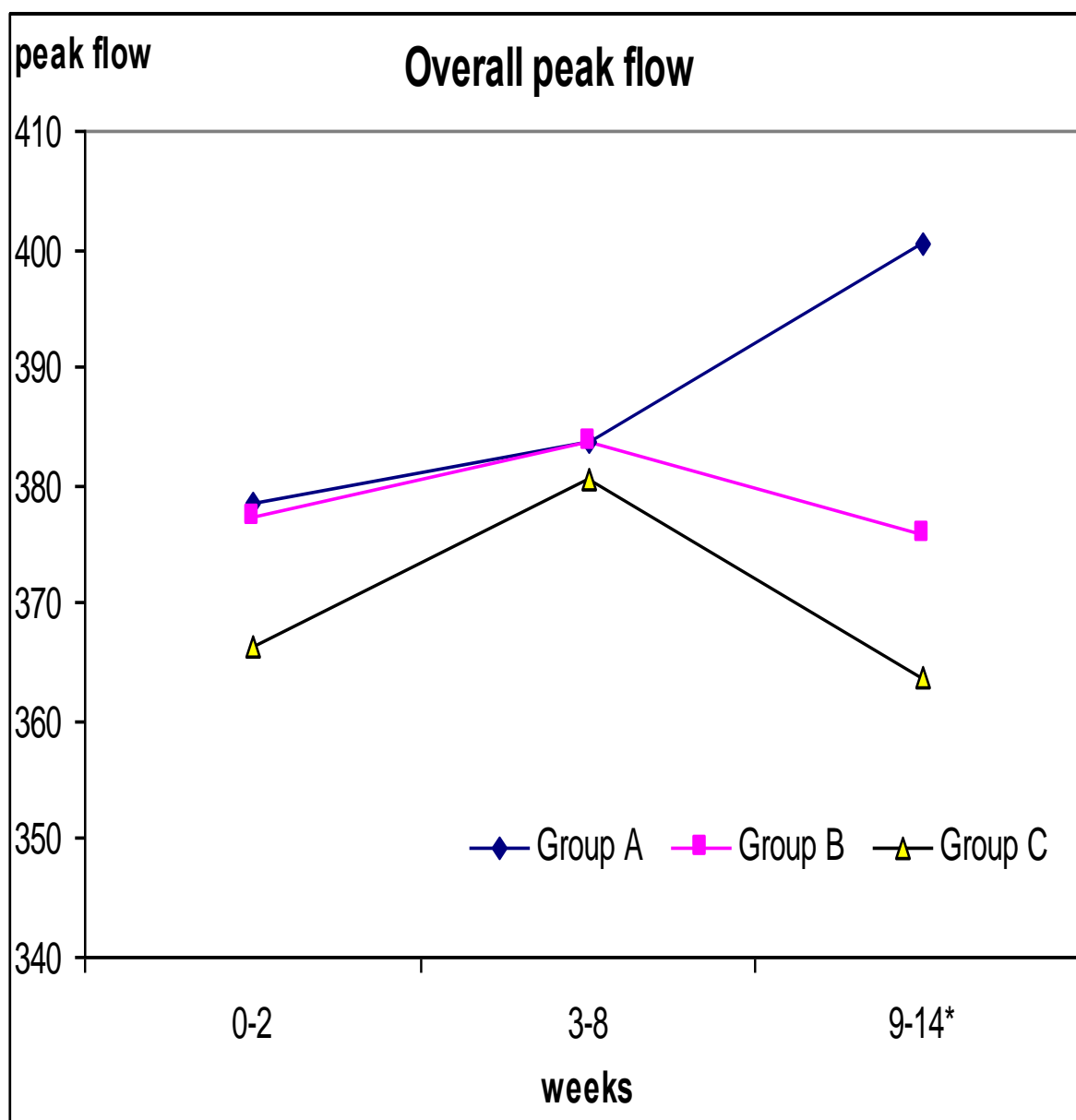


Figure 24: Average PEF readings for the three asthma groups across the 14-week study period

Notes for Figure 24: Group A is represented by the blue line with the diamond shape identifier. There is a continuing trend for group A of PEF scores at the completion of the 14 weeks as noted by the * at the 14 weeks data collection point.

Figure 24 shows that groups B and C demonstrated similar PEF scores across the 14 weeks. There was a decrease in their PEF scores during the clinical phase (phase 3) that continued into the post-treatment six-week period. The observation of an upward trend of improving PEF scores in group A was the same as that observed for their am and pm PEF scores. This improvement in the lung function of group A across the time period of 14 weeks was a significant finding ($P<0.05$).

4.3 Physiological markers of health change

4.3.1 Immune response in asthma: IgA

Baseline readings of IgA levels for all asthma participant groups were captured in phase 1, during the first two weeks of the 14-week study. These baseline readings were assessed using a one way ANOVA for group differences (homogeneity across asthma groups).

IgA levels: post-treatment, eight weeks (phase 2)

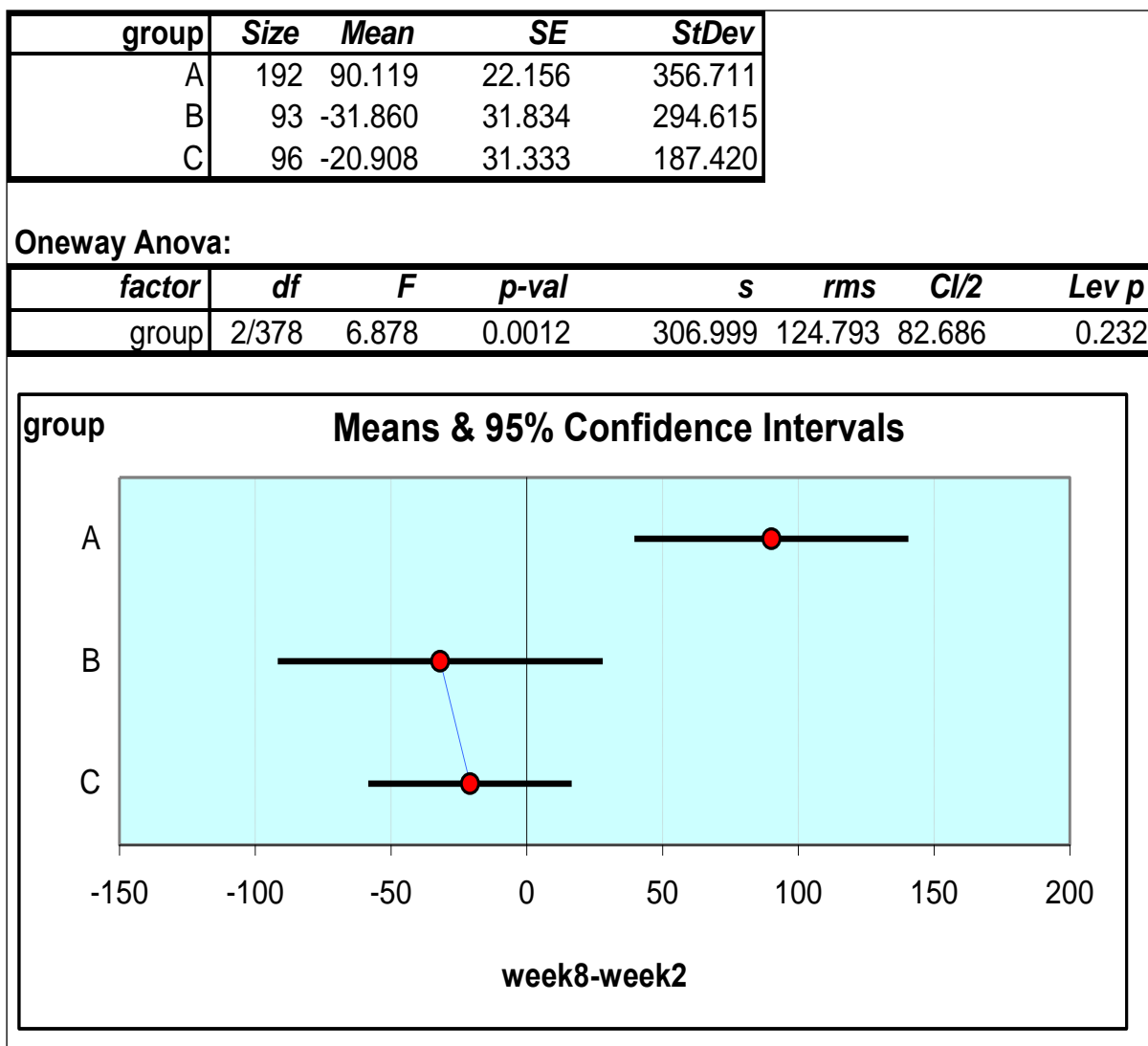


Figure 25: Differences between groups A, B and C, at eight weeks; comparing baseline readings (phase 1) with post-treatment readings at eight weeks (phase 2)

Legend: IgA levels are indicated on the X axis (-150/ +200). The groups of asthma subjects are displayed on the Y axis. The heavy horizontal black line shows the range of IgA in each group with a mean score indicated by the red dot on the line.

Notes for Figure 25:

An increase in IgA level is seen in group A at the end of the treatment (phase 2)

Baseline readings of the asthma participants had shown homogeneity across the groups. There were differences in IgA levels between the asthma participant groups A, B and C, when baseline readings (phase 1) were compared with post-treatment readings at eight weeks (phase 2). In the clinical phase where group A was receiving the 18 chiropractic treatments, the mean level of IgA increased by 90 for group A ; higher than that observed in groups B and C.

IgA levels: six weeks post-completion of treatment (phase 3)

Figure 26 shows the differences between groups A, B and C, comparing baseline readings (phase 1) with the six weeks post-treatment readings at 14 weeks (phase 3).

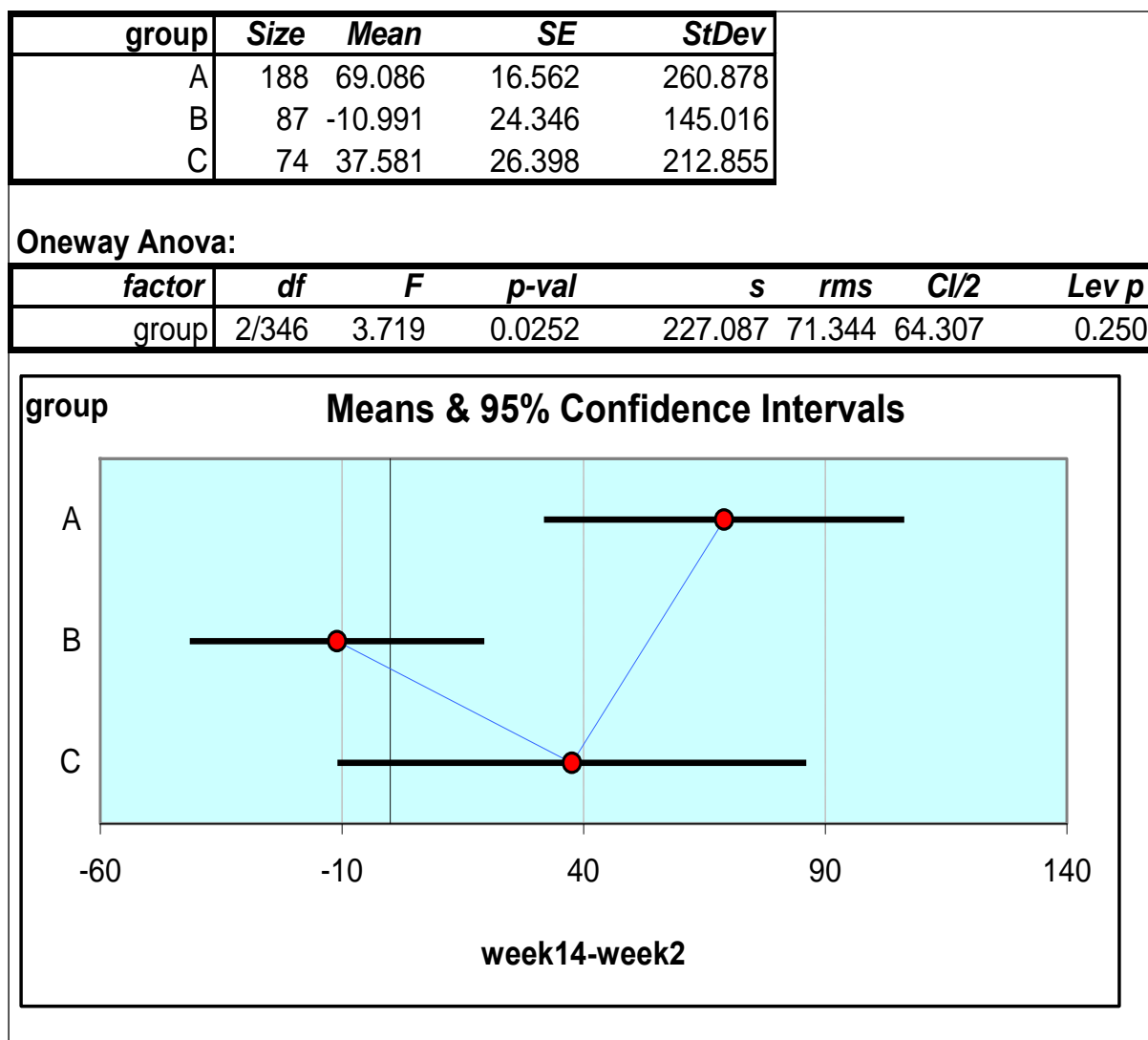


Figure 26: IgA levels measured from levels at 2 weeks prior to the treatment (phase 1) and six weeks post treatment phase at 14 weeks data collection (phase 3)

Legend: IgA levels are indicated across the bottom of the graph (-60/ +140). The groups of asthma subjects are displayed on the left-hand side. The heavy horizontal black line shows the range of IgA in each group with a mean score indicated by the red dot on the line.

Notes for Figure 26: An increase in IgA level seen in group A.

Group A's mean IgA levels at 14 weeks had increased by 69, as compared to the baseline readings.

Group B's mean IgA levels decreased by -10.991 from the baseline readings to the 14-week post-completion data collection.

Group C's mean IgA levels increased by 37.581 from the baseline readings to the 14-week post-completion data collection.

IgA levels: percentage changes of groups over three periods of data collection

	% Change between	% Change between	% Change between
Groups	2 to 8 Wks	8 to 14 Wks	2 to 14 Wks
A	57.89	65.79	60.53
B	17.65	41.18	35.29
C	22.22	16.67	22.22
D	50	25	25

Summary for IgA % decrease in subjects from:

groups	2 to 8 Wks /%	8 to 14 Wks /%	2 to 14 Wks /%
A	42.11	34.21	39.47
B	82.35	58.82	64.71
C	77.78	83.33	77.78
D	50.00	75.00	75.00

Table 15: IgA percentage changes of groups A B C and D

Legend: IgA percentage (%) changes over three periods of the study data collection, from left to right: from baseline readings at two weeks (phase 1) to post-treatment at eight weeks (phase 2); from post-treatment at eight weeks (phase 2) to 14 weeks post-completion (phase 3); from baseline readings at two weeks (phase 1) to 14 weeks post-completion (phase 3).

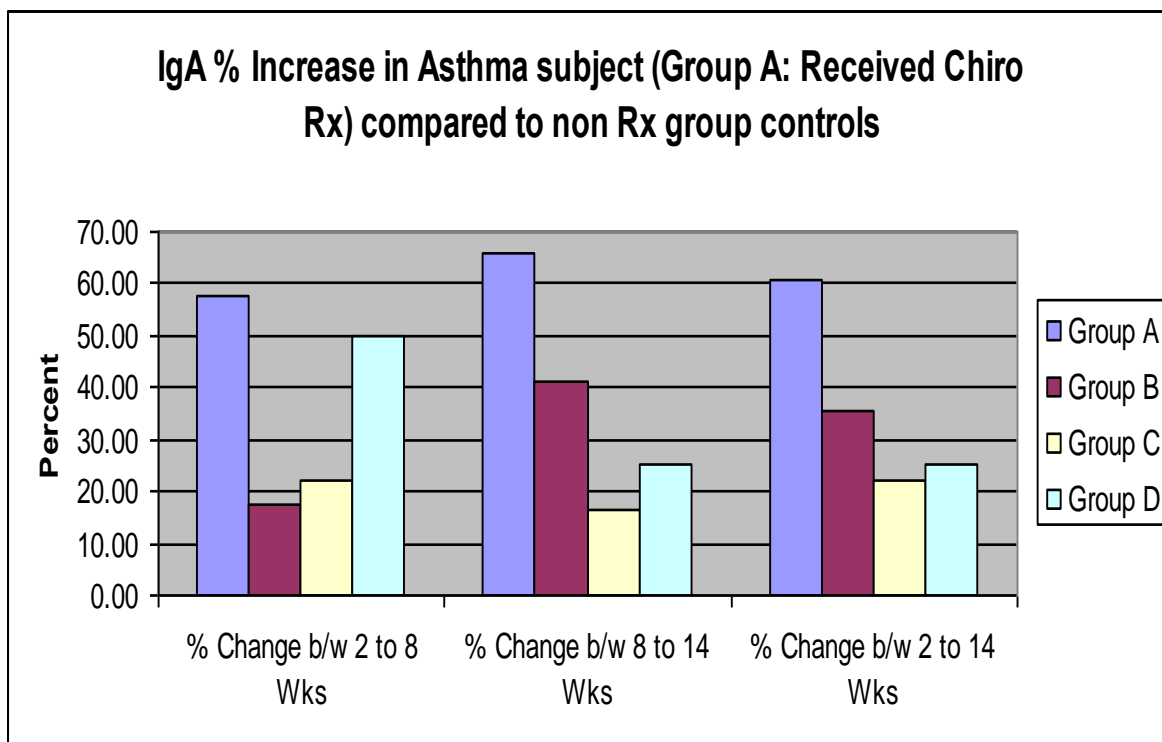


Figure 27: IgA across three periods of data collection

Legend: There are three sets of four bars representing the three data time review periods. In each of the three sets, IgA% changes for groups A B C and D are shown. Moving across from the left, the blue bars on the left of each time review period, is the IgA levels of group A. then the brown bar is group B, the cream bar is group C and the pale blue bar is group D.

Notes Figure 27: An increase in IgA % changes for group A is observed for each time period of analysis.

IgA percentage change between baseline, (phase 1) and week eight (phase 2)

See Figure 27 (first set of four bars groups ABCD)

Group A demonstrated an increase in IgA levels from the baseline readings to after the treatment or clinical phase at eight weeks (phase 2) data collection of 57.89 where group B showed a percentage change of 17.65 over this phase of clinical attendance.

IgA percentage change between week eight, (phase 2) and week 14 (phase 3)

See Figure 27 (second set of four bars groups ABCD)

Group A demonstrated an increase in IgA levels of 65.79 as a percentage change between week eight, (phase 2) and week 14 (phase 3). Group B was also showed an increase in IgA as a percentage change of 41.18 between week eight, (phase 2) and week 14 (phase 3).

The difference in the percentage change increase between group A and group B lessened during this six-week period, following completion of the clinical phase (phase 2). It was during the six weeks post-treatment period that a noteworthy percentage increase in IgA levels was observed for group B. Group B demonstrated an increase in its percentage change of IgA levels in this period more than other data collection periods. Of note, there had been no observed increase in IgA levels as a percentage change for group B between the baseline (phase 1) and week eight (phase 2) which was from the data collection following treatment or clinical attendance phase.

IgA percentage change between baseline recordings week two (phase 1) and week 14 (phase 3)

See Figure 27 (third set of four bars groups ABCD)

There was an increase in IgA for both groups A and B between baseline recordings (phase 1) and week 14 (phase 3) with an IgA increase percentage of 60.53 in group A and of 35.29 in group B. This indicates the IgA percentage change in group B observed during the clinical attendance phase 2 was not sustained into the six weeks following up to the data collection at 14 weeks (phase 3). IgA levels in group A, observed to increase during the clinical phase

were then sustained through to the end of the trial (phase 3). The observation of increased IgA levels in group A, at all three data collection points indicates that there was a sustained percentage change in the IgA levels over the 14 weeks. This level of IgA change was only observed in the asthma subjects of group A who had received the series of chiropractic treatments.

Percentage change in groups C and D were less disparate when viewed as a time period from baseline recordings at weeks zero to three (phase 1) to week 14 (phase 3).

4.3.2 Stress response in asthma: cortisol

Baseline readings of cortisol levels for each group were captured at phase 1, during the first two weeks of the 14-week trial.

Baseline readings were assessed using a one-way ANOVA for group cortisol differences (homogeneity across groups).

Phase 1 cortisol levels: baseline reading, first two weeks of trial

Figure 28 shows baseline readings of cortisol levels across the three asthma groups A, B and C were similar at the start of the trial.

