THE USE OF LOW DOSE TRICYCLIC ANTIDEPRESSANTS AT HEIDEVELD COMMUNITY HEALTH CENTRE

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DEDICATION

This is dedicated to my beloved parents Abdullah and Zainab Banderker for all their love and support.

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To my friends and colleagues, for their friendship, support and encouragement.

DECLARATION

I, Shahida Abdullah Banderker, hereby declare that the work on which this research is based is my original work (except where acknowledgements indicate otherwise), and neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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ABSTRACT

AIM OF STUDY:

To describe how doctors are prescribing low dose antidepressants at Heideveld Community Health Centre.

OBJECTIVES:

1. To determine how many patients are being prescribed low dose antidepressants at Heideveld Community Health Centre.

2. To see what sort of dosages are being prescribed as low dose most frequently.

3. To see if indications for the use of low dose tricyclic antidepressants are being recorded.

4. To identify the indications for the use of low dose tricyclic antidepressant.

METHOD:

A total of 500 patient folders were reviewed. 50 patient folders, (10 folders each from five medical officers), were systematically sampled, per day, for ten days over a two week period. Records were reviewed and data was captured on a data capture sheet. Demographic data: age and gender was recorded. The dose of the antidepressant per patient was recorded. The indication for its use was recorded. Where the indication of its use was not recorded, this was also documented.

RESULTS:

1. Of the 500 folders reviewed, a total of 153 (30,6%) of the patients were prescribed low dose tricyclic antidepressants at the consultation, during the time that the study took place.

2. The minimum dose used was 10mg and the maximum dose used was 75mg of tricyclic antidepressant. The median dose used was 25mg.

3. 83% of the folders had reasons for the use of low dose tricyclic antidepressant recorded. 17% of the folders had no reason recorded.

4. The reasons for using low dose tricyclic antidepressants, were for chronic pain syndromes, insomnia, somatic symptoms and for psychological or psychiatric reasons (anxiety or depression related symptoms).

CONCLUSION

Low dose tricyclic antidepressants were justifiably prescribed for the many non-psychiatric and psychiatric conditions that respond to it, at Heideveld Community Health Centre.

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1. INTRODUCTION

I am at present a medical officer at the Heideveld Community Health Centre. I have been working at this centre, for the past nine years, and have found primary health care to be extremely rewarding.

The Heideveld Community Health Centre, serves the people of Heideveld, Surrey Estate, Welcome Estate, Vanguard Estate, Manenberg, Bonteheuwel, Guguletu and Langa. The patients served at our clinic come mainly from poor socio-economic backgrounds. The social, cultural, political, and economic problems experienced, are enormous, and these impact heavily on their physical and mental health, as well.

We provide a comprehensive service to our patients, with a multidisciplinary team on our staff. The staff at the clinic includes five medical officers, nursing staff, a part-time surgeon, a social worker, a radiographer, a physiotherapist, a dentist, two pharmacists, three pharmacy assistants, and two psychiatrically trained nurses.

Our health centre is known for its good quality care and services provided, in the community.

Due to the large number of patients, and on-going shortage of staff, it has become almost routine for non-pharmacy staff members to assist at the pharmacy, where there is often a huge waiting queue of patients at the end of the day. It was after helping out at the pharmacy that our physiotherapist commented that she wondered why almost all of the patients attending our clinic were on Amitriptyline, a tricyclic antidepressant, and they were not psychiatric patients. (Our patients attending the psychiatric clinic, had separate blue folders, compared to our usual yellow folders, or the more recent folders of patients attending

the psychiatric clinic, then had a bold letter "P" on the side of the folder). Thus she knew the difference between the folders. She commented that she thought, we were prescribing it as a means to "solve all the people's problems rather than counselling them for their depression, because of the limited time available for consultations."

(Amitriptyline and Imipramine were the only two tricyclic antidepressant drugs available, to be prescribed by us, medical officers, on the open pharmaceutical code. The other antidepressants were available on restricted codes, to psychiatrists only).