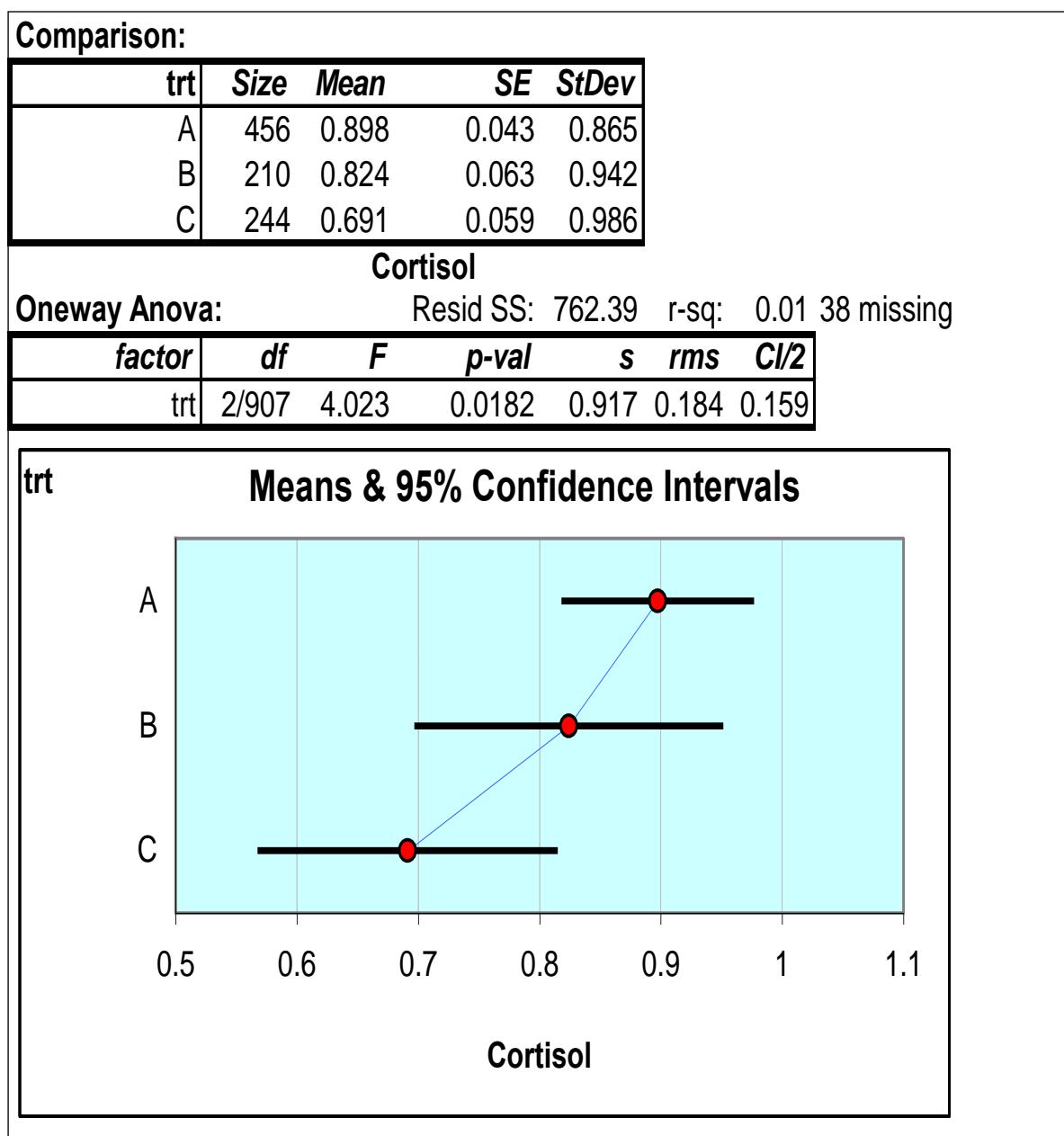
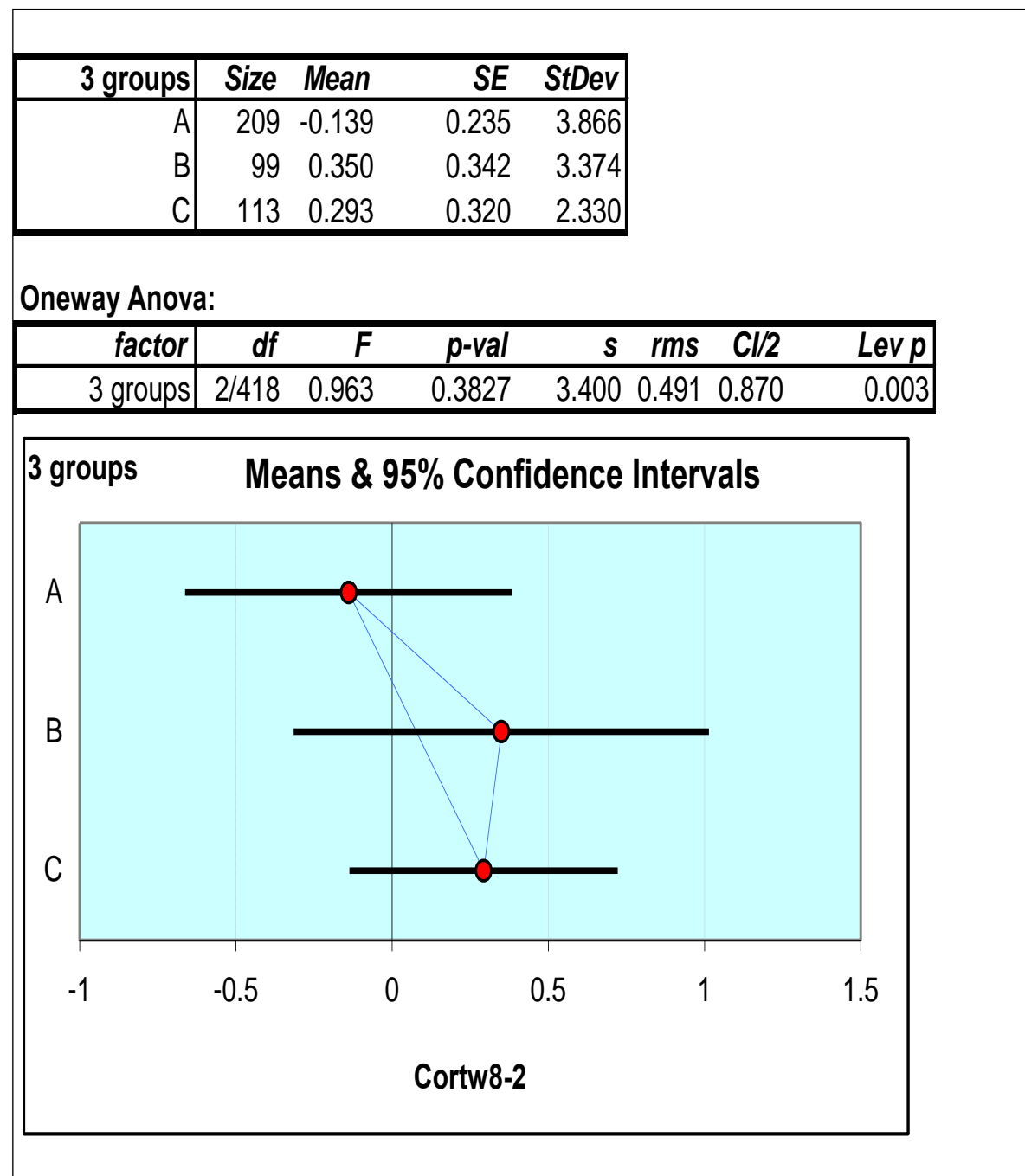


Figure 28: Baseline cortisol readings (phase1) of asthma groups

Legend: Cortisol levels are indicated across the bottom of the graph (0.5/1.1). The groups of asthma subjects are displayed on the left-hand side. The heavy horizontal black line shows the range of cortisol in each group with a mean score indicated by the red dot on the line.

Phase 2 cortisol levels: post-active treatment, eight weeks

Post-treatment, week eight (phase 2), cortisol level comparisons were made to determine any difference across the three asthma subject groups of the trial as shown in Figure 29.



Notes for Figure 29: post treatment (phase 2) cortisol readings of asthma groups

Legend: Cortisol levels are indicated across the bottom of the graph (0.5/1.1). The groups of asthma subjects are displayed on the left-hand side. The heavy horizontal black line shows the range of cortisol in each group with a mean score indicated by the red dot on the line.

Figure 29 shows cortisol concentrations groups A and B were not significantly different at the post treatment data collection (phase2). In the data analysis it had been observed that cortisol concentration for participants of group A had a tendency to increase with treatment commencement in the clinical phase (phase 2). The data of each participant of group A was analysed separately to determine whether this observed tendency for an increase in cortisol was the result of an aberration. There were no aberrations determined. It remained therefore that there was a tendency for cortisol to increase with treatment commencement for asthma participants in group A; although not more than a 'spike' of increase was observed across all the asthma participants in group A.

The cortisol concentrations remained relatively unchanged for groups B and C. There were no significant changes in cortisol concentrations from the baseline recordings at weeks zero to three (phase 1) to post-treatment at week eight (phase 2) for any of the asthma participants in groups A, B and C.

Phase 3 cortisol levels: six weeks post-treatment, 14 weeks (phase 3)

Group A cortisol level changes at the six weeks post-treatment period data collection (phase 3) suggested a magnitude of difference in cortisol concentration (see Figure 30). When observations were made comparing group A to groups B and C, in terms of baseline recordings of cortisol at weeks zero to three (phase 1) to the six weeks post-treatment period data collection (phase 3), significant differences were observed.

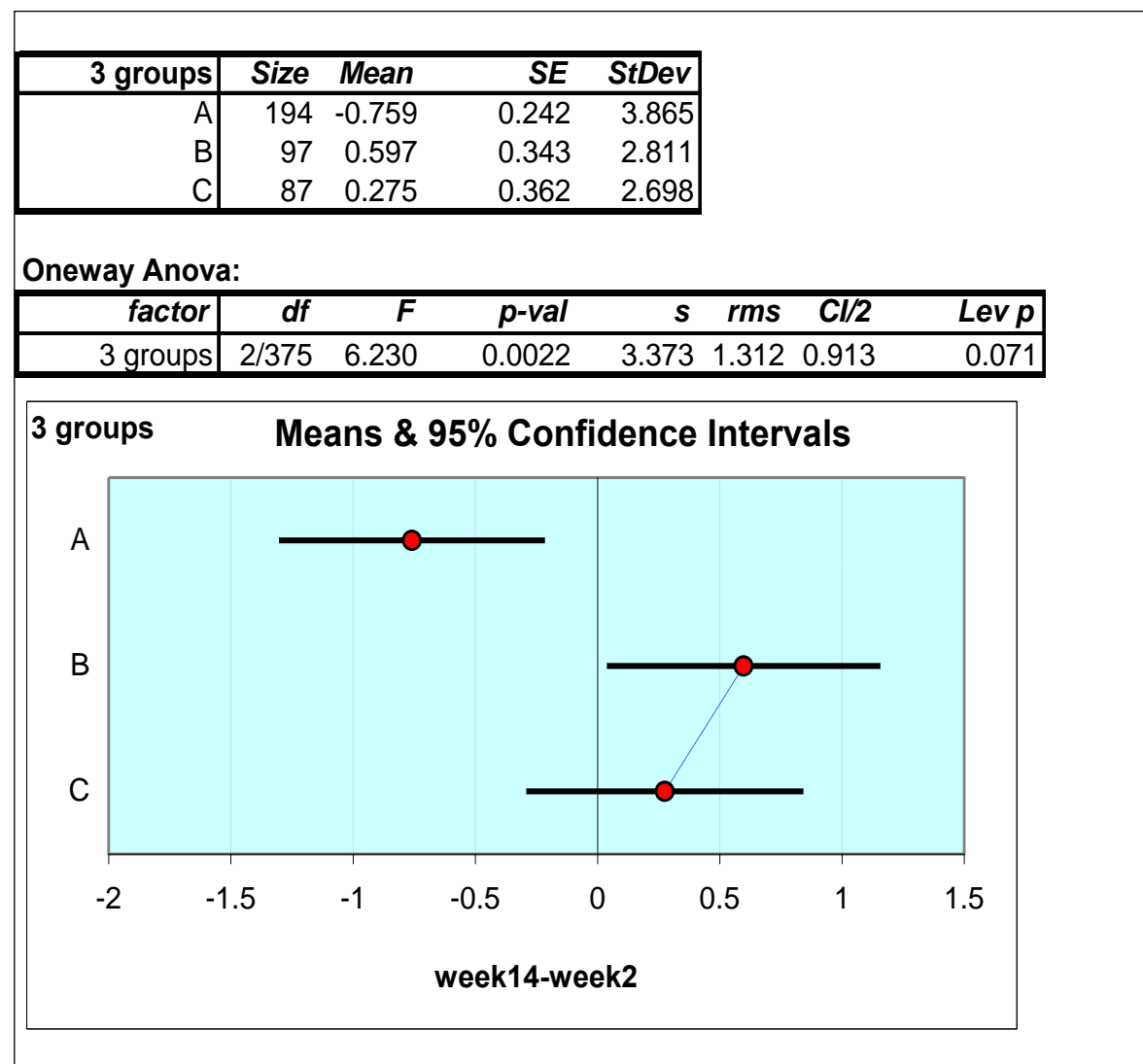


Figure 30: six weeks post treatment (phase 3) cortisol readings of asthma groups

Legend: Cortisol levels are indicated across the bottom of the graph (0.5/1.1). The groups of asthma subjects are displayed on the left-hand side. The heavy horizontal black line shows the range of cortisol in each group with a mean score indicated by the red dot on the line.

At 14 weeks, cortisol concentrations observed in group A had decreased by 0.759 on average, which was significantly lower than those of groups B and C ($P < 0.002$).

Cortisol levels: percentage changes in groups over three periods

In examining changes in cortisol from baseline to week 8 and from baseline to week 14

between groups one way ANOVA was used. Subject effects were adjusted using two-way ANOVA and were not significant in their effects.

Table 16 shows the study groups' cortisol percentage (%) changes over the three periods of the study data collection, from left to right: from baseline readings at two weeks (phase 1) to post-treatment at eight weeks (phase 2); from post-treatment at two weeks (phase 1) to 14 weeks post-completion (phase 3); and from post-treatment at eight weeks (phase 2) to 14 weeks post-completion (phase 3).

	% decrease between	% decrease between	% decrease between
Groups	2 & 8 Wks	2 & 14 Wks	8 & 14 Wks
A	48.7	67	69.2
B	49	37	12
C	47.1	24	23
D	3	2	4

Table 16: Percentage decrease in group cortisol levels over three periods of data analysis

Cortisol levels across the groups are demonstrated as percentage decrease changes between time periods of the study (three milestones of data collection during the study).

Figure 31 is a summary graph for cortisol decrease in groups A, B, C and D.

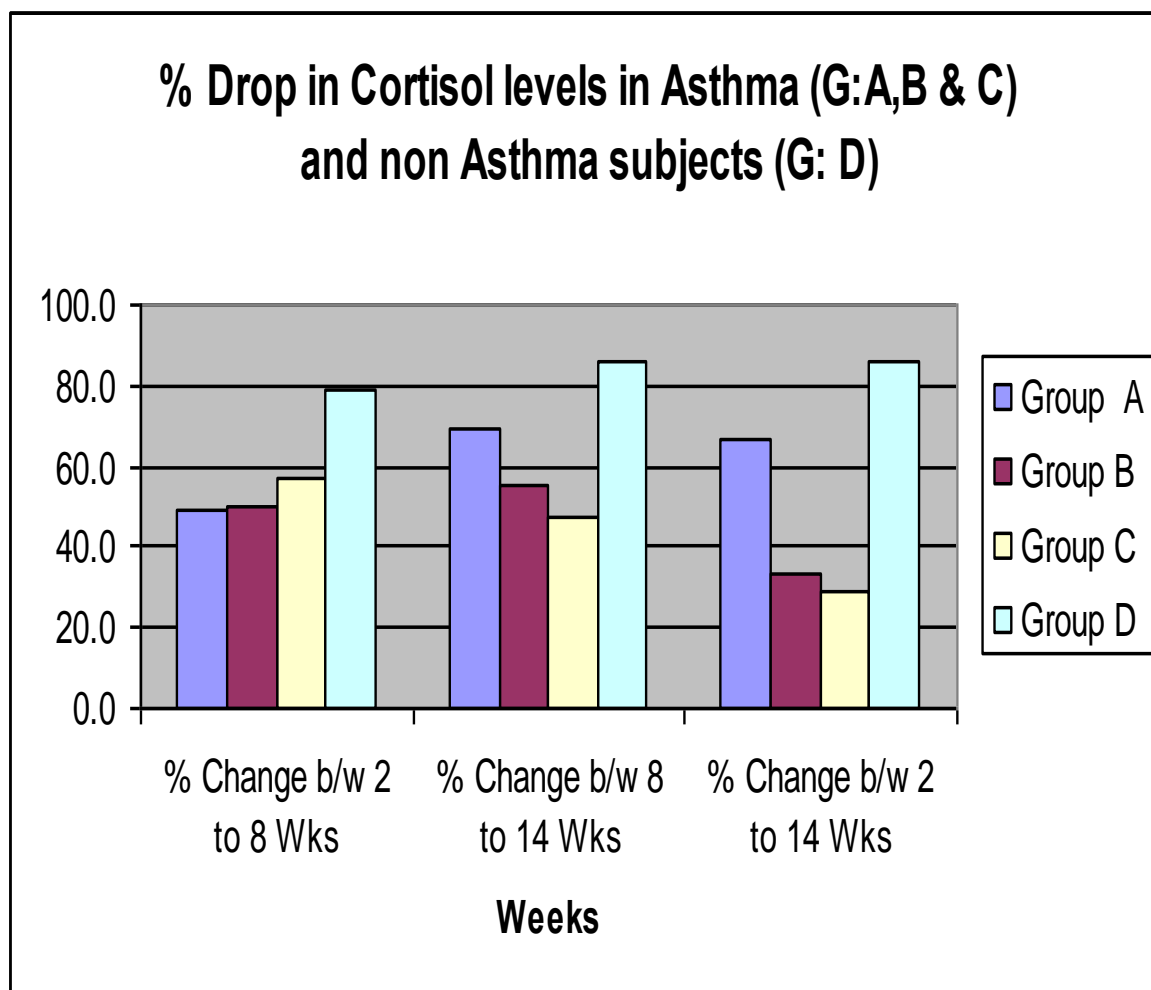


Figure 31: Cortisol decrease across three periods of data collection

Legend: There are three sets of four bars representing the three data time review periods. In each of the three sets, cortisol % decrease changes for groups A B C and D are shown. Moving across from the left, the blue bars on the left of each time review period, is the cortisol levels of group A. then the brown bar is group B, the cream bar is group C and the pale blue bar is group D.

Notes for Figure 31:

A greater decrease of cortisol occurred following chiropractic treatments in group A compared to group B in two periods of analysis, following the treatment (phase 2) and the time period of baseline to six weeks post-treatment, at 14 weeks (phase 3).

Groups A, B and C had similar baseline readings of cortisol concentration at the beginning of the trial at weeks zero to three (phase 1). There was notably less difference in cortisol concentrations across the three asthma participant groups A, B and C at the end of the treatment period at eight weeks (phase 2).

Group A demonstrated percentage decreases in cortisol concentrations over two periods of data collection at higher levels than the other asthma participant groups B and C. The greatest percentage decrease observed in group A relative to group B was in the period from the baseline readings at weeks zero to three (phase 1) to the six weeks post-treatment final data collection at 14 weeks (phase 3). The decrease in cortisol concentrations was noted for group A relative to group B after treatment (phase 2).

Group A demonstrated a 67% decrease in cortisol concentrations from the baseline readings at weeks zero to three (phase 1) to the six weeks post-treatment completion period at 14 weeks (phase 3). Over this same data collection period, group B showed a 37% decrease in cortisol concentrations and group C showed a 24% decrease in cortisol concentrations at 14 weeks (phase 3). Group D (non-asthma participant group) showed unremarkable % changes in cortisol concentrations throughout the trial.

Group A demonstrated a 69.2% decrease in cortisol concentrations from eight weeks post-treatment (phase 2) to the final data collection period at the six weeks post-treatment completion period at 14 weeks (phase 3). Over this same data collection period, group B showed only a 12% decrease in cortisol concentrations and group C showed a 23% decrease in cortisol concentrations at 14 weeks (phase 3).

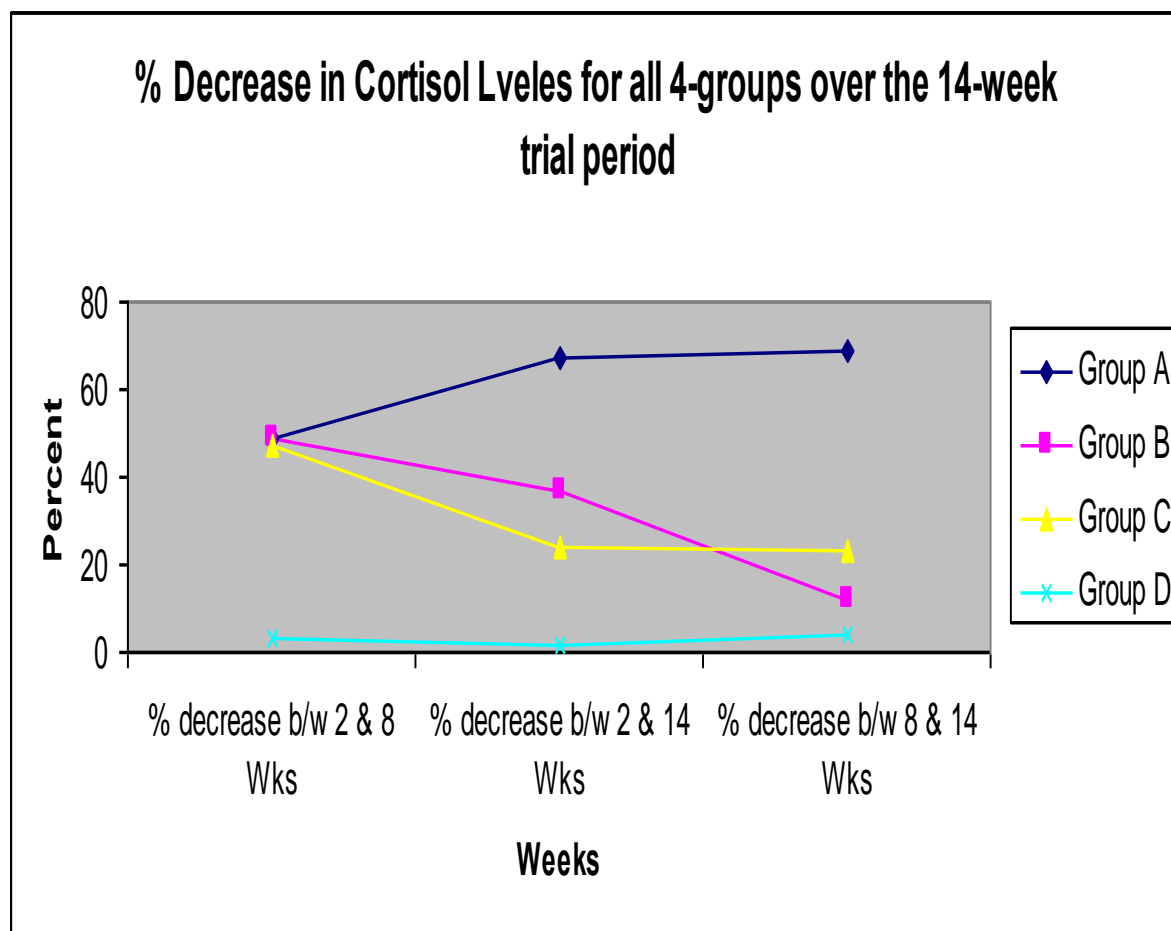


Figure 32: % decrease in cortisol levels for all groups A B C and D over 14 weeks

Legend: The dark blue line has a diamond identifier represents group A. The pink line with square identifier is representing group B. The yellow line with triangle identifier is representing group C.