Were there really so many patients on antidepressants, and why were they on these drugs? Knowing that doctors (myself included), generally referred psychiatric patients to the psychiatric sister, (seeing that she was always available to consult, as well as having a visiting psychiatric consultant on a weekly basis), it seemed obvious that not all the patients would have come for psychiatric reasons. The alleged abundant usage of the antidepressants was therefore, most probably for non-psychiatric reasons. I thus decided that this would be an interesting and useful study, for me and for the health centre, to undertake, looking at the prescribing habits of doctors at the Heideveld Community Health Centre, when prescribing antidepressants.

2. LITERATURE REVIEW

I searched the literature using Medline, limited to English publications, from January 1980-December 2003, and also used relevant reference books.

The tricyclic antidepressants are a group of drugs that have been found to have antidepressant properties.

The tricyclic antidepressants, have a characteristic three ring nucleus, and their actions closely resemble the phenothiazines chemically and to a lesser extent their pharmacological actions as well.[1] They were initially useful as antihistamines, and then later used as antipsychotics.[1] They are now commonly used for depression, anxiety and numerous other non-psychiatric conditions. Amitriptyline and Imipramine are the prototypes of the class of tricyclic antidepressants.[1]

Absorption, distribution, metabolism, and excretion of tricyclic antidepressants are very variable in different individuals. Their onset of action is slow and usually ranges from 2-3 hours. Between 3 and 8 hours, a peak plasma concentration is achieved. Plasma half life ranges from 10-20 hours for a dose. The drug is metabolised by the liver and excreted by the kidneys.[1]

Tricyclic antidepressants have immediate anticholinergic and sedative effects, but the antidepressant effect takes about 6 weeks. Sleep or pain modification response also varies among individuals. The tricyclics act primarily on the central nervous system by inhibiting the uptake of biogenic neurotransmitter amines. They have variable sedative and anticholinergic actions.[1, 52]

Recent articles suggest the potential benefits of tricyclic antidepressants in a number of non-psychiatric conditions.

Leo Hollister[1] in his introduction to the chapter on antidepressants, states that depression can be readily diagnosed, if it is the main complaint. In practice, this is rarely the case. He states that a host of other complaints mask the true depression, and the general feeling is that anybody with vague, complaints, that cannot be medically explained, is suspected of being depressed.

The symptoms of both depression and anxiety often occur together. Some of the symptoms described by anxious or depressed patients include headache, tiredness, insomnia, chronic pain, musculoskeletal aches and pains, strange tastes, or strange cutaneous sensations.

Moore[2] in his article, states that 30-40% of patients attending general practitioners, who are depressed, are not being diagnosed, as depressed. Many patients, especially those with physical complaints, or less severe depression are thus missed. He also states that doses of antidepressants, being prescribed for patients who are diagnosed as being depressed, are "below the therapeutic threshold."

Psychiatrists often start off with low dose tricyclics, and within one to two weeks, push patients up to full dose for therapeutic effects in the treatment of clinical depression.

Richeimer[3] describes low dose tricyclics as being <50mg, and he describes full dose tricyclics as anything >150mg.

Broadhead [4] in his study, after reviewing numerous articles, states that tricyclics may have "specific beneficial effects" on all of the common physical symptoms of depression, in depressed patients. It is now well documented that tricyclics are used successfully in other psychiatric illnesses, such as panic disorders, obsessive compulsive behaviours, agoraphobias attention deficit disorders[8] and bulimia[8] as well as non psychiatric disorders, such as peptic ulcer disease[8,] irritable bowel syndrome[11] tension headaches, prophylaxis of migraine,[9, 10] functional chest pain,[11, 12] smoking cessation programmes, urinary incontinence,[13] enuresis[13] chronic pelvic pain[14] neuropathic cancer pain[15] chronic muscle pains,[16] chronic lower back pain[17] insomnia,[23] chronic pain syndromes, neuropathies,[17,18,19,20] tinnitus,[26,27] cutaneous dysesthesia syndrome[19] and fibromyalgia syndrome[6].

Broadhead[4] also states in his article, that doctors often do not document psychiatric diagnoses, when prescribing psychotropic medication. Reasons for this poor documentation were thought to be due to "inadequate evaluation of the patients by the physicians, a lack of proper physician training and a lack of vocabulary for describing recognised psychological distress in patients, poor record keeping, or physicians' reluctance to record a mental disorder as the diagnosis." He also suggested that the patients treated, did not necessarily have a psychiatric disorder but may have had illnesses responding to tricyclics.

Broadhead [4] also stated that during visits to a primary care physician within one year, 65% of patients were prescribed tricyclic antidepressants, both for psychiatric and non psychiatric reasons. He also suggested that "current estimates that only 55% of tricyclic prescriptions are

based on an appropriate diagnosis are probably too low, and may reflect the omission of the tricyclic antidepressant-responsive diagnoses."

Ornstein[5] also highlighted the high prevalence and wide inter-practice variations of depression diagnosis and the use of antidepressants in primary health care. They also stated that more than 40% of patients in their study had received antidepressants, but had not received a diagnosis of depression.

Jencks[75] stated that mental symptoms are recognised and managed in many cases where a mental diagnosis is NOT made. He also stated that "psychotropic drugs are often prescribed, WITHOUT a recorded diagnosis of mental disorders." He also makes mention of the fact that subjects who received treatment without a diagnosis tended to be patients with established other diagnoses, who had a shorter consultation time and were more likely to have a follow-up appointment.

He states that one needs to consider that doctors could be deliberately under- diagnosing patients with depressive disorders, to "reduce stigma" or for "future insurance eligibility" purposes, or due to the "poor specificity of the diagnostic categories (e.g. depression not otherwise specified versus adjustment disorder with depressed mood.)"

"General practitioners frequently do not detect depressive states, tend to under- treat depression and fail to take up evidence-based guidelines in the area of depression," according to Anderson [74]. In his study, Anderson found that doctors considered antidepressants

important and had increased prescribing of antidepressants, but some of them were sceptical about the increase in prescribing antidepressants and they were uncertain about the correct criteria for diagnosing and treatment of depression. He also found that general practitioners lacked the ability to recognise depression in the depressed patients in their own practices.

A study, according to Olfson[73] revealed that the greatest increase in prescribing antidepressants, in their study, was for patients with adjustment disorders and less severe psychiatric disorders. A depressive disorder was diagnosed in 59% of patient visits in the 1993-1994 National Ambulatory survey amongst medical care of children and adolescents. The study did not provide information about dosages, or duration of the antidepressant used or the specific condition for which the medication was prescribed. The authors stated that they were "uncertain about the reliability of the diagnosis established by the prescribing doctor".

Somatisation is the most common presentation of psychiatric disorder in both general and hospital practices, and for most patients, it is the presenting feature of anxiety and mood disorders.[34]

According to Kroenke[71] 10-15% of primary care patients present with somatoform disorders. He stated that studies showed that somatoform disorders produce significant impairment in patients' functioning and quality of life which could compare to mood and anxiety disorders. Somatoform disorders are also associated with increased health care costs and services, since patients present frequently, more diagnostic tests get done on them, they get prescribed more

medication on their frequent visits and may be referred more often to specialists and be subjected to more surgical and diagnostic procedures. Patients with these disorders may be more difficult and challenging to care for and may be a source of frustration for both the patient and the doctor treating the condition.

Epstein[48] stated that a symptom such as chronic fatigue can be a symptom associated with almost any medical disorder or almost any psychiatric disorder as well. From his reviews, more than two thirds of chronically fatigued patients have coexistent psychiatric illnesses. Approximately half of the patients had depression and the remainder had anxiety or somatoform disorders.

Sheehan [65] found somatisation to be common among older primary care attendees and was associated with depression and chronic physical disorders. Rates of depression in these patients were also higher in the older patients with lower social support. He also stated that older people with psychological distress were more likely to present with somatic symptoms, in a system that was likely to "under-detect and under-treat psychiatric disorders." It was shown that depression in the elderly is often unrecognised. Somatisation was suggested as a reason for under-detection. Medical illnesses causing somatisation and depression, is more common in older people, therefore a clear understanding of the prevalence and association of somatisation among older people is needed.