Notes for Figure 32: A continuing increasing percentage change of decreasing cortisol is observed in group A.

Figure 32 shows that the cortisol levels in group A demonstrated a sustained decrease when compared to the other two asthma groups B and C at 14 weeks.

The magnitude of decreased cortisol levels for group A was statistically significant ($P < 0.05$) for the six-week period post-completion of the trial between weeks eight to 14.

4.4 Clinical recordings

4.4.1 Levels of spinal dysfunction and chiropractic treatment

At the conclusion of the clinical phase, all asthma participants' files were collected from the participating clinics. Also collected were 756 clinical recording sheets used during the clinical phase of the trial. A review of these 756 clinical recording sheets confirmed that the participating chiropractors had used a clinical recording sheet at each appointment with an asthma participant. The review showed that there was a clear indication of the treatment given to the asthma participants in group A.

The clinical recordings were confirmed as showing levels of spinal dysfunction that had been treated in the asthma participants. All clinical recording sheets were checked for compliance with the prescribed method of recording. Each clinical recording sheet was checked to ensure there were clear markings of each segment of the spine with an X or equivalent indication of treatment of one or more levels of spinal dysfunction on the schematic drawing of the spine. . Some of the clinical recording sheets had more notes on clinical observations and asthma comments, but these had been recorded on areas outside the schematic drawing of the spine. The level of compliance and consistency of use of the clinical recording sheets was assessed as reasonable for the purposes of this clinical trial. The Figure 33 demonstrates the various spinal segments or spinal levels of the asthma participants in group A treated by the 19 participating chiropractors during the clinical phase of the trial (phase 2).

Chi-squared test was used to compare the proportions of prevalence for all the 25 spinal levels ($\chi^2_{24} = 1181.5$; $p - value < 0.001$). T6 was observed as receiving the most treatment. Figure 33 shows that the proportion of treatment of certain levels of spinal dysfunction.

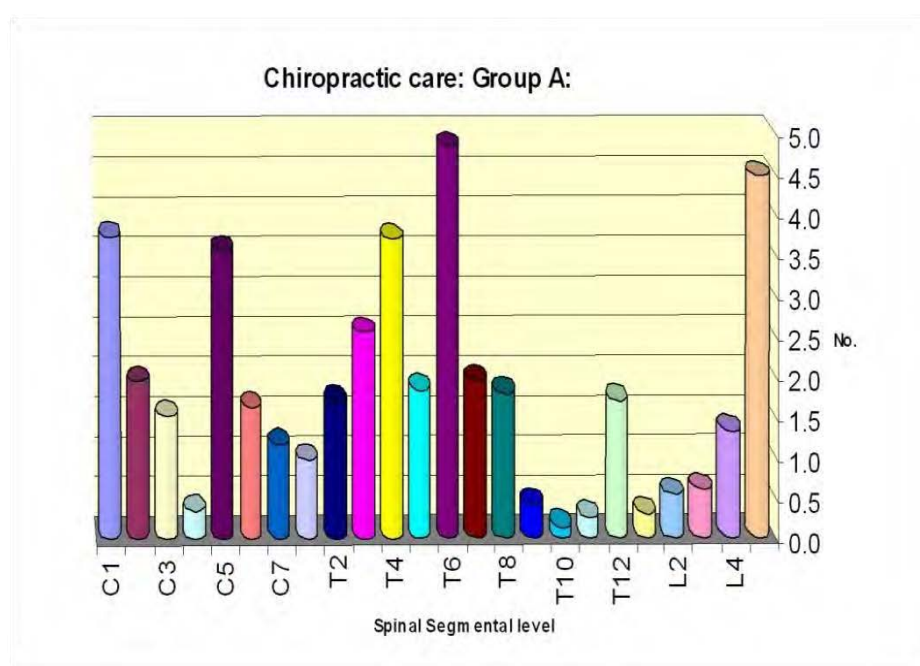


Figure 33: Display of levels of the spine treated in the asthma participants of group A

An analysis of the prevalence of the spinal levels identified on the 756 clinical recording sheets across the possible 25 spinal segments to be marked is shown in Table 17.

<i>Spinal level</i>	<i>Prevalence (%)</i>
C1	161 (7.80)
C2	84 (4.07)
C3	66 (3.20)
C4	15 (0.73)
C5	154 (7.46)
C6	70 (3.39)
C7	50 (2.42)
T1	42 (2.04)
T2	73 (3.54)
T3	110 (5.33)
T4	160 (7.76)
T5	79 (3.83)
T6	209 (10.13)
T7	84 (4.07)
T8	77 (3.73)
T9	18 (0.87)
T10	6 (0.29)
T11	11 (0.53)
T12	73 (3.54)
L1	13 (0.63)
L2	23 (1.11)
L3	26 (1.26)
L4	57 (2.76)
L5	193 (9.36)
S1	209 (10.13)
Total	2063 (100)

Table 17: The prevalence of spinal levels in asthma during the treatment phase (phase 2)

4.4.2 Analysis of proportion of findings across spinal regions

A further analysis of the clinical recordings of the spinal levels treated was conducted. For this purpose the segments of the spine were aggregated into a number of regions. The proportion of treatment of these 15 spinal regions was then determined. A chi-squared goodness-of-fit test was conducted to test if the proportions of spinal dysfunction prevalence were equal across all regions. In order to obtain an adequate sample size, the spinal levels were aggregated into 15 regions. The results of the 'regions' analysis showed that the highest proportion of spinal dysfunction was found in spinal regions T6 and S1 (See Figure 34).

The proportions of spinal dysfunction are significantly higher for regions C2-4, T4, T6, L5 and S1. The differences in regions was significant (chi-squared= 204.44, 14 d. f. P= 0.00). The groupings of the spinal segments by regional analysis are seen in Table 18.

Spinal region	No. of clinical findings	Proportion
C1	161	0.08
C2-4	165	0.08
C5	154	0.07
C6-7	120	0.06
T1-2	115	0.05
T3	110	0.05
T4	160	0.08
T5	79	0.04
T6	209	0.10
T7	84	0.04
T8	77	0.04
T9-12	108	0.05
L1-4	119	0.06
L5	193	0.09
S1	209	0.10

Table 17: Proportional levels of spinal dysfunction determined for treatment by region

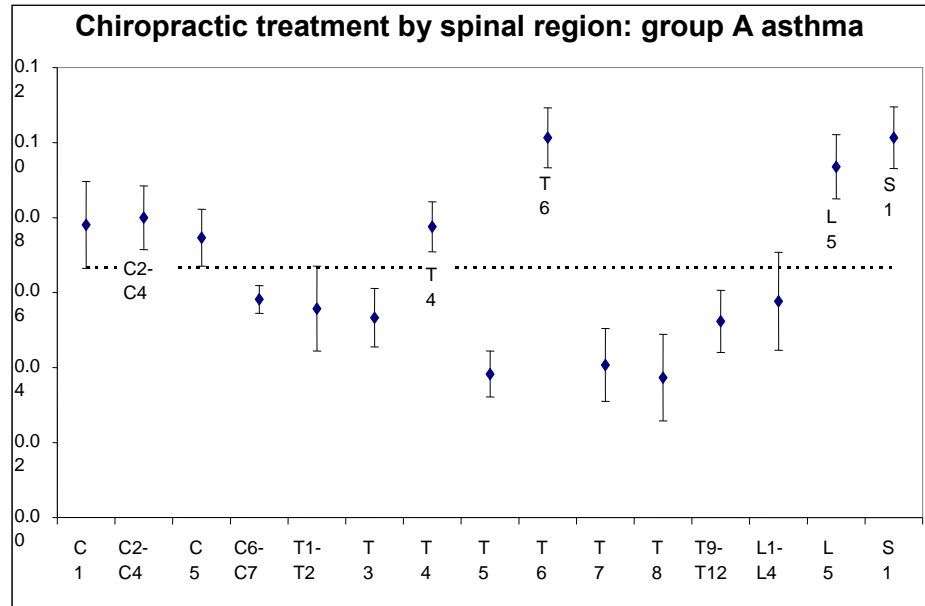


Figure 34: The treatment of spinal dysfunction in group A seen as by spinal region

Legend: spinal regions demonstrated by vertical lines, regions most prevalent in the treatment records of group A, are seen above the horizontal dotted line.

Chapter 5 – Discussion

Emphasis is given in this discussion to some key outcomes from, and implications of, the research conducted through the clinical trial. Results are discussed with reference to the research questions posed in this thesis. There is reflection on the research in terms of its design limitations, and on its practical implications.

Chiropractic is discussed as a non-pharmaceutical approach to asthma linked with research of the healthcare of individuals with chronic multi-factorial conditions such as asthma.

Finally the potential role for chiropractic and other CAM to lead a collaborative patient-centred delivery research model for the emerging healthcare system is suggested.

An overview of the results of the trial

The greatest improvements in all results of the six research measures were noted in group A at the final data collection point of 14 weeks (phase 3).

The observed decrease in self-reported symptoms and in the use of reliever medications was statistically significant ($P < 0.05$). The physical and mental health domain improvements of the SF-36 at phase 3 were statistically significant ($P < 0.05$) and a significant finding of improvement for the DASS locus of negative emotions was noted for group A ($P < 0.05$).

Both groups A and B showed increased IgA levels during the clinical phase of the trial indicating that some physiological effect occurred in both groups from attending appointments at the participating clinics for treatment. A percentage increase of 41.2 was noted in group B; the percentage increase for group A was 65.8 as opposed to the percentage increase of 16.7 for group C who were monitored from home. However, only group A was observed to sustain the increased IgA levels at 14 weeks (phase 3).

There was an increase in cortisol levels in response to the commencement of chiropractic treatment for group A (phase 2); this was followed by a decreasing level of cortisol for this

group, a statistically significant finding ($P < 0.05$) at the end of the trial (phase 3). This biphasic pattern of cortisol change in response to chiropractic treatment in asthma has not previously been observed. An upward trend of improving PEF scores was observed in group A, notably commencing after chiropractic treatment had finished at 8 weeks (phase 2). This indication of improved lung function continued as an upward trend of improving PEF scores for this group and was a statistically significant finding ($P < 0.05$) at the final data collection point of 14 weeks (phase 3).

5.1. The role of patient-centred questionnaires

5.1.1 Disease specific

As depicted in Figures 9 and 10 (Chapter 4), there was a continuing improvement in self-reported changes in asthma symptoms in the group receiving the chiropractic treatment. The greatest improvement was noted in group A at the final data collection point (phase 3). The reported decrease in symptoms was statistically significant ($P < 0.05$).

When the asthma participants were receiving treatment (phase 2), a decreased use of ‘reliever’ asthma medication was self-reported. This improvement was statistically significant ($P < 0.05$). A further decrease in the self-reported need to use asthma reliever medication, was a statistically significant finding ($P < 0.05$) at the end of the trial (phase 3).

Group B also had demonstrated a decrease in reported asthma symptoms during their clinic attendance but this was not sustained. Any benefit of the clinical encounter or some placebo effect during phase 2, registered in their asthma symptoms, was short lived with symptoms returning at the final data collection point of 14 weeks (phase 3).

These findings of improvements in self-reported asthma symptoms are consistent with other studies examining chiropractic treatment for asthma (48,182). This self-reported improvement in asthma symptoms may explain health consumers persisting in including chiropractic treatment in their individual Asthma Management Plan (AMP).

5.1.2 SF-36 wellness in the individual

As depicted in Figures 11 and 12 (Chapter 4), an improvement in self-reported physical health and mental domains was demonstrated by group A at the post treatment phase of the trial at 8 weeks (phase 2) and again at 14 weeks (phase 3). These findings of physical and mental improvements as measured with the use of the SF-36 was statistically significant ($P < 0.05$) at 14 weeks (phase 3). Interestingly, the findings of the SF36 in the area of the mental domain, indicated that possibly a placebo effect was occurring for group B, which was also statistically significant ($P < 0.05$). This observation suggests that a placebo effect may be a therapeutic factor in the clinical encounter and further research of the non-specific therapeutic benefits of the clinical encounter is indicated. In the absence of a specific outcomes measure for the effects of the clinical encounter, it can only be suggested that some 'non-specific' therapeutic benefits may have been active for both groups A and B during their clinical attendance (phase 2). However, physical and mental improvements observed in group B during phase 2, were not sustained at the final data collection point of 14 weeks (phase 3).

These findings of improvements in self-reported changes in their experience of health within asthma have been observed in other studies of chiropractic treatment for asthma (56, 182) . This self-reported improvement for these health consumers resulting in a sense of improved overall wellbeing is another possible reason for the persistence of the asthma sufferer including chiropractic treatment in their individual Asthma Management Plan (AMP).

The findings for group C who were monitored from home show that there may have been some placebo effect occurring for this group of asthma sufferers (see Figure 13 Chapter 4). Their physical health was observed as decreasing when they knew they were not a part of the clinical attendance phase and in fact only improved slightly by the end of the trial at 14 weeks (phase 3). The same group observed a minor improvement in their mental domains of health over the 8 weeks (phases 1 and 2). This may again be due to some non-specific factors of their mere involvement in the trial.

5.1.3 Depression and Anxiety Stress Scales (DASS)

As depicted in Figures 14 (Chapter 4), group A demonstrated some improvement in their emotional wellbeing in response to chiropractic treatment. In group A, the improvement in the three scales of negative emotion was statistically significant ($P < 0.05$). DASS scales of negative emotion were used in this trial for measuring and monitoring of asthma emotional wellbeing for the first time. This association between asthma and the locus of depression, anxiety and stress, requires more research.

The use of a self-monitored measure of emotional wellbeing may assist in the development of further self-profiling of individual asthma in the AMP. A greater understanding of personal health attributes and any emotional triggers that may explain the risk of an unexplained exacerbation of their asthma is of great value to an AMP. The association of negative emotions with unexplained exacerbations of asthma episodes that persist in an active AMP is a little understood area of asthma management (106, 297). The intrinsic type of individual asthma profile is not well understood in terms of its triggers; this type of asthma profile may have a preponderance of emotional or psycho-social triggers. It is suggested that a self-monitored measure of emotional wellbeing may be used in further asthma research to understand the nature and asthma health risks of an intrinsic type asthma sufferer (237, 298).

5.1.4 The use of questionnaires as asthma self-profiling measures

The results of this trial are an early indicator that some therapeutic benefits may be occurring in the complex multi-factorial nature of asthma from attending the 'typical' chiropractic practice and receiving a program of chiropractic within an AMP. In this trial the research question of whether there is any therapeutic benefit for asthma from chiropractic treatment was addressing the overall health of an individual with asthma.

For this purpose, a disease-specific baseline questionnaire was expanded to include a greater understanding of the individual complexity of this condition with broader data collection. The inclusion of data that may contribute to the further research of an individual asthma sufferer's

personal environment (genetic tendencies, family history, and demographic information, as well as details about their physical home and work environment with psychosocial profiling) was able to offer some insight into the unique profile of each asthma sufferer. This increased array of health factors in asthma may be developed as health-related quality of life profiling that may include a chiropractic-related self-profile of wellbeing for the purpose of further research. This developing research tool could be examined alongside established health-related quality of life questionnaires that have been used in this trial.

It is suggested that the findings of the trial confirm previous studies that self-education in asthma and increased awareness of triggers and within an AMP produce better health outcomes (3, 10).

The findings of individual responses with the patient-centred questionnaires of this trial are considered subjective measures of therapeutic response that support the findings of improvements in more 'objective' measures of biomarkers and lung function over the 14 weeks of the study. However, the patient-centred results of this trial were not only subjective findings in support of the laboratory-based findings. It is suggested that patient-centred questionnaires promote individual self-awareness and contribute to self-determining behaviours in asthma. Self-profiling questionnaires may be used in future patient-centred research as 'self-determining' asthma behavioural research questionnaires. Self-determining behaviour in asthma may be examined in future research for its contribution to the therapeutic benefits observed in asthma participants within their AMP (299).

A combination of a number of these self-profiling questionnaires may be used for future clinical research purposes. Including factors such as 'time and place' within the scope of self-monitoring and self-profiling may contribute to greater understanding of health in individuals with chronic conditions such as asthma.

The healthcare delivery system may benefit from such development of ‘wholistic’ patient-centred self-profiling questionnaires where the measure is truly representative of the experience of the individual in their health (300).

5.2 The role of Peak Expiratory Flow measurements

As depicted in Figure 24(Chapter 4), Groups B and C demonstrated similar Peak Expiratory Flow (PEF) scores across the 14 weeks. There was a decrease in their PEF scores at six weeks post-treatment at 14 weeks (phase 3).

An upward trend of improving PEF scores was observed in group A. This trend of improving PEF scores was most notable for this group after treatment had finished at 8 weeks (phase 2). The improved lung function was statistically significant at week 14 (phase3) for the asthma participants in group A ($P < 0.05$).

Group B had attended the participating clinics for six weeks of the clinical phase (phase 2) and were unaware of when their treatment would start. A rise in the PEF scores was observed for this group during phase 2. This may have been due to the non-specific therapeutic benefits of the clinical encounter as a placebo effect. Some emotional anticipation of expecting treatment to start on each occasion that they attended the clinic for an appointment may have had a placebo-type effect.

This non-specific therapeutic benefit or placebo effect was short lived. PEF scores for group B were demonstrated as decreasing after the clinical phase had finished at 14 weeks (phase 3). Whereas, the PEF scores for the group that received the treatment (group A) were observed as increasing when measured at 14 weeks (phase 3).

Group C followed a trend of PEF scores similar to Group B, that of a short lived response (see Figure 23). In Group C there may have been some ‘non-specific’ therapeutic benefit occurring such as the enthusiasm of being involved in the trial. There may have been anticipation of treatment commencing. It is also possible that some reversal of these ‘non-specific’

therapeutic benefits occurred for group C resulting in decreased PEF scores after the clinical phase. This may be some placebo-like effect of disappointment or a ‘non-specific’ negative impact on these asthma participants and requires more detailed research. This was observed in the PEF scores of group C who did not attend the clinic, nor had their treatment commenced during the clinical phase. They also did not receive any treatment during the 14 weeks of the study.

Group B may have been demonstrating some similar psychological impact as observed in group C. For group B, at each appointment at the clinic, they were expecting their treatment to commence. Then at the completion of the treatment period, the asthma participants in group B may have been somewhat psychologically disturbed that the anticipated treatment had not occurred during the clinical phase. There may then have been a negative effect from the realisation that they would not be receiving their treatment until after the completion of the 14-week study.

The mind is known to affect body functions. This area of research using the expanding knowledge base of the science of psychoneuroimmunology may be a useful resource in further researching this observed ‘therapeutic impact’ of human to human clinical interaction (166).

5.2.1 Physiological effect of chiropractic treatment

The greatest improvement in PEF scores was noted for group A after the chiropractic treatment had finished. This may indicate some physiological activity coming into effect after a number of chiropractic treatments had been received by the asthma sufferer. A ‘trend’ of improvement in the PEF scores for group A was observed starting in phase 2 and continuing to increase in phase 3 for group A. It appears that a ‘time-lag’ or a ‘window of impact’ may be part of some physiological activity in response to the chiropractic treatment. This requires further research as to the underlying reasons.

It is suggested that this altered physiological response maybe related to the nature of the autonomic dystonia associated with asthma (147, 163, 301). This requires further research. It is suggested that some alteration in the underlying abnormal mechanisms of the ANS may be researched as a plausible biological mechanism to explain these therapeutic benefits from chiropractic treatment for asthma. This plausible mechanism may involve some neuro-physiological reflex activity in response to stimulation of the spine (159, 164) (177) (155).

The trend of improvement observed in the PEF scores of group A indicates that this sustained physiological impact may still have still been active at 14 weeks when the trial was completed (phase 3). This possibility of a continuing trend may be included in future research for the purpose of developing ‘windows of observation’. An improving lung function pattern over time in asthma sufferers may require a number of periods or ‘windows of observation’ (147, 163).

It is suggested that these findings may indicate that such cumulative physiological impact may be an aspect of many CAM manipulative and body-based therapies. A ‘program of care’ in CAM healthcare may be used to examine a number of treatments as being more therapeutic than single clinical applications.

5. 3 The role of laboratory-based assays for IgA and cortisol

5.3.1 IgA levels

As depicted in Figure 27 (Chapter 4), Group A showed their greatest IgA level increase during the clinical phase (phase 2) with a percentage increase of 65.8. IgA level increases occurred in group A at each of the phases of clinical trial and were greater than that seen in asthma participants of groups B and C. The IgA levels for group B showed their greatest percentage level of improvement of 41.2 when observed between 8 weeks (phase 2) and 14 weeks (phase 3).

The percentage increase was less for group B than group A, when IgA levels were compared as baseline recordings (phase 1) with IgA levels at week 14 (phase 3). This period of observation suggests that group A was sustaining their increased IgA levels at 14 weeks (phase 3).

Both groups A and B had improvements in their IgA levels during the treatment phase 2. This indicated that some physiological effect occurred during the treatment phase for both groups. The percentage increase of 41.2 was noted in group B and the percentage increase for group A was 65.8 as opposed to a percentage increase for group C of 16.7. As both A and B attended the chiropractic clinics, both groups may have benefitted from some placebo effect or non-specific therapeutic benefit of attending the clinical environment and/or the clinical encounter. The percentage change in IgA levels observed in Group B who attended the clinic and did not receive treatment may possibly be due to this biomarker of immune response registering some emotional response to the clinical encounter. The clinical attendances of phase 2 may have resulted in a psychoneuroimmune response in both groups of asthma participants (295, 302, 303). The factors of placebo are unknown mechanisms. It may be that this placebo effect observed was only registered in the IgA levels as an immune response, simply because this happened to be by chance, the one outcome measure used in this trial that registered this placebo effect. The placebo is likely to be a more complex factor than this trial was able to suggest with its limited outcome measures focused on placebo effects. There is a need to develop other research measures, subjective and biochemical that may be used for examining some psychoneuro immune response or the placebo effect in clinical research. The knowledge of the science of psychoneuroimmunology (PNI), may contribute to understanding the link between the mind, changes in the nervous system and immunity in asthma. The developments of PNI may offer new measurement tools of the ANS in research of the health of the individual with asthma. New 'whole body' measures of PNI research may be developed for

used in understanding the observed health change in the asthma participants from the chiropractic program of care used in this trial (304).

Overall, the greatest changes in IgA levels occurred in group A. The increase in IgA level seen in group A was significantly higher than that observed in groups B and C in the clinical phase where group A was receiving the 18 chiropractic treatments.

Maintaining a healthy IgA level may promote a healthy lung epithelium in asthma as the lung surface is one of the first lines of defence against pathogenic invasion in extrinsic asthma. Maintaining a healthy IgA level may assist in the immune-responsiveness to inhaled allergens and other triggers for the asthma sufferer. This requires further research (257).

5.3.2 Cortisol levels

As depicted in Figures 31 and 32 (Chapter 4), this clinical trial observed a change in cortisol levels for group A seen to decrease most evidently at 14 weeks (phase 3). The magnitude in decreased cortisol levels for group A was considered to be a statistically significant finding ($P < 0.05$). There was an increase in cortisol as an immediate response to the impact of chiropractic treatment was followed by some regulatory activity. This pattern of response to the stimulation of the chiropractic treatment has not been observed before and requires further research in asthma and non-asthma participants in examining any therapeutic benefits from chiropractic treatment. It is possible that this was indicative of some altered cycling of cortisol; observed at 14 weeks (phase 3) as a decreased level of cortisol. Notably, these findings are for asthma participants. Abnormalities of the ANS associated with asthma may offer some explanation of this observed pattern of response to the chiropractic treatment in this trial (163, 303).

Asthma may also be also a condition of state of 'physiological alertness' that may be associated with some altered stress response to stimulation (279, 305).

In this clinical trial, the asthma participants showed a response to ‘stimulation’ of the spine in the form of chiropractic treatment. There was an increase in cortisol observed initially in group A at the commencement of the chiropractic treatment. This suggests that some cortisol-stimulating response was occurring initially for the asthma participant from chiropractic treatment. This requires further research. There may be a threshold of stress response or some stress response variance in each asthma sufferer; this response to chiropractic treatment may differ from the normal healthy or non-asthma population generally.

It is suggested that an altered survival mechanism of the body may be a part of the abnormal physiological functioning in chronic asthma; the body normal is to constantly respond to physiologically challenging stimuli. Chronic conditions like asthma may have altered levels of circulating cortisol with some alteration of homeostatic feedback mechanisms (273, 306).

5. 4 The role of chiropractic treatment in asthma

Empirical evidence is that physical treatment of a ‘manipulative or body-based healthcare approach’ such as chiropractic for asthma, is addressing the biomechanical function of the thoracic spine, ribcage and related regions. The balanced structure of these physical components of respiration supports healthy mechanics of normal breathing. This clinical trial suggests preliminary findings of other therapeutic benefits beyond the structural improvement in respiratory biomechanics.

There are early indications from this trial that there may also be a relationship between chiropractic treatments and improvements in lung function resulting from neuro-mediated changes in the function of the ANS following chiropractic treatment. It is suggested that research into these underlying pathophysiological mechanisms may further the understanding of neuro-endocrine and immunological factors in relation to lung function in asthma.

A focus of the research question in this trial was to examine chiropractic as it occurs in ‘typical’ chiropractic practice. A series of chiropractic treatments were delivered with ‘mainstream’ chiropractic clinical techniques and all chiropractors identified the levels of

spinal dysfunction treated. The chiropractic program of care was treatment of non-painful spinal dysfunction associated with a comorbidity of asthma. The research question of the clinical trial was examining for any therapeutic benefits from chiropractic treatment. There was consideration in reviewing chiropractic research that there is a lack of any research evidence of efficacy for chiropractic treatment. In this context, the results of this trial are reviewed with a proposed set of criteria for assessing scientific validity of chiropractic treatments. This may contribute to further research and development of criteria for examining for evidence of efficacy in chiropractic research.

5.4.1 Spinal segments identified

As depicted in Figure 33 (Chapter 4), some spinal segments were identified as being treated more often than others. The spinal segments of C1, C5, T4, T6, L5 and S1 were identified as being treated at a proportionally higher rate than the other levels of the spine. T6 was the most frequently treated single level of the spine in the asthma participants. When there was a grouping of spinal levels by regions, T6 and S1 were determined as the prevalent levels of spinal dysfunction treated in the asthma participants.

This observation of a preponderance of treatment of the spine at one level in asthma, promotes the question of what a chiropractor does in clinical practice when treating the spine.

One suggestion from within the chiropractic profession, concerning adjustment or manipulation of the ‘spinal subluxation’ is that a chiropractic treatment removes ‘subluxations’. It is suggested that this means chiropractic treatment of a clinical presentation of spinal dysfunction is to resolve the dysfunction (142, 284). The clinical recordings of 756 chiropractic treatments in this trial of asthma participants demonstrated that the preponderance of treatment of spinal dysfunction in the asthma participants of this trial was at C1, C5, T4, T6, L5 and S1 levels. This observation suggests the chiropractic treatment in this trial did not result in the ‘removal’ of spinal dysfunction at those levels; the same spinal levels

were repeatedly treated in these asthma participants. This may be due to the chiropractic clinical technique persistently determining dysfunction at that level of the spine; or some other reason yet to be established.

The trial findings of therapeutic benefits for asthma from the series of chiropractic treatments suggest that a persistent treatment at these identified spinal levels was a contributing factor to the observed therapeutic benefits. Further research is indicated.

It is possible that treatment of spinal dysfunction in this trial of asthma participants may have had a cumulative stimulating effect at these levels of the spine. A biological mechanism may be involved that involves some activity of somato-viscero-somatic reflex cycling. Spinal level of involvement in this cycling may result in it being a persistent clinical finding of spinal dysfunction when examined by the chiropractor.

One suggestion is that the chiropractic treatment produced therapeutic benefits as this stimulation assisted in modulation the function of the ANS in these asthma participants. This requires further research.

Also, improvements in lung function and biomarkers were associated with a 'time-lag' of physiological changes in asthma in response to chiropractic treatment suggest a cumulative stimulating effect at these levels of the spine. This requires further research

These early findings suggest a period of time may have been required for the biological mechanism involved to become active in response to the prolonged stimulation of spinal levels of dysfunction of 18 chiropractic treatments. Certain spinal levels may be involved in abnormal cycling of the autonomic nervous system (ANS) in its dysfunction associated with asthma (147, 163, 303).

5.4.2Chiropractic treatment protocols

The observations of treatment of certain levels of spinal dysfunction concur with chiropractic clinical protocols regarding the treatment of the spine with a comorbidity of asthma. The participating chiropractors recorded treatment of T 6 as the most prevalent level of the spinal dysfunction in the asthma participants of this trial. Early chiropractic writings cite spinal levels in relation to treating presentations of asthma where hospital inpatients were not responding to the asthma treatment of the day. The treatment of T4 and T5 was reported to have a benefit in 75% of these medically non-responsive hospital patients (149). The chiropractic treatment of dysfunction at the thoracic levels 4 and 5 (T4 and T5) may suggest there may be a relationship between these thoracic vertebrae and some signs of sympathetic depletion associated with some aberrant somato-autonomic reflex activity. This imbalance of the autonomic nervous system, associated with asthma sufferers' airway compromise, has been suggested in the historical chiropractic literature as the plausible biological mechanism of therapeutic activity in response to chiropractic treatment (35, 38, 307) and (36).

The old chiropractic technique known as the Meric System was a clinical construct of observed associations of organ dysfunction from the earliest literature of chiropractic practice (181). These historical references may still influence chiropractors today. Standard anatomical charts for the display of the autonomic nervous system (ANS) are displayed in healthcare clinics. These educational anatomical charts show several levels of the spine with the sympathetic and parasympathetic parts of the ANS cycling, in their anatomical distribution. The Meric System may have some influence on what a chiropractor does in clinical practice. The suggestion behind the historical use of the Meric System is palpation of the spine for 'tone' as an indication of healthy function (308). The chiropractor in their use of clinical techniques to determine the level of spinal dysfunction may or may not be aware of the historical association of levels of the spine and organ dysfunction as co-morbidity in the clinical presentation.

There is a suggestion that a spinal level of dysfunction, though not a causative agent of organ dysfunction, may play some role in the chronic facilitation of somato-autonomic reflexes in organ dysfunction (164). This is an area of research interest for chiropractic and other CAM manipulative and body-based health approaches (309).

5.4.3 Relationship - spinal dysfunction and organ dysfunction

Some chiropractors continue a tradition of checking for any relationships between the structure and presentations of comorbidities in their practice (310). The chiropractor recognises an essential relationship between the structural integrity of the whole spine with efficient weight-bearing and good posture as part of the healthy functioning of the body. In the clinical practice of chiropractic, the whole spine, its segments and related areas are assessed for dysfunction. The treatment of the spinal dysfunction has a clinical aim of structural and functional integrity of the whole spine, its segments and related areas. This aim is to have healthy spinal function with efficient weight-bearing and good posture associated with healthy functioning of the body. Any co-morbidity in the clinical presentation may or may not be the focus of the treatment. The chiropractor is educated to determine if the co-morbidity associated with a clinical presentation of spinal dysfunction requires concurrent care from another health provider. The chiropractor uses their clinical judgement to refer to a medical practitioner when indicated (25).

The Gonstead approach is considered a mainstream technique; and the only one in the trial to have a history of accessing certain levels of the spine in treatments to ensure healthy function of the ANS. This systematic approach to chiropractic treatment includes awareness of the healthy balanced function of the autonomic nervous system. The Gonstead chiropractic clinical technique, suggests the function of the sympathetic or the parasympathetic system are to be considered when treating the spine; not treating the thoracic spine (sympathetic) and the sacrum (parasympathetic) in the same treatment (286).

5.4.4 Treatment of painful and non-painful spinal dysfunction

The origin of the spinal dysfunction can be musculoskeletal or non-musculoskeletal. Chiropractic treatment is used in painful musculo-skeletal dysfunction and non-painful musculo-skeletal dysfunction. The nature of the chiropractic treatment will be varied by the chiropractor depending on the clinical presentation (79). However the same chiropractic clinical techniques will be used in both painful and non-painful presentations of spinal dysfunction to determine the level of spinal dysfunction to be treated on each clinical attendance.

Research of the efficacy of chiropractic treatment as a healthcare approach is in its infancy. The chiropractic treatment of levels of spinal dysfunction may be viewed for future research purposes as a series of ‘therapeutic stimulations’ of the spine. The observed therapeutic benefits in the asthma participants may be due to neurobiological mechanisms of underlying abnormalities of the ANS. The neurophysiological response occurring with a series of ‘therapeutic stimulations’ or chiropractic treatments of the spine is to be further researched.

There has been a significant growth of spinal manipulative therapy (SMT) in developed countries over the last 20 years that is continuing. The biomedical model of SMT has been an area of much research by chiropractors and other health providers of SMT (311, 312). The published research of SMT is research by many providers of SMT (130). Despite this broader use of SMT by many health providers, any benefits of SMT as opposed to other non-manipulative healthcare approaches in musculoskeletal pain syndromes, is still debated (126, 129, 313). The varied nature of SMT as a manipulative and body-based therapy makes it difficult to use a sham in researching for therapeutic efficacy from SMT that may not be like the SMT of another provider of SMT. This may possibly explain the limited evidence of any therapeutic efficacy of SMT in published research where more benefit than a sham is the established minimum standard for evidence of efficacy (314).

5.4.5 Assessing for scientific validity

Research into chiropractic treatment has theorised about the neurobiological mechanisms of health and disease as plausible scientific explanations to explain patient-reported benefits from chiropractic treatment (155, 159, 164, 277). Theories which may explain the therapeutic benefits of chiropractic treatment include the nerve compression, ANS reflex and pain relief theories (164). Though there are a number of theories that support plausible neurobiological mechanisms, they are proposed by the different clinical technique groups of the chiropractic profession and there has been little research investigation without the bias of a particular chiropractic clinical technique in the research modelling. This research is often to substantiate one clinical technique ‘approach’ or school of thought and not representative of the whole profession (315).

There is a dearth of research examining the efficacy of chiropractic treatment in terms of its scientific validity. This lack of research to establish evidence of efficacy was considered in the background to the trial. There are unsubstantiated claims of chiropractic treatment and the number of theories explaining the effects of chiropractic treatment over thirty years ago remain unsubstantiated (164, 170, 316).

In the clinical trial, asthma participants received treatment for painless spinal dysfunction. They received ‘typical’ treatment from chiropractors in ‘typical’ chiropractic practices. The research question of what a chiropractor does in clinical practice was designed to have no particular technique examined for the purposes of this research. This trial did not use a ‘specific manipulative procedure’. This trial used four mainstream clinical techniques as chiropractic treatment ‘typical’ of chiropractic practice. There were some therapeutic benefits for asthma from the ‘typical’ chiropractic treatment used in this trial. The ‘typical’ chiropractic treatment is presented here for research purposes as what a chiropractor does in clinical practice when treating levels of spinal dysfunction. This is to be representative of

what may be known clinically as a ‘specific manipulative procedure’ or particular chiropractic clinical technique procedure, manipulation or chiropractic adjustment.

The clinical concepts of manipulable lesion, subluxation, adjustment and manipulation were exchanged for a common term of chiropractic treatment of spinal dysfunction. A set of biomarkers was used with other research tools to monitor what may be changing in the asthma participants before, during and after receiving a series of chiropractic treatments.

Haldeman’s original criteria are presented below and discussed with regard to the research findings and observations of this thesis. This discussion is intended to promote further thought for the chiropractic profession as a developing research body.

The four criteria by which chiropractic treatment may be assessed for scientific validity are (164):

Criterion I:

A specific manipulative procedure must demonstrate consistent clinical results under controlled conditions in treating a specific pathologic process, organ dysfunction, or symptom complex.

The clinical results of this trial demonstrated a positive physiological impact observed as an improvement in the condition of asthma under randomised controlled conditions. Chiropractic treatment of levels of spinal dysfunction in the asthma sufferer was measured with a number of health research tools. These included laboratory-based objective outcomes of immune and stress response and lung function changes, and a number of self-reported health-related quality of life instruments. Signs of autonomic imbalance in asthma were monitored with the biomarkers of stress response and immune response. This measurement showed a steady improvement in lung function, the symptom complex of asthma and the underlying abnormalities of the autonomic nervous system associated with asthma. The therapeutic

benefits observed were seen in response to a ‘program of chiropractic care’ that involved a series of chiropractic treatments of asthma participants.

Criterion II:

The specific manipulative process must demonstrate a specific effect on the musculoskeletal system to which it is applied.

In clinical practice musculoskeletal presentations are with or without pain.

As closed systems of inherent logic, chiropractic clinical techniques each have a different approach with an intended therapeutic impact on the musculoskeletal system in the delivery of their treatment. The impact on the musculoskeletal system is dependent on the intended effect of the clinical technique. A number of measuring/monitoring systems are used within each of these chiropractic techniques; however a ‘gold standard’ of measuring change in the musculoskeletal system before and after ‘typical’ chiropractic treatment is administered has yet to be established.

In managing painful conditions of the musculoskeletal system, chiropractors and other providers using manipulative procedures have standards of self-scaling pain, ranges of motion and pre and post treatment mobility using established patient centred questionnaires. These measurements of the outcomes of effectiveness for musculoskeletal therapy include pressure or tenderness on palpation, self-reporting of mobility and ease of movement. These and other measures may be developed and standardised for use in the chiropractic practice of treating painful spinal conditions across all chiropractic clinical techniques.

There is an impact on the musculoskeletal system whether the intended therapeutic impact is for a non-painful musculoskeletal presentation or for a painful musculoskeletal presentation. The findings of this trial suggest that in a comorbidity of asthma, a non-musculo-skeletal presentation, certain levels of the spine were treated more than others. It is suggested that when the chiropractic treatment is for a non-painful musculoskeletal presentation, the

particular measuring/monitoring systems used within each chiropractic clinical technique e.g. self-scaling pain, ranges of motion and pre and post treatment mobility may be less useful. It is suggested that for treatment of spinal dysfunction of a non-painful condition measures may be developed with laboratory-based physiological measurement systems. These may be used before and after the chiropractic treatment to measure the impact attributable to the chiropractic treatment of painless spinal dysfunction.

Criterion III:

The musculoskeletal effect caused by the manipulation must be shown to have a specific influence on the nervous system.

Chiropractic clinical techniques all have an intended therapeutic impact in clinical presentations with or without pain. The neuromediated effect on the nervous system in response to chiropractic treatment of the musculoskeletal system may occur in several segmental levels above and below the spinal level of chiropractic treatment. The state of the individual's nervous system function within that clinical presentation will influence the neuro-mediated effects through the nervous system. These effects may be most likely occurring in relation to the biological mechanisms associated with local somato-somatic reflexes and feedback loops with the central nervous system (178).

This clinical trial used laboratory-based research measures for monitoring changes in the immune system (IgA levels) and the stress response (cortisol levels) in the individual asthma participants (317, 318). Therapeutic effects may be monitored with a number of indicators of other neuro-mediated changes in the body. Further research could focus on similar appropriate 'measurements' to monitor or assess other effects on the nervous system resulting from chiropractic treatment. Current research examining neurophysiological effects in the nervous system in response to chiropractic treatment may contribute to the development of appropriate 'measurements' of the nervous system for use in future clinical research (319).

The results of this trial suggest that there may be effects on the nervous system that may be dependent on a 'window of measurement' of physiological activity coming into effect. The factor of time for any therapeutic benefit to be registered in the nervous system following chiropractic treatment requires further understanding. This may contribute to the development of research measurements of neuro-mediated changes in the body.

The developing science of psychoneuroimmunology and whole body health may be used as a background in developing other measures of neuro-mediated changes in the ANS and other altered functional states of nervous system health. This may allow the therapeutic benefits of these neurophysiological changes to be measured and monitored in individuals and in specific target conditions as a response to chiropractic treatment. The research and development of acupuncture examining the modulation of the function of the ANS serves as a good example (309).

Criterion IV:

The influence on the nervous system brought about by the manipulation must demonstrate a benefit to abnormal function of an organ, tissue pathology, or symptom complex.

The measurement of any specific therapeutic impact on abnormal function of an organ, tissue pathology, or symptom complex must use biomarkers of health change specific to the organ function or targeted health change as the focus of the chiropractic treatment.

For asthma, this trial used clinical outcome measurements of neuro-endocrine and neuro-immune markers to demonstrate physiological change in relation to the specific organ function which was the target of the treatment.

The treatment of the spine has an influence on the nervous system and the response in organs and tissues of the body is complex (159). Overall systemic changes are mediated by the central nervous system; this can vary depending on the state of function of the central nervous system and the ANS (99, 153, 304).

There are individual variants of tissue pathology or altered function that affect the dynamic cycling of the autonomic nervous system (306, 320). This complex of neurophysiological responses in health and illness is little understood.

It is suggested that in the development of clinical research models, using specific biomarkers of organ functions, healthy tissues and symptom complexes can be used to research the neuro-modulation activity that may occur with chiropractic treatment of spinal dysfunction. The research tools may differ in the examination of neurophysiological changes when the treatment is of painful as opposed to non-painful spinal dysfunction.

5.4.6 Health of the individual with asthma

These preliminary findings suggest that further research may examine a clinical profiling of the individual in their responsiveness to the spinal stimulation of chiropractic treatment. This will also assist in the research and development of the clinically critical question of identifying those individuals who are not likely to respond to the use of spinal stimulation from chiropractic treatment in their asthma management plan (243).

People prefer a focus on themselves personally rather than on their illness. Researching the individual's experience of asthma will contribute to understanding the individual and developing the best approach to managing his or her condition (219). The 3 C's of patient-centred care are suggested as pivotal for asthma management: communication, continuity of care and concordance (finding common ground) (321).