Kroenke and Spitzer[67] in their study showed that females were more likely to have somatic symptoms. They suggested that the greater reporting of most symptoms, including

unexplained symptoms, by females, may account for the increased prevalence of functional syndromes among women, including irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome, and migraine headaches. Depression and anxiety disorders were both strongly associated with symptom reporting in their study. They found that depression had a greater effect on total symptom reporting, while patients with anxiety reported more somatoform symptoms. They state that numerous theories have been proposed to account for the increased symptom reporting in females. On a physiological level, females are more sensitive to external environmental stimuli including stress and men to internal physiological stimuli in noticing, defining and reacting to physical symptoms. Certain psychological factors more prevalent in females are strongly associated with increased symptom reporting especially depressive and anxiety disorders, as well as a history of physical or sexual abuse. Greater expressiveness and less stoicism among females, amplification of somatic symptoms and a lower threshold for seeking health care and gender differences in social roles and responsibilities, are some of the cultural factors postulated for the increased symptom reporting.

Kroenke and Spitzer[67] also stated that interviewing a patient to establish the presence or absence of a somatoform disorder can be time intensive, because the clinician must gather sufficient information from the patient and medical records to ascertain that a physical explanation for somatic complaints is unlikely.

Recognising that depressed patients often present to their doctors with physical symptoms that may mimic other diseases, such as chronic pain, fatigue, gastrointestinal symptoms,

rather than presenting with the usual symptoms of sadness, hopelessness or loss of pleasure in usual activities, is important, in order to treat appropriately and to improve the quality of life and to reduce their excessive use of health care facilities according to De-Wester.[35]

Anxiety is commonly found in adults with depressive disorders, either alone or as a co-morbid disorder. Lenze[46], in his study stated that an estimated 85% of adults with depression experience significant symptoms of anxiety. He also stated that depressed elderly patients were more likely to seek treatment than younger patients, either due to "greater physical illness or greater psychological distress, both of which are associated with geriatric depression and anxiety disorders". He also stated that the elderly patients were more likely to have poorer social functioning and increased somatic symptoms associated with anxiety disorders. High levels of somatic symptoms during treatment, may be interpreted by either the patient or the doctor to be a side-effect of the medication, and could lead to compliance problems or stopping medication too early. His findings also suggested that symptoms of generalised anxiety disorder in patients with co- morbid depression, predict greater severity in depressed elderly patients.

Patients, who present with unexplained physical symptoms, are associated with both higher levels of psychiatric symptoms and abnormal attachment behaviours when compared to patients presenting with organic physical symptoms. Their "medical help seeking behaviour" is a form of "care eliciting behaviour," and as such may be understandable in terms of "attachment style" and may affect relationships with their professional carers, according to

Taylor[49], in his article about attachment types in patients with unexplained physical complaints. This could also account for the increased utilisation of health- care resources. Ballinger[30] reports that "sociocultural and family factors are more important in the aetiology of symptoms of menopausal women, than physiological changes." He reports that anxiety and depression in some women do not respond to oestrogen therapy, but do respond to antidepressants used by them.

In psychosomatic illness, psychological factors may well aggravate, prolong or cause relapses in an illness, whose basis is physical. McDaniel[72] states that despite very difficult life situations, somatically fixated patients tend to present with numerous physical symptoms, and not with anxiety, depression, or trouble with coping. In one of their studies reviewed, more than half of their patients at a practice presented with unexplained medical symptoms. In another study[72] they found that these patients had a 5% higher rate of attending and 5% higher charges and had folders that were almost twice as thick as the average folder.

Psychogenic symptoms are often based on a vicious cycle, e.g. emotional distress causing muscular tension, which causes pain, which in turn worsens anxiety or emotional stress (e.g. fearing pain may be cancer- related), which in turn causes more muscular tension, which again increases pain, etc. thus repeating the cycle and causing increased visits to the health care centres.