An AMP with chiropractic treatment included, examining for any benefits in the health of the individual with asthma in accordance with the WHO definition of health. Health is more than the mere absence of disease, is achieved by accepting that the individual health of each asthma sufferer is a personal profile; only able to be determined by that asthma sufferer (9). This targeted focus of 'optimal health in the individual' encourages a sense of increasing

control for the asthma sufferer with increasing self-awareness of their personal profile of health within their chronic multi-factorial condition, not just the disease process (322, 323).

5.5 The role of a combination of outcome measures

A combination of the findings in this clinical trial is useful in establishing some understanding of what may be the therapeutic benefit of chiropractic treatment. In group A (received treatment), there was a correlation of improvements noted across the patient-centred questionnaires, SF-36 and disease-specific symptoms with findings of depression, anxiety and stress in asthma confirming the improved sense of wellbeing. The laboratory based physiological ‘biomarkers’ confirmed these findings. Peak Flow Meter self-monitoring supported the results of the laboratory based physiological ‘biomarkers’ of immune and stress response (IgA and cortisol levels).

The trend of improved lung function was most significant six weeks after completion of the ‘program of chiropractic care’. Spinal dysfunction at thoracic level 6 (T6) was a main focus of the chiropractic treatment (See Figure 33).

The significantly increased IgA levels coupled with the significant reduction in free unbound cortisol underpinned the results of the patient-centred research tools and the Peak Flow Meter recordings. A reduction of circulating cortisol was associated with the observed reduction in negative emotions. The lung function improvement observed by the asthma participants was associated with increased IgA levels. This is associated with a possible improvement in immune responsiveness for the asthma sufferer to both intrinsic and extrinsic asthma triggers. The reduced cortisol levels may also help to explain the trend of improved lung function observed in the scores of PEF increasing over the 14 weeks period. This trend of improvement in lung function was observed alongside the self-reported increased sense of physical and mental health in the asthma sufferer. The above combination of findings included a reduction in the negative emotions of depression anxiety and stress. These negative

emotions are associated with sudden exacerbations of asthma; an area of asthma management yet to be understood (297).

Combining all these early research observations, the findings of laboratory-based changes in neuro immune and neuroendocrine biomarkers (see Figure 27 and 32) are further corroborated by the improved lung function observed (see Figure 24). The responses from disease-specific, SF36 and DASS questionnaires supported the laboratory-based results with an associated sense of improved physical, mental and emotional wellbeing registered by the asthma sufferers themselves (see Figures 9, 10, 11 and 12). The 18 chiropractic treatments for spinal dysfunction in the asthma participants were predominantly administered at the level of the sixth thoracic vertebra (T6).

5.5.1 The body as a ‘whole’ rather than as the sum of its parts

Using a combination of research tools can be useful if the CAM system being researched sees the body as a ‘whole’ rather than as the sum of its parts. The combined data may assist in new understandings or clues to some aspects of whole health in an individual that are not yet understood.

A series of research tools can be developed to be supportive of each other in the areas of body function and health changes that may be linked in an underlying mechanisms of therapeutic benefits observed.

The findings of this clinical trial suggest that measuring the body as a ‘whole’ with a series of clinical research tools is appropriate for CAM healthcare with the nature of the CAM treatment being examined with a plausible biological mechanism of therapeutic benefit always in place (51).

Maintaining broad observations about the individual in the context of their asthma may require a dynamic perspective of combining all data about the ‘place and time’ in relation to their health profile. (322). Greater data collection from self-monitoring and other health

profiling tools may offer an interrelationship of findings. This is a non-reductionist research approach of 'real time' data modelling with self-monitoring and other health profiling tools with a fully computerised collection process suggested (324). Future research may include the development of a computerised process of 'real time' data collection and modelling. This may benefit future clinical research that seeks to use findings of health in an individual using in combination multi-factorial patient-centred questionnaires with other health profiling tools (325).

5.6 Reflections on the research model and the findings

There were limitations and challenges faced in this trial. They are presented here with discussion for the benefit of future research design.

This was a practice-based model in 'typical' chiropractic practices with RCT research elements. The planning and development cycle for the research design of the trial was lengthy. A number of preliminary studies were required to determine the research design and measurement tools appropriate for the research question. This was followed by the development of laboratory based biomarkers then used in the trial with laboratory technicians then required throughout the trial. There were unexpected costs of advertising as a large number of initial asthma participants interviewed did not progress to involvement in the trial. The rigour of the research data collection across three data collection phases with four groups of trial participants required high levels of participation and cooperation. There were difficulties with recruiting the number of trial participants required with costs of advertising, couriers and office administration ongoing. All participants that commenced the trial were well prepared for their time commitment, diligence required and consistency of data collection of the 14 week trial. However there were only 148 participants who commenced the trial. 142 participants completed the 14 week trial. Only 6 (4%) did not complete the trial.

A priori sample size of 420 participants had been determined for the trial for use in statistical review. This was not achieved. The trial was truncated due to time and resource constraints. The truncation at this lower number of participants is an acknowledged shortcoming of the trial.

This trial had a shortcoming in ‘a lack of defined chiropractic treatment’ in relation to the findings of therapeutic benefit for asthma. This clinical trial examined treatment by chiropractors using varying clinical techniques. The lack of one clinical technique used as the treatment may be considered a weakness in a trial examining for any therapeutic benefits from chiropractic treatment for asthma sufferers.

The chiropractic treatment received by the asthma sufferers in the 100 years of anecdotal reports of therapeutic benefit was likely to have been a range of techniques, from soft to firm to quite noxious in impact. Clinical techniques used in this trial were considered representative of ‘mainstream’ practice and varied from ‘softer touch, postural blocking with trigger point release’ to the hand-rotate and thrust of more forceful manipulation and/or adjustment styles. One clinical technique treated spinal dysfunction with a velocity-based thrust instrument called the ‘Activator’.

This trial used a research design of ‘no treatment’ as opposed to a sham of one clinical technique. This demonstrated some therapeutic benefit for asthma sufferers from chiropractic treatment. A previous study of chiropractic treatment for asthma had used ‘typical’ chiropractors also delivering a sham of their own clinical technique in the research design (56). A sham by definition does not produce a therapeutic benefit. This raises concerns in chiropractic and other CAM research when using a sham. The sham of one clinical technique may be considered therapeutic treatment in another clinical technique

The use of sham may never be effective for chiropractic and CAM healthcare research generally. In fact, there is only one CAM that has developed a sham which is being used

effectively in complex treatment practice-based research and within RCTs. The sham acupuncture needle is contributing to the understanding of the placebo effect of the acupuncture treatment and the effects of the therapeutic clinical encounter; though debated as to whether it is a true sham (81, 326). With the differing forces and techniques used in acupuncture and TCM, the sham is not fully accepted by that CAM as an appropriate research model (327). Without any therapeutic mechanism in place, both the treatment and the sham may produce therapeutic benefits, and contribute to confused research findings.

Particularly for the chiropractor in clinical practice, the lack of a specified clinical technique as the treatment used in the trial is a shortcoming of the trial. These readers may be naturally interested in the specific clinical technique demonstrated in the clinical trial to have offered some therapeutic benefit to the asthma sufferers. The preliminary observation for these chiropractors is that ‘typical’ or mainstream chiropractic treatment used in ‘typical’ practice has some therapeutic benefits for asthma. A description of the specific type of chiropractic manipulative procedure used for treating the asthma participants was not possible.

The specific type of chiropractic manipulative procedure or the most appropriate chiropractic clinical technique for treating presentations of asthma comorbidity will require further research. Such clarification may assist in the development of preliminary research into clinical guidelines for chiropractors involved in the treatment of asthma.

This trial only contributed to research of chiropractic treatment without the use of a sham. This trial has contributed to early observations of therapeutic benefit for asthma from ‘typical’ chiropractic treatment. The use of ‘no treatment’ rather than a sham is suggested as appropriate for future chiropractic and CAM clinical research.

The results of the trial suggest that a wide range of chiropractic clinical techniques produced the observed therapeutic benefit in asthma. The wide range of chiropractic clinical techniques used as the treatment in this trial may be seen as a weakness in that the observed therapeutic

benefits could be interpreted as being from the broader concept of ‘therapeutic touch’ generally.

It is to be noted that the trial specifically examined ‘typical chiropractors’ using mainstream clinical techniques as the treatment for asthma. The chiropractors recorded treatment of specific levels of the spine. They were using their clinical skills and judgement in determining the location and type of treatment required at each appointment and then administering this treatment to each individual asthma participant. A weakness of the trial is recognised in not including questions regarding their clinical reasoning in determining any treatment variation for a participant and why certain levels of the spine were treated more than others. Chiropractors in clinical practice use their clinical techniques and their clinical judgement in treatment decisions. Understanding the clinical decision-making process and the varying influences in that process will be the focus of a future clinical research questionnaire for the further research of chiropractic treatment for asthma.

The trial did not examine a range of providers administering a therapeutic touch. An unanswered question as to whether the broader concepts of ‘therapeutic touch’ were contributing to the findings of this research is valid. This shortcoming of the trial requires further research. CAM manipulative or body-based healthcare all shares a common factor of ‘therapeutic touch’. This common factor of ‘therapeutic touch’ is particularly relevant in the research of manipulative or body-based CAM healthcare. There is a variability of ‘therapeutic touch’ ranging from soft, hard, light or even a painful or noxious stimulation. Laboratory-based neurophysiological research into the nature of ‘therapeutic touch’ examining the somato-viscero-somatic reflexes may form part of the research approach into the plausible mechanism of therapeutic benefits of healthcare such as chiropractic and acupuncture (159, 309). Therapeutic touch, like the placebo, is an integral part of many CAM manipulative or body-based healthcare approaches. Its nature and therapeutic role as a common factor in

manipulative or body-based healthcare is yet to be understood. The common factor of 'therapeutic touch' may be developed with research as to its contribution to the efficacy of any CAM manipulative or body-based healthcare. Research measurements of 'therapeutic touch' as part of the healthcare exchange may be developed for future use in clinical research of chiropractic and CAM healthcare.

Healthcare research has an established pyramid of evidence; randomised controlled clinical trials (RCT) being the pinnacle of research evidence. This pinnacle of RCT examines for therapeutic efficacy with an internal validity of research construct: statistically developed to establish clinical significance or external validity of the treatment in the larger population (76).

Of a lower hierarchy of evidence in this established pyramid is the clinical trial of a pragmatic nature. Research that examines for any contributing factors to findings of therapeutic benefit is often a part of pragmatic clinical research not a RCT (328).

A short coming of the trial is that it was a mixed model of research. The research model examined chiropractic treatment for asthma using a randomised control method with three asthma participant groups with six different outcome measures including two laboratory-based biomarkers. This research focused on health in the individual asthma sufferer and the use of biomarkers to assess for any evidence of clinical efficacy of chiropractic treatment for asthma. The randomisation of the asthma participants examined the impact of the therapeutic interaction of the 'typical' practice setting. The treatment was not specified and controlled for the purposes of the research. The trial examined 'typical' chiropractic treatment in 'typical' chiropractic practice in the 'real world' of the asthma sufferers' daily routine.

The research was a pragmatic trial that included the asthma sufferers' daily routines, self-reporting and home-based data collection. These interactive clinical research elements were seen as an integral aspect of their AMP and an active aspect of the clinical trial for each participant. A short coming of the trial was not using any measure of the self-determining

behaviour within the research model as to whether it had a contribution to the therapeutic benefits observed.

Shortcomings of this trial are acknowledged. The study did not include a comprehensive 'Table 1' of randomisation for reader review of the trial processes. Only a basic table of age, gender and duration of asthma was included in the randomisation of the asthma participants in methods. This is acknowledged as a weakness.

Also, a multivariate analysis was not conducted to examine the impact on the research of the multiple variables across the randomised groupings. This is acknowledged as a weakness.

A shortcoming of the trial was not to have a double-blinding of the chiropractor and participant in the groupings. This would have enabled an examination of the chiropractors in their determination of levels of spinal dysfunction for treatment in asthma sufferers as opposed to non-asthma sufferers. This may have assisted in further observing the reasoning or decision-making process of the participating chiropractors in their clinical judgement of the levels of spinal dysfunction treated in the asthma sufferers. As the 'no treatment' group, group B asthma participants were not examined at all. This meant only asthma participants were treated and group B asthma participants were not touched.

Consequently, the 'no treatment' model of research may be considered a shortcoming of the trial which could have been overcome with a non-asthma participant group included in the clinical phase of the trial. This group could have been presented to the participating chiropractors as an asthma group to be examined but not treated.

This trial was limited in the use of only one therapeutic window; at 14 weeks or the end of the study. The clinical trial demonstrated some therapeutic benefits which are to be further researched in examining anecdotally reported benefits of chiropractic treatment for asthma. Although some of these benefits and physiological changes were sustained at 14 weeks a

second or even third window to observe any ‘therapeutic physiological activity’ may have been able to demonstrate any further sustained health improvements in the asthma participants. A research design that allows for observing cumulative therapeutic benefit over time is important for non-pharmaceutical treatment in CAM clinical research.

This trial’s research design included single blinding of the asthma participants in group B as to when their treatment would commence; the chiropractor needed to know whether treatment was to be given. This was to examine for the impact of receiving treatment compared to the participants who received all the benefits of the ‘typical’ practice except for treatment (group B). As this research model had no sham of the treatment there was no placebo effect from the chiropractor delivering the sham. There was however a placebo effect observed in the response of group B; whose participants experienced a change in their immune response and their DASS which indicated some anticipation factor that was not sustained after the clinical phase. These placebo-driven benefits of a non-specific nature observed in this trial may also be due to other as yet not understood factors of the chronic illness being examined (329).

A short coming of this clinical trial is that it has made a limited contribution to the understanding of placebo effects in the chiropractic clinical encounter.

It is suggested that the nature of this pragmatic trial may have allowed the group that attended the clinic but did not receive treatment to develop some awareness after a few weeks that they would not be receiving any treatment. Equally, the group that did receive the treatment may have become aware that this was going to happen throughout the clinical phase. While the blinding of the participants was carefully managed, there was no provision in the research trial to confirm participants in group B did not realize during the trial that they were in the ‘no treatment’ group. The trial did not use any research method to measure this question of successful blinding of participants in this trial.

A short coming of this trial was that it did not further factor in the ritual of the chiropractic clinical encounter and use more research tools for a more thorough examination in its research design.

The research of placebo as a valid therapeutic factor in patient-centred healthcare is suggested. A number of randomised groups of participants may examine the factors of the clinical encounter with patient-centred questionnaires to measure and monitor for any contributing therapeutic benefit. This may require randomised groupings involved in several phases of a research model. The participants informed of treatment and ‘no treatment’ phases and of the research value of their self-determining behaviours. This approach may see patient-centred elements of clinical research as contributing factors of therapeutic exchange in the clinical encounter (326). Clinical research tools that measure the ability of a patient to discern a therapeutic benefit occurring are a part of a patient-centred research approach (314). This clinical research approach is interactive; researcher, patient and caregiver give this research model the ability to be developed, working with its own strengths and weaknesses in examining the less understood area of placebo (212, 321).

5.7 Conclusions and future directions

The following summary of the results of the clinical trial are presented here and considered in the context of the aims and objectives as well as the limitations of this trial discussed earlier. This is followed by a direction of future research.

The first aim of this study was to determine if a ‘program of chiropractic care’ defined for the purposes of this trial as a ‘series of 18 chiropractic treatments’ produces any therapeutic benefit in the condition of asthma. Improvements in Peak Flow Meter monitoring of lung function (PEF), self-reported asthma signs and symptoms and two biomarkers of neuro-endocrine and immunological health changes indicated some therapeutic benefits for asthma

sufferers. The mechanism by which these early signs of therapeutic benefit may be occurring is not yet understood.

The second aim was to examine whether ‘a program of chiropractic care’ defined for the purposes of this trial as a ‘series of 18 chiropractic treatments’ may have any beneficial effects on the health of the individual with asthma. The use of a health-related Quality of Life questionnaire, the SF-36 short form and a self-scoring scale of negative emotional locus in asthma (DASS), showed early indications of improvement in the physical, mental and emotional health of the individual asthma sufferer within their experience of asthma with a ‘series of 18 chiropractic treatments’.

The third aim was to contribute to healthcare research and understanding of the pathophysiological mechanisms underlying asthma. The trial has demonstrated changes in two biomarkers of neuro-endocrine response and immune-responsiveness for the asthma participants who received the treatment. There is an early indication that healthier function of the respiratory system is demonstrated with the improving of PEF scores over the 14 weeks (see Figure 24, Chapter 4). These results suggest that there may be an impact on an underlying relationship between cortisol, IgA levels and the pathophysiological mechanisms that contribute to compromised lung function in asthma. Research of these underlying asthma pathophysiological mechanisms is indicated. It is suggested that research of neuro-endocrine and neuro-immunological factors as precipitating factors of the inflammatory pathway associated with asthma may contribute to greater understanding of asthma.

The fourth aim was to examine whether ‘a program of chiropractic care’, defined for the purposes of this trial, as a ‘series of 18 chiropractic treatments’ may have any role in managing asthma within an AMP. The findings of lung improvement (see Figure 24, Chapter 4) show that some therapeutic benefit for the asthma sufferer in their AMP may be occurring. The indication of overall positive improvement in the health of an individual with asthma was

documented with the use of self-monitoring in this trial. This self-monitoring may produce discernible self-determining health behavioural changes of therapeutic benefit for asthma (14). These early findings of ‘a program of chiropractic care’ within an AMP indicate that this is a practical and effective approach to researching chiropractic treatment for asthma. A patient-centred approach to asthma is an appropriate research model for further research.

The clinical trial also achieved *the specific objective of using patient-centered questionnaires for self-monitoring by the asthma sufferer in their AMP*. Patient-centred questionnaires were used in assessing the impact of a chiropractic program of care alongside the asthma sufferer’s medical management. The preliminary findings of this trial showed the possible contribution of the patient-centred questionnaires to the health of the asthma sufferer within their AMP. Further research of the appropriate use of self-monitoring for health changes in their asthma is encouraged as it increases the understanding of the asthma sufferers themselves.

Finally, *a combination of research tools (objective and subjective) was used to quantify any therapeutic benefits for asthma from ‘a program of chiropractic care’*. The research measures of the trial were a set of biomarkers of physiological change (objective or ‘hard’ measures) alongside a patient-centered set of questionnaires (subjective or ‘soft’ measures). While each has validity as a research measurement tool, the results from the softer measures of patient-centered questionnaires were corroborated by the use of a set of laboratory-based or ‘hard’ measures of biomarkers (IgA and cortisol).

Future research directions

From the introductory and background sections of this thesis it is apparent that endeavours underlying the development of the thesis extend to questions of how chiropractic is researched and how chiropractic as representative of CAM may be researched in the emerging healthcare delivery system.

The findings of this clinical trial of ‘a program of chiropractic care’ within an AMP indicate that a patient-centred approach to asthma is an appropriate research model for further research of chiropractic and other CAM modalities.

Health behavioural change is seen as a way of motivating people towards ‘keeping well’. A new style of research design for healthcare is emerging from the current predominantly ‘illness based medical model’ to a ‘model of health behavioural change’. This model may examine the nature of clinical decision-making in a patient-centred paradigm. Moving people towards ‘keeping well’ requires individual understanding of each person in their environment (76). Chronic illnesses such as asthma are particularly well suited to this research approach.

This new and developing research model of patient outcomes-centred healthcare may be used to address questions that are relevant to all health stakeholders relating to inefficiencies of healthcare delivery and the limited success to date of improving health outcomes for chronic multi-factorial conditions such as asthma (330).

Consumer driven healthcare can lead to greater choice in healthcare access as well as promote financial responsibility of consumers themselves. Patient satisfaction is an important measure of quality healthcare is. The health consumer is likely to become more selective in provider assessment, using provider report cards, to seek out both high patient satisfaction and good clinical outcomes (193).

The increasing use of CAM by health consumers makes it incumbent upon governments and health regulatory bodies to increase their understanding of its appeal and foster research to

understand its therapeutic mechanisms (331, 332). With over 80% of the world's population using some non-pharmaceutical healthcare, it is essential that any therapeutic benefits of CAM systems be investigated (4). This means placing the spotlight on research design and methodologies and other aspects.

Patient-centred models and integrative healthcare

Patient-centred healthcare means taking into account the patient's individual view of where their health goals should be taking them as well as their desire for information. It has a focus on the patient outcomes. It includes sharing decision-making and responding respectfully and iteratively to the presence of other health providers involved in the care of that patient whether by the patient's own decisions or by virtue of inherent respect for the patient's wellbeing (333).

Patient-centred healthcare has a focus on sound clinical judgement of the members of the provider team having regard to outcome objectives understood by the team and established with input from the patient; and further, sharing of knowledge and experience. This creates a patient-centred model of integrative health, focused on patient outcomes and patient self-determining behaviours -for long term results (334).

'Integrative medicine' and 'integrative healthcare' exist as concepts that adjust healthcare alliances to new theories of healthcare service delivery. These are considered methods of healthcare delivery that intend to involve health providers with a team approach to healthcare services. There are not as yet established models of this healthcare for the purposes of comparative effectiveness research (335, 336).

Chiropractic as a healthcare profession is in need not only of respect from the larger healthcare community, but professional unity. It is suggested that chiropractic research is in its infancy as a self-critical research discipline (337, 338).

Finally, it is suggested that this trial indicates that rigorous chiropractic clinical research would assist in the development of chiropractic as well as other CAM modalities as a healthcare choice in the emerging integration of a patient-centred healthcare delivery (28, 339).

Glossary

The following is a list of terms that appear in the thesis. Terms presented here may have different meanings. The following definitions are used in the context of this research study.

Activator Method – this is a chiropractic clinical technique used in treatment of spinal dysfunction. The Activator method uses an ordered series of ‘isolation tests’ conducted with the patient lying face down on the treatment table. A precise set or series of ‘instructed movements’ is required of the patient. The chiropractor notes changes in leg lengths of the prone patient during each of these ‘isolation tests’. These leg length changes are associated with different parts of the spine and related areas and assist in identifying levels of spinal dysfunction. A spring-loaded alterable velocity-based thrust instrument or mechanical hand-held device is used to deliver a thrust to a specific joint identified as showing dysfunction.

Acupuncture – this is a procedure of inserting and manipulating needles into various points on the body to relieve pain or for therapeutic purposes. Acupuncture is part of a whole Complementary and Alternative Medicine system (CAM) known as Traditional Chinese Medicine (TCM). TCM encompasses diet, the use of Chinese herbs, massage, and moxibustion (heat application on needle). Acupuncture, as a separate and simple treatment intervention, is usually administered by an acupuncturist but may also be used as an adjunctive therapy by many health providers.

Adjunctive therapy – this is a therapy occurring alongside a primary healthcare approach. The primary healthcare approach is taken to deliver the therapeutic effectiveness and the adjunctive therapy is taken to supplement the effect but not to supplant the efficacy of the primary healthcare approach.

Adjustment – this is a term used to describe treatment applied within a chiropractic clinical technique. A chiropractic adjustment is a clinical correction to an area of dysfunction as determined by the chiropractor using a chiropractic clinical technique. Typically, an adjustment treats spinal dysfunction (subluxation) of one or more levels of the spine or a related area, as identified by the chiropractor. An adjustment may be delivered by hand or by instrument depending on the chiropractic clinical technique.

Asthma – this is a common chronic disorder of the airways that is complex, recognised by the individual's limited capacity to breathe out. It is associated with a sense of chest tightness, excessive mucous production and a persistent cough.. The reversibility of an episode of asthma distinguishes asthma from other chronic lung conditions such as chronic obstructive pulmonary disease.

Asthma co-management – the patient and the medical provider are in a co-operative collaboration within the Asthma Management Plan. The plan is individually tailored for the asthma sufferer by the medical provider, encouraging shared responsibility in decision-making by the patient with a focus on self-education about their asthma profile. Co-management of the AMP requires the individual asthma sufferer to be more directly involved in his or her own asthma management decisions, with an emphasis on self-awareness. For the purposes of this clinical trial, this co-management approach to asthma saw the asthma participants active in their AMP and choosing to participate in a clinical trial of chiropractic intervention within their AMP.

Asthma Management Plan (AMP) – an active plan of management is shared between the medical doctor and the patient. There was an AMP endorsed by the Asthma Foundation of Australia, with the imprimatur of Australian health regulators, in operation during this clinical trial (2000-2003). The AMP requires the patient to self-monitor actively with the use of Peak Flow Meters measuring their lung function daily as their Peak Expiratory Flow.

Measurements are diarised and results recorded, enabling self-alerts to assist decision-making about their asthma health status. The shared decision-making between the medical doctor and the patient is taken to be a co-management approach. The patient is afforded some joint responsibility concerning the direction of his or her asthma management.

Chiropractic – this is a system of healthcare focusing on the balanced function of the nervous system and the interrelationships of structure and function in the health of the body.

Chiropractic treatment of dysfunction of the spine involves manipulation and adjustment of spinal segments and related areas. The chiropractor treats abnormal function (subluxation) of specific spinal segments or vertebrae clinically determined by the chiropractor as levels of spinal dysfunction. Chiropractic clinical management includes patient education about diet, lifestyle, exercise and other self-help advice.

Chiropractic clinical techniques – in a chiropractic practice, clinical techniques are used to determine the health needs of a patient and the therapeutic approach to be used for a patient.

Chiropractic clinical techniques differ as they depend on the particular philosophy and understanding of chiropractic being practiced. Each chiropractic clinical technique includes an assessment, examination and treatment approach.

Clinical techniques – clinical techniques are used to determine the health needs of a patient and the therapeutic approach to be used for a patient. These clinical techniques may differ as they depend on the particular healthcare system philosophy and understanding of healthcare being practiced.

Co-management in healthcare –co-management in healthcare requires more than a sharing of patients between healthcare providers. Case management strategy, including the actual achievement of agreed health outcomes for a patient, is co-managed by a team of healthcare

providers. Proactive co-operation between involved health providers is expected. There is a sense of equality not hierarchy inherent in this model.

Complementary and Alternative Medicine (CAM) – this is a medical system, practice or product not thought of as standard care in that society. In Australia, CAM connotes a non-conventional medical system.

Conventional medicine – this is the healthcare system considered by a society as their normal or conventional approach. Conventional medicine is seen as mainstream healthcare positioning that medical management approach as the rule or standard. This approach is usually administered by a doctor of medicine and an inclusion of any non-medical or adjunctive therapy is determined at the judgment of the doctor of medicine.

Gonstead Technique – this is a chiropractic clinical technique used in treatment of spinal dysfunction. The Gonstead Technique uses diagnostic monitoring of skin temperature change, X-ray analysis and palpation of the paraspinal tissues. The Gonstead Technique includes a pre-defined manner of manual adjustment to the precise level of the spine determined as showing the primary dysfunction.

Hawthorne effect – this is a confounding effect observed in research involving human exchange. It can be due to the potential effect of the enthusiasm of the participants involved in research or a clinical trial. This human factor of participation may skew research results of research with human participation required.

Integrative healthcare – this is an approach of shared responsibilities between healthcare providers that offer a seamless continuum of decision-making within a patient-centred healthcare paradigm and without hierarchical leadership. This involves a collaborative team approach for the benefit of the individual patient.

Integrative medicine – this is a combined approach of conventional and other (particularly Complementary and Alternative Medicine) therapies and services, offering a wholistic approach. It is a concept that considers some or all of the physical, psychological, social and spiritual wellbeing of the person. A characteristic, distinguishing this from ‘integrative healthcare’, is that the integrative effort is, to a material extent, by delegation from the provider of conventional medicine.

‘Mainstream clinical techniques’ - the term is used to describe treatment according to a number of different clinical techniques known to be used routinely by chiropractors in a ‘typical chiropractic clinic’. The actual day-to-day chiropractic treatments of the participating chiropractors were the experimental intervention in the clinical trial. The participating chiropractors were specifically requested to use their normal clinical techniques.

Manipulation – this is a term used in to describe treatment applied by a variety of chiropractic clinical techniques. Manipulation describes the manual delivery of a clinical correction by hand to a joint or joints to increase the range of motion. This is often the spine or spinal segments or vertebrae but includes other joints. The term manipulation is used by chiropractors, manipulative therapists, manipulative physiotherapists, osteopaths and medical providers of manipulative therapy.

Motion Palpation and Diversified Technique – this is a chiropractic clinical technique used in treatment of spinal dysfunction. Motion Palpation seeks to determine aberrant joint motion, especially fixations. This is done with active and passive movement of the joints and the corrections are manual manipulations of the joints determined to be limited in their range of motion. Diversified Technique uses many procedures to introduce motion into the spinal segment.

Placebo – this is a perceived effect recognised as a factor in human research and comes from the Latin ‘I shall please’. The powerful impact of the brain or mind on the body is seen with

the placebo effect. In clinical trials, the placebo effect can be caused by subjective perception of a therapeutic effect. The placebo effect can also occur as a normal consequence of human exchange in healthcare relationships. The mechanism of the placebo effect is not fully understood. It has been a confounding factor in some health research, and is recognised as an aspect of all clinical research to be measured. Increasingly it is measured as a legitimate contributing factor in the therapeutic benefits being examined.

Program of chiropractic care – this clinical trial examined an experimental intervention of a series of chiropractic treatments. This was described for this research purpose as a program of chiropractic care for the asthma participants. This program involved 18 separate appointments at the participating chiropractic clinics, as a six-week program of three times weekly chiropractic treatment.

Sacro-Occipital Technique (SOT) – this is a chiropractic clinical technique used in treatment of spinal dysfunction. The Sacro-Occipital Technique focuses on the cerebro-spinal fluid (CSF) and its flow within the spinal column. The SOT chiropractor uses triangular-shaped wedges or ‘blocks’ that reposition the pelvis, as well as manual treatments of specific dysfunction in the spine and related areas.

Sham – this is the administering of a pre-determined ‘like’ intervention in a clinical trial. The ‘sham’ is deemed by the researchers to have no therapeutic benefit and is able to be applied to participants without their realising any difference between the two applications. The ‘sham’ is to be ‘non-therapeutic’ and as a control and in the research outcomes offer no therapeutic benefit. For non-pharmaceutical research purposes such as this study, the validity of ‘sham’ is discussed as there is no established biological mechanism for therapeutic effect in the research model.

Spinal dysfunction – this is a loss or a restriction of normal movement and functioning of the spine. Spinal dysfunction, determined by a chiropractic clinical technique, refers to a loss or a restriction of the normal movement and functioning at specific vertebral levels.

Spinal levels – the term spinal levels refers to spinal vertebrae one by one, from the base of the skull to the sacrum/base of the pelvis. These spinal levels start below the skull and are called Cervical level (C) 1 through 7; Thoracic level (T) 1 through 12; and Lumbar level (L) 1 through 5.

Traditional medicine – this is a healthcare system, generally antecedent to the development of conventional medicine, considered by a society as the native or traditional approach usually administered by someone other than a doctor of medicine.

Typical or mainstream chiropractic – the ‘typical’ of anything is regarded as being a characteristic example, and ‘mainstream’ is regarded as being characteristic of an established field of activity. In this trial these terms are used regarding the experimental intervention described here:

Typical chiropractic clinic - the term is used to describe the daily practice of chiropractic, in actual practice settings, by chiropractors using their normal clinical techniques. This study was conducted in actual practices of the participating chiropractors. Specifically, normal daily practice routines were to be the research setting for the clinical trial. All participating clinic staff was required to maintain the normal procedures and protocols of the practice.

Vertebral subluxation – in general medical terminology, a ‘significant structural displacement’ is called a subluxation. In chiropractic terminology, a dysfunctional spinal segment or vertebral level, whether displaced significantly or not, is a subluxation. In vertebral subluxation, altered functioning of the spinal segment may irritate nerve roots and the blood vessels, which branch off from the spinal cord between each of the vertebrae. This

irritation may cause pain and dysfunction in muscle, lymphatic and organ tissue, as well as neurologic imbalance in the normal body processes.

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Story of this thesis

I am a registered chiropractor in full-time private practice and my practical and philosophical interest in the Australian healthcare system has remained my primary motivation throughout this candidature.

I have additional healthcare qualifications – a Doctor of Osteopathy (Sydney College), Diploma of Acupuncture (Australian Acupuncture Association), a Postgraduate Diploma in Western Herbal Medicine (Southern Cross School of Herbal Medicine), a Postgraduate Diploma in Chinese Herbal Medicine (Cathay Herbal) and I am a member of the Australian College of Nutritional and Environmental Medicine. My breadth of study and some 29 years as a primary health provider in private practice have inspired an interest in health systems and a patient-centred health paradigm. My research interest in the benefits of chiropractic treatment for patients presenting with a co-morbidity of asthma, developed while completing a Master of Science (Chiropractic) at Macquarie University, Sydney Australia. A continuing interest in patient-centred healthcare and the development of self-monitoring and individual health measurement systems underpinned my further study and research. I enrolled in the Department of Human Geography at Macquarie University focusing my PhD candidature on researching the traditions of clinical research methodology for use in developing a patient-centred health paradigm where individual responsibility for health outcomes could be measured and monitored. The initial focus was on understanding the individual experience of health within the experience of a chronic multi-factorial condition. Asthma was being examined as an example of a chronic multi-factorial condition with a unique profile of triggers in each individual.

While enrolled for this candidature in the Department of Human Geography, the Department of Chiropractic requested my involvement in a research grant for a clinical research trial of asthma and chiropractic. My candidature was considered an appropriate fit with the research project that had an interest in examining asthma and chiropractic. This research project team

was to have multi-disciplinary expertise as it would involve the Departments of Chiropractic, Biological Sciences and Human Geography. Being involved in a co-ordinated team that was to develop a clinical research trial of asthma and chiropractic, sat well with the research paradigm of my thesis. The team of multi-disciplinary researchers provided an excellent opportunity to develop my involvement in patient-centred health paradigms. My interest in clinical research models that might be able to examine a more integrative approach to health was accommodated with the opportunity to work with a number of different researchers on one project. The ability to develop research skills with these different disciplines in one team would foster self-critical thinking of ways to research within Evidence-Based Medicine (EBM) and Complementary and Alternative Medicine (CAM) and approach to the practice of chiropractic.

I was interested in the clinical reality of what a chiropractor does in practice. I had a research interest in the diversity of clinical techniques within the chiropractic profession and the range of clinical terms used in general chiropractic practice. I had previously been responsible, in 1992, for a pilot study examining chiropractic clinical findings when examining the spines of asthma sufferers.

From the outset of my involvement in the asthma project, I was directly involved in the clinical research modelling and the decision to use practising chiropractors in their 'typical' practices as part of this clinical research trial. I was interested in developing a selection of research tools for non-pharmaceutical healthcare or CAM treatments within a research design that may examine underlying biological mechanisms of treatment and individual health changes.

My involvement in the multi-disciplinary team led to my contribution to the writing of the funding proposal for a research trial involving asthma participants and an experimental intervention of actual practice-based chiropractic treatments.

As the trial took shape and began to be implemented, my involvement in its practical requirements and other research protocols also increased. My PhD candidature in clinical research of healthcare paradigms saw my role developing around the clinical research trial. My involvement included researching the appropriate research outcomes for use in the clinical trial. I played a major role in all the preliminary studies required for this selection process of the clinical research design. I was directly involved in developing and then maintaining clinical research protocols and standards of the trial. I have to date, made significant contributions to the writing of drafts for several co-authored papers on the study; yet to be published. My co-authors Dr Ray Hayek and Dr Sinan Ali have approved my writing of this thesis about the asthma study.

During my candidature, there was some re-organisation at Macquarie University which resulted in changes to the affiliations and responsibilities within the faculty. This saw my supervisors and eventually my department change. The shift in the focus of my candidature from the Department of Human Geography to the Department of Chiropractic seemed appropriate in view of my involvement in the clinical component of the asthma research trial. Subsequently, a second change of supervisors was required again due to unexpected university staff changes. All the changes required me to adapt on a continuing basis during the candidature, between a focus on theoretical constructs and the co-ordination of practical and research issues in the multi-site clinical trial. In summary, there have been a number of unexpected changes during my candidature, each requiring re-familiarisation and re-establishment of candidature research priorities.

The concept, design and execution of this clinical trial required and justified the range and diversity of academic input and research expertise given to it by the multi-disciplinary team. Co-ordination of research analysis required data to be duly examined in the context of

individual areas of expertise as well as 'in committee'. The requirement for review and discussion across the asthma research team has certainly resulted in unexpected time delays.

The timelines for trial completion, data collation and analysis, discussion of results, presentation of papers and co-ordination across the multi-disciplinary asthma research team has made this journey at the same time both challenging and satisfying.

My experience as a PhD candidate is that a well-organised collaborative approach to multi-disciplinary research is needed for CAM and chiropractic healthcare programs to be a part of the emerging healthcare system. The team approach to research may also foster a productive and self-critical research discipline for the development of chiropractic healthcare.

I thank Peter, Eleanor and Rosalind for their love and support during my involvement in this study and the writing of the thesis.

Appendix

Appendix

1. Ethics approval for the trial



6 November 2003

Dr Ray Hayek
Centre for Chiropractic
Department of Health & Chiropractic
Macquarie University NSW 2109

Reference: HE26SEP2003-R02633

Dear Dr Hayek

FINAL APPROVAL

Title of project: *A multisite trial: Chiropractic and asthma with physiological markers*

Your responses to the outstanding issues raised by the Committee have satisfactorily been addressed. You may now proceed with your research.

Please note the following standard requirements of approval:

1. Approval will be for a period of twelve months. At the end of this period, if the project has been completed, abandoned, discontinued or not commenced for any reason, you are required to submit a Final Report on the project. If you complete the work earlier than you had planned you must submit a Final Report as soon as the work is completed. The Final Report is available at <http://www.ro.mq.edu.au/ethics/human/forms>
2. However, at the end of the 12 month period if the project is still current you should instead submit an application for renewal of the approval if the project has run for less than three (3) years. This form is available at <http://www.ro.mq.edu.au/ethics/human/forms>. If the project has run for more than three (3) years you cannot renew approval for the project. You will need to complete and submit a Final Report (see Point 1 above) and submit a new application for the project. (The three year limit on renewal of approvals allows the Committee to fully re-review research in an environment where legislation, guidelines and requirements are continually changing, for example, new child protection and privacy laws).
3. Please remember the Committee must be notified of any alteration to the project.
4. You must notify the Committee immediately in the event of any adverse effects on participants or of any unforeseen events that might affect continued ethical acceptability of the project.
5. At all times you are responsible for the ethical conduct of your research in accordance with the guidelines established by the University (<http://www.ro.mq.edu.au/ethics/human>).

If you will be applying for or have applied for internal or external funding for the above project it is your responsibility to provide Macquarie University's Research Grants Officer with a copy of this letter as soon as possible. The Research Grants Officer will not inform external funding agencies that you have final approval for your project and funds will not be released until the Research Grants Officer has received a copy of this final approval letter.

Yours sincerely

Catrina Mackenzie

Dr Catriona Mackenzie
Chair, Ethics Review Committee (Human Ethics)

COPY



11 March 2002

Dr Ray Hayek
Department of Health & Chiropractic
Macquarie University

Reference: 26MAY2000-R042
FILE: 02/146

Dear Dr Hayek,

Title of project: "A multisite trial: chiropractic and asthma with physiological markers"

Thank you for your recent correspondence. Approval for renewal of the above application has been granted, effective 11 March 2002. The following are standard requirements attached to approval of all projects:

1. Approval will be for a period of twelve months. At the end of this period, if the project has been completed, abandoned, discontinued or not completed for any reason you are required to submit a Final Report on the project. If you complete the work earlier than you had planned you must submit a Final Report as soon as the work is completed. This form is available at http://www.ro.mq.edu.au/eth_hum3.htm
2. However, at the end of the 12 month period if the project is still current you should instead submit an application for renewal of the approval if the project has run for less than three (3) years. This form is available at http://www.ro.mq.edu.au/eth_hum3.htm. If the project has run for more than three (3) years you cannot renew approval for the project. You will need to complete and submit a Final Report (see Point 1 above) and submit a new application for the project. (The three year limit on renewal of approvals allows the Committee to fully re-review research in an environment where legislation, guidelines and requirements are continually changing, for example, new child protection and privacy laws).
3. Please remember you must notify the Committee in writing regarding any alteration to the project.

MACQUARIE UNIVERSITY
SYDNEY, NSW, 2109 AUSTRALIA

Chair: Ph: (02) 9850 8865 Fax: (02) 9850 8892 E-mail: cmackenz@scmp.mq.edu.au
Deputy Chair: Ph: (02) 9850 9859 Fax: (02) 9850 9890 E-mail: swyver@aces1.aces.mq.edu.au
Secretary: Ph: (02) 9850 7854 Fax: (02) 9850 8799 E-mail: rachael.krinks@mq.edu.au
http://www.ro.mq.edu.au/eth_hum.htm



25 July 2000

Mr Ray Hayek
Department of Chiropractic
Macquarie University

Reference: 26MAY2000-R042(JU)

Dear Mr Hayek,

Project Title: "A multisite trial: chiropractic and asthma with physiological markers"

The requested information and amended forms have now been reviewed and approved. You may proceed with your research.

With best wishes,

Associate Professor Judy A Ungerer
Chair, Ethics Review Committee (Human Research)

MACQUARIE UNIVERSITY		
SYDNEY, NSW, 2109 AUSTRALIA		
Telephone: (02) 9850 8045	Facsimile: (02) 9850 8062	E-mail: judy.ungerer@mq.edu.au
Telephone: (02) 9850 7854	Facsimile: (02) 9850 8799	E-mail: rachael.krinks@mq.edu.au



3 August 2001

Dr Sinan Ali
Department of Biological Sciences
Macquarie University

Reference: 01/04/LAB

Dear Dr Ali,

FINAL APPROVAL LETTER

Project title: "Multicentre Asthma trial"

At its meeting on 26 July 2001 the Biosafety Committee granted final approval for laboratory work on samples relating to the above project to commence.

Approval is for a 3 year period. At the end of 12 months you are required to submit a progress report (if the project is continuing). Upon completion of the project or if it is discontinued for any reason you should submit a final report. Both forms are located at http://www.ro.mq.edu.au/eth_bio3.htm.

Please note it is your responsibility as Chief Investigator to notify co-investigators (and your supervisor if you are an Honours or Postgraduate student) of the approval and conditions of approval, if any.

Please remember that you must notify the Committee in writing and apply for Committee approval if you wish to change the project aims or procedures in any way or if you wish to add investigators to your project. You must also notify the Committee in writing immediately in the event of any unforeseen events that might affect continued acceptability of the project. At all times you are responsible for the conduct of your research in accordance with the guidelines established by the University. These guidelines can be found at www.ro.mq.edu.au/ethics.htm and www.ro.mq.edu.au/eth_bio2.htm.

Please cite the above reference on future correspondence.

Yours sincerely,

A/Professor Millar Whalley
Chair, Biosafety Ethics Committee

**MACQUARIE UNIVERSITY
SYDNEY, NSW, 2109 AUSTRALIA**

Chair: Telephone: (02) 9850 8200
Biosafety Officer: Telephone: (02) 9850 8185
Secretary: Telephone: (02) 9850 7854

E-mail: mwhalley@rna.bio.mq.edu.au
E-mail: dveal@rna.bio.mq.edu.au
E-mail: rachael.krinks@mq.edu.au

Appendix

2. Consent forms



PARTICIPANTS CONSENT FORM

Dear Participant,

You are invited to participate in a clinical study of patients with asthma and chiropractic care being conducted at Macquarie University by Dr. Ray Hayek (Chief investigator; Ph [REDACTED]), Dr. Sinan Ali (9850 6420), Dr. Peter Curson (9850 6420), Dr. Robyn Beirman (9850 6420) and Dr. Sue-Ellen McKelvey ([REDACTED]). The study is looking at the relationship between chiropractic manipulation of the spine and its health benefits to the people with asthma.

During the study, you will maintain your current medical treatment and prescribed management of asthma. The Doctor involved with this study, may need to ask you some questions about your current asthma treatment and management.

I understand that my participation in the study is voluntary. I may withdraw my consent and discontinue participation at any time without having to give a reason and without penalty or prejudice. I understand that no payment is involved.

Like with any medical procedure, some complications may occur following chiropractic care. These are:

- Muscle soreness – happens in one out of 1,000 cases (it may last up to 3 days).
- 'Sympathetic storm' sign – happens in one out of 50,000 cases (harmless stress response that lasts for 5 minutes).
- Moderate stroke – happens in one to three out of 1,000,000 cases.

Chiropractors in the study are licensed to practice and will give you safety-screening test before the procedure. If you experience any pain or discomfort, you can contact either your chiropractor or the Project Coordinator Mrs. Chandrika Subramanyam (Tel: 02 [REDACTED]) for help.

I understand that I will be receiving free chiropractic care for 6 weeks, total of 18 sessions. Each session will take between 15 to 30 minutes. This is to take place at approved clinics involved in this university study.

I understand that I will be required to have X-rays of the spine, free of charge. This is to exclude any underlying problems for which the chiropractic care is not suitable. These include bone disease like arthritis and fractures.

I understand that I will be asked for morning and evening saliva samples for the period of 14 weeks.

Any information or personal details gathered in the course of the study are confidential and will be treated as such. No individuals will be identified in any publications of the results. Data will be stored at the Department of Chiropractic with the chief investigator Dr. Ray Hayek

MACQUARIE UNIVERSITY-NSW 2109 AUSTRALIA
Tel: (02) 9350 6420 - Fax: (02) 9350 6066
Email: asthma@mq.edu.au

YOUR SALIVA SAMPLES WILL NOT BE USED FOR DNA ANALYSIS

I _____, have read and understand the information above.
Participant (Parent/Guardian, if under 16 years)

The questions I have asked have been answered to my satisfaction. I agree to participate in this study, knowing that I can withdraw at any time. I understand that I will be given a copy of this form to keep.

Participant's (Parent/Guardian) signature:

_____ **Date:** _____

Investigator: _____ Signature: _____

Date: _____

The ethical aspects of this study have been approved by the Macquarie University Ethics review Committee (Human Research). If you have any complaints or reservations about any ethical aspect of your participation in the study, you may contact the Research Ethics Officer: Telephone (02) 9550 4444, fax (02) 9550 4444, Email kdesilva@vc.mq.edu.au. The matter will be treated in confidence, investigated and you will be informed of the outcome.

Please fill out and return this form in the reply paid envelope provided



Group D

PARTICIPANT CONSENT FORM

Dear Participant,

You are invited to participate in a clinical study conducted at Macquarie University by Dr. Ray Hayek (Chief investigator; Ph ~~9850 6062~~), Dr. Sinan Ali (~~9850 8144~~), Dr. Peter Curson (~~9850 8146~~), Dr. Robyn Beirman (~~9850 8092~~), Dr Sue-Ellen McKelvey (~~9851 8144~~). The study will look at the relationship between chiropractic manipulation of the spine and its health benefits to the people with asthma. Your role in this trial, being a non-asthmatic, is to act as a 'control' subject.

Please read the following information and fill out the bottom portion before returning it in the enclosed envelope.

I understand that my participation in this study is voluntary, and that I may withdraw my consent and discontinue participation at any time without giving any reason and without penalty or prejudice.

I understand that as a control patient, I will not receive any chiropractic treatment during the 14- week program of care.

I understand that I will give saliva samples 3 days per week; twice daily for the entire 14 weeks I am involved in the trial.

Any information or personal details gathered in the course of this study are confidential and will be treated as such. No individuals will be identified in any publication of the studies results. Data will be stored at the Trial Head Office in E78, with the Project Coordinator Mrs Chandrika Subramanyam (98506420)

Participant to sign

I ----- have read and understand the above information.

Please print name

Participant signature (parent/guardian if under 16 years) -----

Date: -----

Investigator to sign

Investigator: ----- Signature: -----

Date: -----

YOUR SALIVA SAMPLES WILL NOT BE USED FOR DNA ANALYSIS

The ethical aspects of this study have been approved by the Macquarie University Ethics review committee (Human Research). If you have any complaints or reservations about any ethical aspects of your participation in this study, you may contact the Research Ethics Officer: Telephone (02) 9850 7854, fax (02) 9850 7854, Email: kdesilva@vc.mq.edu.au. The matter will be treated in confidence, investigated and you will be informed of the outcome.

Macquarie University Ethics Officer: Telephone (02) 9850 7854, fax (02) 9850 7854, Email: kdesilva@vc.mq.edu.au. The matter will be treated in confidence, investigated and you will be informed of the outcome.

Appendix

3. Questionnaire:
Asthma profiling and disease-specific

Set 1

1



Asthma Information Questionnaire

Asthma Trial 2001

Code:

Name _____

Address _____

_____ Post Code _____

Age _____ Date of Birth ____/____/____ Sex _____

Height _____ Weight _____

1. Which of the following best describes your occupation? (*please tick*)

- | | |
|--------------|--------------------------|
| Student | <input type="checkbox"/> |
| Office Work | <input type="checkbox"/> |
| Professional | <input type="checkbox"/> |
| Tradesman | <input type="checkbox"/> |
| Blue Collar | <input type="checkbox"/> |
| Home Duties | <input type="checkbox"/> |
| Unemployed | <input type="checkbox"/> |
| Pensioner | <input type="checkbox"/> |
| Other _____ | |

2

2. How long have you lived at the current address? *(please circle)*

less than 1 yr
1 – 4 yrs
5 – 10 yrs
more than 10 yrs

3a. Is your dwelling/house –

(please tick)

Free-standing house? ☐
Semidetached house? ☐
Terrace house? ☐
Flat? ☐
Caravan? ☐

b. located on -

½ acre house block? ☐
more than 1 acre house block? ☐

4. Approximately, how old is your dwelling/house? *(please circle)*

1 – 5 yrs
6 – 15 yrs
16 – 25 yrs
26 – 50 yrs
over 50 yrs

5. Is the floor of your general living:

(please tick)

On the ground? ☐
On second level? ☐
On third level? ☐
Higher than 3 stories? ☐
Other _____

6. Materials used for **external** walls are mostly:

☐
Brick ☐
Timber ☐
Fibro ☐
Other _____

7. Materials used for **internal** walls are mostly:

☐
Brick ☐
Timber ☐
Plaster ☐
Fibro ☐
Other _____

8. Materials used for **roof** are mostly:

Iron ☐
 Tiles ☐
 other _____

9. Materials used for **floor** are mostly

timber ☐
 cement ☐
 other _____

10. The floor covering in the **bedroom** you sleep in is mostly:

Carpet ☐
 Timber floor ☐
 Tiles ☐
 other _____

11. The floor covering in **living areas** is mostly:

Carpet ☐
 Timber floor ☐
 Tiles ☐
 other _____

12. Have you ever noticed surface mould (mildew) within the house? (*please circle*)

YES / NO

13. For what months of the year is the house regularly heated?

Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

14. In winter, is the house **heated** mostly by:

(*please tick*)

Open fire? ☐
 Fluted gas heater ☐
 Electric heater ☐
 Other _____

15. In summer, is the house **cooled** mostly by:

Fixed ceiling fan? ☐
 Portable electric fan? ☐
 Evaporative cooler? ☐
 Air-conditioning? ☐
 Other _____

16. Do you have **air-conditioning** at work? (*please circle*)

YES / NO / NOT APPLICABLE

17. Are your **cooking appliances** at home operated by:

GAS? / ELECTRICITY?

Other _____

18. Do you have pets in your house? YES / NO

If yes, please circle

Cat
Dog
Bird
other _____

19. Have you ever smoked?

No ☐ (go to question 22)
Yes ☐

20. How many years have you smoked for? _____

21. Are you currently smoking? YES ☐

a) No, I stopped less than 3 months ago ☐

b) No, I stopped 4 - 6 months ago ☐

c) No, I stopped 7 - 12 months ago..... ☐

d) No, I stopped more than 12 months ago..... ☐

22. Do any people in your house smoke?YES / NO

If YES, do they smoke:

a) Daily ?..... ☐

b) Weekly? ☐

c) Monthly ? ☐

23. Have you got any known allergies?..... YES / NO

If yes, please specify
.....
.....

24. Do you take any vitamin supplements regularly?YES / NO

a) Vitamin A & B ☐

b) Vitamin C ☐

c) Other _____

25. Were you born in Sydney? YES / NO

Other place

26. Have any members of your immediate family ever suffered from asthma?

	Please circle	
Mother	YES / NO	
Father	YES / NO	
Sister/s	YES / NO	X
Brother/s	YES / NO	X

27. At what age did your first asthma attack occur?.....

5

28. When did you have your last attack?.....

29. How frequently have the attacks occurred in the last 12 months?

- a) None in the past year ☐
- b) 1-6 attacks in the past year ☐
- c) 1-3 attacks per month ☐
- d) 1-3 attacks per week ☐
- e) daily ☐

30. Please tick the appropriate box to indicate how often you have experienced the following symptoms in the last 12 months associated with asthma?

	Never	Occasionally	Most days	Every day
CHEST				
Cough				
Phlegm				
Wheeze				
Tightness in the chest				
Difficulty breathing				
NASAL				
Sneeze				
Runny nose				
Blocked nose				
Itchy nose				
Sinus problems				
EYE				
Red eye(s)				
Itchy eye(s)				
Watery eye(s)				
OTHER				
Hives or itchy skin				
Migraine headaches				
Vomiting				
Diarrhoea				

31. How has your **usual** asthma (*not your bad attacks*) interfered with your normal daily activities in the last 12 months?

- a) No asthma symptoms in the last 12 months ☐
- b) Able to perform all normal daily activities ☐
- c) Able to perform most normal daily activities ☐
- d) Unable to perform normal daily activities ☐

6

32. How have your **bad** asthma attacks (*not your usual asthma*) interfered with your normal daily activities in the last 12 months?

- a) No asthma attacks in the last 12 months ☐
- b) Able to perform all normal daily activities ☐
- c) Able to perform most normal daily activities ☐
- d) Unable to perform normal daily activities ☐

33. How often have you taken any of the following medications for asthma or wheezy breathing in the past 12 months?

Please circle all relevant medications ↓	a) Never	b) A few times in the last 12 months	c) A few times a month	d) A few times a week	e) On most days	f) Frequently, on most days
i) Puffer or nebuliser reliever. eg Ventolin, Asmol, Bricanyl, Berotec, Respolin, Airmir, Atrovent, Serevent, Foradile, Oxis						
ii) Tablet reliever. Nuelin, Theodur,						
iii) Puffer preventer eg Intal, Intal Forte, Tilade						
iv) Puffer steroid preventer eg Becotide, Becloforte, Aldecin, Pulmicort, Flixotide, Respocort						
v) Oral tablet preventer Sinulair, Accolate						
vi) Oral steroid tablets eg Prednisone or Prednisolone						

7

34. In the last month, how many times per day did you take your bronchodilator puffer?

- a) Rarely..... ☐
- b) Once per day..... ☐
- c) Twice daily..... ☐
- d) 3-4 times per day..... ☐
- e) More than 4 times per day..... ☐

35. During what period of the day are your asthma attacks most severe?

- a) During the early hours of the morning / upon wakening..... ☐
- b) During the middle of the day..... ☐
- c) During the afternoon / early evening..... ☐
- d) Late at night / during sleep..... ☐

36. Do you ever wake at night with chest tightness, wheeze or cough?

- a) Never..... ☐
- b) A few times per year..... ☐
- c) A few times per month..... ☐
- d) A few times per week..... ☐
- e) Most nights..... ☐

37. Upon awakening, do you experience chest tightness / difficulty in breathing / wheezing/coughing?

- a) Never..... ☐
- b) A few times per year..... ☐
- c) A few times per month..... ☐
- d) A few times per week..... ☐
- e) Most mornings..... ☐

38. Are your attacks of asthma or wheeze brought on or made worse by any of the following?

	Yes	No	Don't know
a) Contact with cosmetics/perfumes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
b) Contact with insecticides	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c) Contact with cigarette smoke.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
d) Eating certain foods / drinks.....	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
e) Other (please describe)			

8

39. Are your attacks of asthma or wheeze brought on or made worse by any of the following?

	Yes	No	Don't know
a) House cleaning, Bed making, or Sweeping?.....			
b) Working with particular gases/dusts/fumes/smells?...			
c) Mowing the lawn / exposure to grasses?.....			
d) Exposure to pollens?.....			
e) Other (please describe) _____			

f) Sudden upset or worries			
g) Being in an airconditioned room?.....			
h) Other (Please describe) _____			

i) Contact with cats.....			
j) Contact with dogs.....			
k) Contact with birds or feathers.....			
l) Contact with other animals.....			
m) Other (please describe) _____			

40. Which is/are the worst month(s) of the year for your asthma?
(please tick as many as is required)

Same all year round..... ☐

January	February	March	April
May	June	July	August
September	October	November	December

9

41. Do certain weather conditions or changes in temperature bring on your asthma or wheeze, or make it worse?

	Yes	No	Don't know
a) Sudden changes in weather			
b) Cold weather			
c) Hot weather.....			
d) Rapid change in temperature			
e) Other(please describe)_____			

42. Do attacks seem to occur

	Yes	No	Don't know
a) In the house?			
b) In the classroom?			
c) At your workplace?			
d) Outdoors?			
e) Other (please describe)_____			

43. Do certain rainfall conditions bring on your asthma or wheeze, or make it worse?

	Yes	No	Don't know
a) Wet weather			
b) Dry weather			
c) Storm			
d) Other (please describe)_____			

44. Do certain wind conditions or changes in wind direction bring on your asthma or wheeze, or make it worse?

	Yes	No	Don't know
a) Windy weather (in general)			
b) Wind from a particular direction			
c) Other (please describe)_____			

45. Do certain localities bring on your asthma or wheeze, or make it worse?

10

- a) Sea side / low altitude locality
b) Mountain areas / high altitude locality
c) City environs / dense living
d) Plains environs / farm living
e) Other (please describe) _____

Yes	No	Don't know

**Thank you for taking the time to complete
this Questionnaire.**

Appendix

4. Questionnaire:

SF – 36

CODE:

Short Form 36 (SF-36) Standard US Version 1.0: English

SF-36 HEALTH SURVEY

INSTRUCTIONS: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

(circle one)

Excellent 1
 Very good 2
 Good 3
 Fair 4
 Poor 5

2. Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago 1
 Somewhat better now than one year ago 2
 About the same as one year ago 3
 Somewhat worse now than one year ago 4
 Much worse now than one year ago 5

SF-36 Standard US Version 1.0: English (continued)

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

(circle one number on each line)

ACTIVITIES	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
a. Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing several flights of stairs	1	2	3
e. Climbing one flight of stairs	1	2	3
f. Bending, kneeling, or stooping	1	2	3
g. Walking more than a mile	1	2	3
h. Walking several blocks	1	2	3
i. Walking one block	1	2	3
j. Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(circle one number on each line)

	YES	NO
a. Cut down on the amount of time you spent on work or other activities	1	2
b. Accomplished less than you would like	1	2
c. Were limited in the kind of work or other activities	1	2
d. Had difficulty performing the work or other activities (for example, it took extra effort)	1	2

SF-36 Standard US Version 1.0: English (continued)

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(circle one number on each line)

	YES	NO
a. Cut down the amount of time you spent on work or other activities	1	2
b. Accomplished less than you would like	1	2
c. Didn't do work or other activities as carefully as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

(circle one)

Not at all 1
 Slightly 2
 Moderately 3
 Quite a bit 4
 Extremely 5

7. How much bodily pain have you had during the past 4 weeks?

(circle one)

None 1
 Very mild 2
 Mild 3
 Moderate 4
 Severe 5
 Very severe 6

SF-36 Standard US Version 1.0: English (continued)

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all 1
 A little bit 2
 Moderately 3
 Quite a bit 4
 Extremely 5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks -

(circle one number on each line)

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	None of the Time
a. Did you feel full of pep?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt calm and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and blue?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
h. Have you been a happy person?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

SF-36 Standard US Version 1.0: English (continued)

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(circle one)

- All of the time 1
- Most of the time 2
- Some of the time 3
- A little of the time 4
- None of the time 5

11. How TRUE or FALSE is each of the following statements for you?

(circle one number on each line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
a. I seem to get sick a little easier than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

Appendix

5. Questionnaire: DASS (scoring)

Depression, Anxiety Stress Scale (DASS)	Code:	Date:
--	-------	-------

Please read each statement and circle a number 0,1,2 or 4 which indicates how much the statement applied to you *over the past week*. There are no right or wrong answers. Do not spend too much time on any statement.

The rating scale is as follows:

- 0 Did not apply to me at all
- 1 Applied to me to some degree, or some of the time
- 2 Applied to me to a considerable degree, or a good part of the time
- 3 Applied to me very much, or most of the time

1	I found myself getting upset by quite trivial things	0	1	2	3
2	I was aware of dryness of my mouth	0	1	2	3
3	I couldn't seem to experience any positive feeling at all	0	1	2	3
4	I experienced breathing difficulty (eg. Excessively rapid breathing, breathlessness in the absence or physical exertion)	0	1	2	3
5	I just couldn't seem to get going	0	1	2	3
6	I tended to over-react to situations	0	1	2	3
7	I had a feeling of shakiness (eg. Legs going to give way)	0	1	2	3
8	I found it difficult to relax	0	1	2	3
9	I found myself in situations that made me so anxious I was most relieved when they ended	0	1	2	3
10	I felt that I had nothing to look forward to	0	1	2	3
11	I found myself getting upset rather easily	0	1	2	3
12	I felt that I was using a lot of nervous energy	0	1	2	3
13	I felt sad and depressed	0	1	2	3
14	I found myself getting impatient when I was delayed in any way (eg. Lifts, traffic lights, being kept waiting)	0	1	2	3
15	I had a feeling of faintness	0	1	2	3
16	I felt that I had lost interest in just about everything	0	1	2	3
17	I felt I wasn't worth much as a person	0	1	2	3
18	I felt that I was rather touchy	0	1	2	3
19	I perspired noticeably (eg. Hands sweaty) in the absence of high temperatures or physical exertion	0	1	2	3

Please turn the page

Reminder of rating scale:

- 0 Did not apply to me at all
 - 1 Applied to me to some degree, or some of the time
 - 2 Applied to me to a considerable degree, or a good part of the time
 - 3 Applied to me very much, or most of the time
-

20	I felt scared without any good reason	0	1	2	3
21	I felt that life was worthwhile	0	1	2	3
22	I found it hard to wind down	0	1	2	3
23	I had difficulty in swallowing	0	1	2	3
24	I couldn't seem to get any enjoyment out of the things I did	0	1	2	3
25	I was aware of the action of my heart in the absence of physical exertion (eg, sense of heart rate increase, heart missing a beat)	0	1	2	3
26	I felt down-hearted and blue	0	1	2	3
27	I found I was very irritable	0	1	2	3
28	I felt I was close to panic	0	1	2	3
29	I found it hard to calm down after something upset me	0	1	2	3
30	I feared that I would be 'thrown' by some trivial but unfamiliar task	0	1	2	3
31	I was unable to become enthusiastic about anything	0	1	2	3
32	I found it difficult to tolerate interruptions to what I was doing	0	1	2	3
33	I was in a state of nervous tension	0	1	2	3
34	I felt I was pretty worthless	0	1	2	3
35	I was intolerant of anything that kept me from getting on with what I was doing	0	1	2	3
36	I felt terrified	0	1	2	3
37	I could see nothing in the future to be hopeful about	0	1	2	3
38	I felt that life was meaningless	0	1	2	3
39	I found myself getting agitated	0	1	2	3
40	I was worried about situations in which I might panic and make a fool of myself	0	1	2	3
41	I experience trembling (eg, in the hands)	0	1	2	3
42	I found it difficult to work up the initiative to do things	0	1	2	3

*Lovibond S.H., Lovibond, P.F. Depression Anxiety Stress Scales (DASS)
Australia, Psychology Foundation of Australia: 1995*

Appendix

6. Peak flow meter reading

CODE:

2121

Peak Flow Meter Record Sheet

This is your Peak Flow Meter (PKM) record sheet. Each time you take a PFM reading, please record the results using the instructions set out below. Only record the highest (1) of (3) tries, and take any medications after you have completed your reading.

How to use a PFM

1. Hold the meter without obstructing the scale.
2. Breathe in as deeply as you can and place lips tightly around mouthpiece, biting lightly.
3. Blow as **hard and as fast as possible – in a short sharp blast**. Do NOT cough or spit into the meter as this may effect its normal functioning.

How to chart your reading

On Tuesday, Thursday and Sunday of each week we would like you to take (2) readings per day – (1) at 8am and (1) at 8pm. Please mark the exact time reading is taken i.e. 8.07.

Mark your AM (morning) results in the grey columns and PM (evening) results in the white columns with a dot or a cross. An example is given below:

Week 1	
14/3/01	
AM	PM
8.01	7.43
450	450
400	400
300	300
200	200
100	100
50	50

← Date
← Exact time sample is taken
← Peak Flow Measurement

Please mark on this scale of 1 - 10 the severity of symptoms you are experiencing as you take your PFM reading. Ten (10) represents an emergency trip to the doctor, and One (1) represents having no symptoms at all.

Week 1						Week 2					
29/01		31/01		3/2		5/2		7/2		10/2	
AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
8.15	7.50	7.30	7.50	8.15	7.30	8.15	8pm				
650	650	650	650	650	650	650	650	650	650	650	650
600	600	600	600	600	600	600	600	600	600	600	600
550	550	550	550	550	550	550	550	550	550	550	550
500	500	500	500	500	500	500	500	500	500	500	500
450	450	450	450	450	450	450	450	450	450	450	450
400	400	400	400	400	400	400	400	400	400	400	400
350	350	350	350	350	350	350	350	350	350	350	350
300	300	300	300	300	300	300	300	300	300	300	300
250	250	250	250	250	250	250	250	250	250	250	250
200	200	200	200	200	200	200	200	200	200	200	200
150	150	150	150	150	150	150	150	150	150	150	150
100	100	100	100	100	100	100	100	100	100	100	100
50	50	50	50	50	50	50	50	50	50	50	50

Scale of symptoms – PLEASE MARK

High 10											
5	5	5	5	5	5	5	5	5	5	5	5
Low 1											

REMINDER:
FILL IN YOUR
QUESTIONNAIRES
THIS WEEK

*from week 3 - handwriting became extremely untidy + erratic
 - ? chiropractic + ment?

CODE: 2121

Peak Flow Meter Record Sheet

asthma attack

Week 3						Week 4						Week 5						Week 6					
12/2	14/2	17/2	19/2	21/2	24/2	26/02	28/02	3/03	5/3	7/3	10/3	12/2	14/2	17/2	19/2	21/2	24/2	26/02	28/02	3/03	5/3	7/3	10/3
AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
				1040	730	730	870	730	870	725	870	725	870	730	870	730	870	730	870	730	870	870	870
650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650
600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600
550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550
500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500
450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450
400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400
350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350
300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250
200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200
150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50

Scale of Symptoms

Please mark the severity of your asthma symptoms with a dot or a cross each time you take a saliva sample. 10 = Severe; 1 = None

10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

← Exema →
 Started + allergic eyes

— usually cannot run long distance — this was amazing →

(Tues, Wed, Thurs + Fri — lots of cross country running at school (2nd place))

CODE: 2121

Peak Flow Meter Records Sheet

Week 7						Week 8						Week 9						Week 10					
12/3	14/3	17/3	19/3	21/03	24/3	26/3	28/3	31/3	2/4	4/4	7/4	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
730	8p	730	730	8	8	745	8p	730	8	8	730	730	8p	8p	8p	8p	8p	730	730	8p	8p	8p	8p
650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650
600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600
550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550
500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500
450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450
400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400
350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350
300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250
200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200
150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50

Scale of Symptoms

Please mark the severity of your asthma symptoms with a dot.

Mark each time you take a saliva sample. 10 = Severe; 1 = None

10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

asthma REMINDER:
 - asthma
 - allergies
 - eye allergy
 - coughing
 - 1/2 of sinus congestion

eye
 allergy

eye allergy

eye allergy

eye allergy

head
 crawling
 in
 evening

CODE: 2121

Peak Flow Meter Records Sheet

Week 11						Week 12						Week 13						Week 14					
9/4	11/4	14/4	16/4	18/4	21/4	23/4	25/4	28/4	30/4	2/5	5/5	9/4	11/4	14/4	16/4	18/4	21/4	23/4	25/4	28/4	30/4	2/5	5/5
AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
6.45	8pm	7am	8pm	8am		8	8	8	8pm	8am		8	8	8	8pm	8	8	8	8	8	8	8	8
650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650
600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600	600
550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550	550
500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500
450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450	450
400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400	400
350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350	350
300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300	300
250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250	250
200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200
150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150
100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50

Scale of Symptoms

Please mark the severity of your asthma symptoms with a dot
Or a cross each time you take a saliva sample. 10 = Severe: 1 = None

10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

butch
sore
throat,
eye allergy
persists, still
using drops.

Croaky
voice
little
wheezy.

REMINDER:
FILL IN YOUR
QUESTIONNAIRES
THIS WEEK

Appendix

7. Clinical recording sheet

Please ensure you complete the page clearly at the time of each appointment.

Date: _____ Time: _____ Patient: _____ Code: _____

Any increase/decrease in signs or symptoms	Yes/No	Other Comments
Any other new therapy	Yes/No	
Any other problems?	Yes/No	

Treatment Steps:

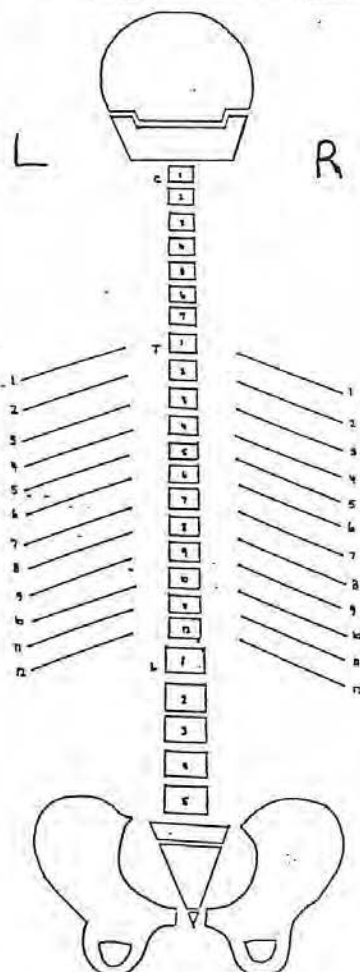
1. Tick box below pre-adjustment protocol

PA	<input type="checkbox"/>
G	<input type="checkbox"/>
M	<input type="checkbox"/>
LL	<input type="checkbox"/>
AL	<input type="checkbox"/>
XR	<input type="checkbox"/>

FT	<input type="checkbox"/>
MP	<input type="checkbox"/>
SP	<input type="checkbox"/>
N	<input type="checkbox"/>
IT	<input type="checkbox"/>

2. Indicate precise area of spinal dysfunction/ subluxation

e.g. ☒ 2 or ☐ 2 or ☒ 3



3. Please write below findings (o/e) and describe adjustments or tech. Jargon (Rx)

O/E
Rx

Key:

PA Postural Analysis
G Gait Observation
M Mobility Observation
LL Leg Length
AL Arm Length
XR X-ray Analysis

FT Fossa Test
MP Motion Palpation
SP Static Palpation
N Nervoscope
IT Isolation Tests

AM ☐ Activator Method
G ☐ Gonstead Technique
SOT ☐ Sacro Occipital Technique
MP ☐ Motion Palpation Technique

Doctor sign on completion

Appendix

8. Participant information package



(Insert date)

Dear «First»,

Thank you for your interest in the Asthma Trial, conducted by the Macquarie University Stress and Spine Research Unit. We appreciate the time you have taken to contact us.

In this letter you will find enclosed a consent form, which we want you to read carefully and sign. It is essential to the trial that this be completed prior to your participation, and returned to us in the 'reply paid' envelope provided. We also ask that you return the tear off -section below, indicating your preference of chiropractic clinic location.

During the trial, we will maintain contact with you mainly by mail or telephone. In addition, we have organised an asthma meeting on Saturday afternoon from 2pm-4pm on (insert date) for those who wish to meet our research team and discuss the asthma trial. However, as we understand that many of you are leading busy lives and will not have time or means to attend this meeting, attendance is not compulsory for your participation in the trial. It is simply intended as an information gathering and sharing session. If you are unable to make the meeting, we ask that you make alternative arrangements to pick up your asthma trial package from the university prior to (insert date) – which includes a peak flow meter and saliva tubes.

The final thing is a referral for a full spinal x-ray. This is free of charge and an essential to the trial. In order to give our specialists enough time to report on your x-ray, please ensure that you have attended one of the 3 outpatient clinics – Summer Hill, Eastwood or Epping, by (insert date). If you have problems with this, please phone the asthma trial hotline on 9850 6420 to discuss options. Phone numbers for the clinics are written on the top of the referral form.

If there is anything that you do not understand after reading the consent form, or wish to have a brief chat about some trial details, please call us on 9850 6420, send us a fax on 9850 6066 or Email us on asthmatrial@mq.edu.au

Once again thank you for your interest in this trial. We look forward to receiving your response soon.

Yours faithfully,

Kate Boyce
Asthma Trial Coordinator
 Encl.



PARTICIPANTS CONSENT FORM

Dear Participant,

You are invited to participate in a clinical study of patients with asthma and chiropractic care being conducted at Macquarie University by Dr. Ray Hayek (Chief investigator; Ph [REDACTED]), Dr. Sinan Ali (9 [REDACTED]), Dr. Peter Curson (9 [REDACTED]), Dr. Robyn Beirman (9 [REDACTED]) and Dr Sue-Ellen McKelvey ([REDACTED]). The study is looking at the relationship between chiropractic manipulation of the spine and its health benefits to the people with asthma.

During the study, you will maintain your current medical treatment and prescribed management of asthma. The Doctor involved with this study, may need to ask you some questions about your current asthma treatment and management.

I understand that my participation in the study is voluntary. I may withdraw my consent and discontinue participation at any time without having to give a reason and without penalty or prejudice. I understand that no payment is involved.

Like with any medical procedure, some complications may occur following chiropractic care. These are:

- Muscle soreness – happens in one out of 1,000 cases (it may last up to 3 days).
- 'Sympathetic storm' sign – happens in one out of 50,000 cases (harmless stress response that lasts for 5 minutes).
- Moderate stroke – happens in one to three out of 1,000,000 cases.

Chiropractors in the study are licensed to practice and will give you safety-screening test before the procedure. If you experience any pain or discomfort, you can contact either your chiropractor or the Project Coordinator Mrs. Chandrika Subramanyam (Tel: 02 [REDACTED]) for help.

I understand that I will be receiving free chiropractic care for 6 weeks, total of 18 sessions. Each session will take between 15 to 30 minutes. This is to take place at approved clinics involved in this university study.

I understand that I will be required to have X-rays of the spine, free of charge. This is to exclude any underlying problems for which the chiropractic care is not suitable. These include bone disease like arthritis and fractures.

I understand that I will be asked for morning and evening saliva samples for the period of 14 weeks.

Any information or personal details gathered in the course of the study are confidential and will be treated as such. No individuals will be identified in any publications of the results. Data will be stored at the Department of Chiropractic with the chief investigator Dr. Ray Hayek

MACQUARIE UNIVERSITY, NSW 2109 AUSTRALIA
Tel: (02) 9850 6420 • Fax: (02) 9850 6066
Email: asthmatrial@mq.edu.au

YOUR SALIVA SAMPLES WILL NOT BE USED FOR DNA ANALYSIS

I _____, have read and understand the information above.
Participant (Parent/Guardian, if under 16 years)

The questions I have asked have been answered to my satisfaction. I agree to participate in this study, knowing that I can withdraw at any time. I understand that I will be given a copy of this form to keep.

Participant's (Parent/Guardian) signature:

_____ **Date:** _____

Investigator: _____ **Signature:** _____

Date: _____

The ethical aspects of this study have been approved by the Macquarie University Ethics review Committee (Human Research). If you have any complaints or reservations about any ethical aspect of your participation in the study, you may contact the Research Ethics Officer: Telephone (02) 9594 1144, fax (02) 9594 1145 Email kdesilva@vc.mq.edu.au. The matter will be treated in confidence, investigated and you will be informed of the outcome.

Please fill out and return this form in the reply paid envelope provided



Thank you for your interest in taking part in the Asthma Research Trial, conducted by the Macquarie University Stress and Spine Research Unit. We appreciate the time you have taken to contact us. As you have been computer randomized into a group who will receive treatment during the trial, please read the following break-down of the 14-week program that we ask each participant to read carefully before agreeing to take part in this important health research.

Week 1 and 2 of the trial are a ‘pre-treatment’ phase

During this time you will take saliva samples and peak flow meter readings at 8am and 8pm, 3 days per week. We will also ask you to fill out 3 questionnaires, which ask questions pertaining to your asthma and general health. This information is invaluable to future comparisons, which we will make between your overall pre-treatment and post-treatment wellness.

Week 3 to week 8 (inclusive) is the treatment phase

At this stage you will visit a university preferred chiropractic clinic 3 times weekly for 6 weeks.

You will make all of your own appointments (with our assistance if needed).

Treatment times will vary – but a good estimate is 20 minutes. You will receive 18 chiropractic sessions all up – valued at over \$500. As part of the trial protocol you may be randomized into a group that is receiving a ‘placebo’ chiropractic treatment. You will not be told of this, and will continue treatment as normal. If you do fall into this group, you will be given a gift certificate for chiropractic treatment at one of our out-patient clinics when the 14 weeks have finished.

Whilst you undergo your treatment sessions, you will also continue saliva samples, peak flow meter readings and fill out another questionnaire regarding your general health.

Week 9 to week 14 (inclusive) is a ‘post treatment’ phase

The post treatment saliva samples and peak flow meter readings are taken just as they were in weeks 1 and 2. These samples are very important to our analysis of your progress during the 14-weeks. Via lab testing, these samples will provide evidence of how much your overall wellness has improved from chiropractic treatment.

Please read the following consent form – sign it and return it, along with the clinic location form. We will require you to attend one seminar for approximately 1 ½ hours

on a Saturday afternoon. It is compulsory to participation that you be there to pick up saliva tubes etc. Please indicate on the clinic location form provided that you will be attending, and return it within the week.

The team would appreciate your involvement in this study very much. Anecdotal evidence suggests that chiropractic treatment is beneficial in relieving asthma symptoms, but this study will only succeed with your generous support.

Yours faithfully,
Kate Boyce
Asthma Trial Coordinator
Ph 02 9850-6420

Welcome to the Asthma Trial!

Following is an outline of what to expect during the 14 weeks that you participate in this trial. Whilst we have tried to make this package easy to read and informative, if you would like to find out more about the asthma research we are currently undertaking – we will also hold a non-compulsory seminar. The seminar is optional for all participants, and will take place if numbers are sufficient. There is a package to be collected.

What you will find in the package:

1. AN X-RAY REFERRAL FORM

Before you begin the trial, it is imperative that you have a spinal X-ray taken. This is at no cost, and can be done at either Eastwood, Summer Hill or Epping chiropractic clinic. The phone numbers for these clinics are listed below. If you have any problems the project office is available to assist on (02) 9850 6420.

Eastwood:

Summer Hill:

Epping:

2. QUESTIONNAIRES

There are 3 questionnaires to fill out in the first week of the trial. These are used to gauge your general health, as well as compare against other questionnaires that you will take **during week 7 of the trial and week 14. The first 'Asthma', 'SF36' and 'Depression, Anxiety Stress Scale' questionnaires are included in your package** – the next sets will be posted out to you during the trial. **Please fill out the questionnaires and return them in the 'postage paid' A4 envelopes provided.**

3. Saliva collection, tubes and instructions, labels, storage and transport

The method of assessment in this trial is saliva. In other cases you might have been asked to give blood or urine samples, but for the purposes of this asthma trial – saliva assays give the most accurate readings. It is extremely important to the study that you take saliva samples twice daily, three times per week for the entire 14 weeks of the trial. Saliva samples should be collected specifically at 8am and 8pm on Tuesday, Thursday and Sunday of each week. All of the collection tubes that you will need are included in the package - this **includes 14 'weekly' bags (one for each week)**. Please put 6 tubes in each bag - 3 with blue lids and 3 with white lids. The white lids indicate a morning sample and the blue lid indicate an evening sample.

You are also provided with sticky labels, please write on these the day, date and the exact time a sample is collected. At the end of each week place 6 samples into one bag and stick **on the appropriate label, such as 'week 1' (labels are provided). Your labelled samples must be immediately frozen until they are transported to the Chiropractic Centre or the project office. We would very much appreciate you personally delivering your saliva samples, kept frozen during transit. The times you should do this are outlined on the 'before you begin' notice.** If you are unable to get to the clinics or the trial office at Macquarie University, please phone us (02 9820 6420) and we will make other arrangements.

4. Peak flow rates

Whilst we assume that most people will be familiar with how to use a peak flow meter, instructions are provided on the record page.

5. Timeline

'Before you begin' outlines what you must do before you begin your saliva samples, as well as anticipating the steps you will need to follow during the 14 weeks you are involved in the asthma trial. It is a good idea to keep this sheet close by as it is an overview of the entire trial.

6. Your Next Appointment

We have included a wallet sized appointment record for your convenience. If you are **randomised into the 'treatment group'** we strongly suggest that you make all of your chiropractic appointments as quickly as possible. The clinics are prepared to take all 18 appointments – and to secure dates and times, this is the best option. It is necessary that you schedule 3 appointments per week for 6 weeks (week 3 to week 8 inclusive).

7. Saliva Collection

Below are instructions on how you should take a saliva sample. Please be completely aware of these instructions before taking your sample, and if you have any questions contact the hotline.

Saliva samples should be taken at 8am and 8pm Tuesdays, Thursday and Sunday of every week for the entire 14 weeks of the trial.

Any inhaled steroid medications such as Becotide, Becloforte, Pulmicort, Flixotide or Respocort should be taken after saliva sample is taken.

Step 1 Morning samples – use tube with a clear lid

Evening samples – use tube with a blue lid

Write the day, date and exact time of starting the saliva collection on the labels which we have provided for you, and stick the label on the tube. This is what the label will look like



Step 2 Think or smell some a favourite or bitter food to stimulate saliva flow. Collect saliva only. Do not collect phlegm that you cough up from your throat.

Step 3 Remove the lid of the tube and hold it pressed against your lower lip. Lean forward and allow the saliva to flow into the tube (you can push it with your tongue). Repeat **until you have filled the tube over 3/4 full, bubbles don't count.**

Step 4 **Put the lid back on the tube, place in a bag labelled 'Week #' and put directly into the FREEZER.** This is what that label will look like.



Once again, thank you for your time and participation. If you have any questions, please phone the trial hotline.

Kate Boyce
Project Coordinator



How to give your saliva samples

- Samples should be given on **Sundays, Tuesdays and Thursdays** at **8.00** am and **8.00** pm.
- If you use a steroid medication, **take it after** you have given your spit sample. Steroid medications include Becotide, Becloforte, Pulmicort, Flixotide, Respocort.
- Try to finish eating or smoking at least 15 minutes before you spit so that your sample is not full of bits of food.

1. Prepare a tube for the saliva. Write on it the day, date, the exact time of starting saliva collection and am / pm. Use a tube with a blue lid in the morning and one with a white lid in the evening.
2. We need saliva, **not** phlegm coughed up from your throat. A small piece of clean cotton wool in your mouth will help to stimulate saliva flow.
3. When you have some saliva under your tongue, remove the lid from the tube and hold the tube so that it is pushed against your lower lip. Then lean forward and allow the saliva to flow into the tube - you can push it with your tongue. Chew the cotton wool again, wait until you have some more saliva under your tongue then spit again into the tube.
4. Fill the tube if you can but we need the tube at least half full with saliva. Bubbles on top don't count.
5. When you have enough saliva, screw the lid firmly onto the tube and put it in the bag labelled for that week.
6. Store the tubes of saliva in the freezer - not in the fridge.
7. On the record chart, enter the time of your sample collection chart under the correct date.

BEFORE YOU BEGIN!

- Step 1** Before beginning it is essential that you have had a spinal X-ray taken at either the Eastwood, Summer Hill or Epping Chiropractic clinic.
- Step 2** Prior to beginning saliva collection and peak flow meter monitoring please organise all 18 clinic appointments
- ** Whilst you do not have treatment for the first 2 weeks of the trial, we recommend that you make all the appointments before beginning, to ensure your availability of days and times
- Step 3** Please ensure that you have sent your first set of questionnaires - Asthma, Depression Anxiety Stress Scale and SF36, to the Asthma Trial Office.
- Step 4** Begin taking saliva samples on the Tuesday at 8am and 8pm, 2 weeks prior to your first chiropractic appointment. Do not forget that these samples should be frozen immediately after collected. Saliva samples should be personally delivered to either the Asthma Trial head office at Macquarie University or the clinic you are allocated to on weeks **3, 7, 11, and 14**. Please take every precaution to keep the samples frozen during transit.

<i>Trial Timeline</i>	<u>My Starting Date:</u> <i>(insert date month)</i>
Week 1	<ul style="list-style-type: none"> • Make clinic appointments for week 3 to week 8 inclusive (total of 18 visits). • Begin taking saliva samples and peak flow meter readings twice daily at 8am and 8pm on Tuesday, Thursday and Sunday of each week.
Week 2	<ul style="list-style-type: none"> • Continue for the 2nd week of pre-treatment saliva and peak flow meter monitoring.
Week 3	<ul style="list-style-type: none"> • 1st week of chiropractic treatment (3 times weekly for the next 6 weeks). <p>Continue taking saliva samples peak flow meter readings at usual intervals</p>
Week 7	Send second set of Questionnaires into the Asthma Trial head office.
Week 8	<ul style="list-style-type: none"> • Last week of Chiropractic Treatment. <p>Continue saliva samples and peak flow meter readings for the remainder of the trial.</p>
Week 14	<ul style="list-style-type: none"> • This is the last week of the trial. <p>Your last saliva sample and Peak Flow Meter Reading will be at 8pm on Sunday night.</p> <ul style="list-style-type: none"> • Please send the final set of questionnaires and any other information you still have into the Asthma Trial Head Office.
<i>Thank you for your participation</i>	<u>My Finishing Date:</u> <i>(insert date month)</i>