Numerous studies have been done to confirm the efficacy of tricyclics in the treatment of non- psychiatric disorders. Many of these are not "purely non-psychiatric" and may often be

accompanied by an axis 1 diagnosis such as "psychological factors affecting physical condition" in DSM III-R classification. Cunha[36] states that antidepressants are recommended by some clinicians to treat irritable colon, even when there is no evidence of depression, since this illness may represent a type of "masked depression" in the elderly.

Many patients with chronic pain syndromes have been treated successfully with antidepressants, whether or not if they had depression. In most of the cases, chronic pain is accompanied by mild depression.[6] It is not clear if painful states represent depressive states or if patients become secondarily depressed, because of the chronic pain states.

It was found that low dose tricyclics helped in relieving pain in patients with rheumatoid arthritis either with or without pain, but it did not have a significant effect on depression, in patients who had it.[6]

Richeimer[3] stated that antidepressants are analgesic, if they relieved depression which gave rise to pain, but some were shown to be analgesic in the absence of depression.

Chronic pain is a common presentation in the primary health care setting. It is often very frustrating to both patient and doctor alike. Among the conditions under the chronic pain syndromes are chronic lower back pain, fibromyalgia, chronic tension headaches, neuropathy, chronic pelvic pain, post herpetic neuralgia and cancer pain. The treatment of patients with chronic pain syndromes requires a multidisciplinary approach.[3]

Antidepressants are considered to be the first choice of treatment for patients with diabetic peripheral neuropathy, in numerous studies reviewing and evaluating the drug therapy of patients with diabetic peripheral neuropathy, according to Wright.[21]

Chronic phantom limb pain is a sequel of amputations. Interactions between pathophysiological mechanisms in the peripheral and central nervous systems may be responsible for the initiation and maintenance of chronic phantom limb pain as reported in Wright's article.[21]

Tricyclic antidepressants provided partial symptomatic relief for patients with predominantly sensory neuropathy in patients with AIDS and AIDS related complex, according to Cornblath et al.[20] The most common type of peripheral neuropathy associated with Human Immunodeficiency Virus infection, affecting 10-30% of patients with HIV, according to him, is predominantly sensory neuropathy.

Orsulak[8] states that lower doses of antidepressants were effective in patients with chronic pain. He also reported that tricyclic antidepressants are far superior to placebo in migraine prophylaxis. Preventative treatment is often given daily for months or years. Interestingly enough, Silberstein[9] reports that most migraine preventative medications were designed to treat other disorders. (e.g. propanolol for hypertension, valproate for epilepsy), before it was used for preventative treatment.

The National Heart, Lung and Blood Institute working group on insomnia[42] revealed that from 30 to 40 percent of adults indicate some level of insomnia within any given year and

about 10 to 15 percent indicate that the insomnia is chronic, severe or both. They reported that the prevalence of insomnia increased with age and was more common in women. They reported that patients with chronic insomnia frequently complained about "fatigue, mood swings, irritability, depression and impaired daytime functioning." They reported that insomnia appeared to "contribute to increased rates of absenteeism, health care utilisation, and social disability."

Simon et al[41] states that "epidemiological surveys have shown that sleep disturbance is more prevalent among the elderly, those with chronic medical illness and those with anxiety or depressive disorders." They also stated that prevalence rates of self reported sleep difficulty range from 10-40% and this, in itself, leads to poor general health, increased absenteeism, and an increased use of medical services. They also found that the patients with insomnia had more illnesses and a higher prevalence of depression, functional impairment and increased health care visits which might reflect the confounding influence of chronic medical illness and/or depression.[41]

In addition, they also reported that both insomnia and depression made independent contributions to disability and health care utilisation, but that it could also be part of a vicious cycle, in which insomnia can lead to a depressed mood and loss of interest, which often leads to functional impairment and likewise, insomnia can also be a mediator between depression and disability.

Similarly, Walsh[40], in their study reported that insomnia is associated with "higher than normal levels of anxiety, depression, medical illness and social disability."Walsh[40] concluded

that there had been a "dramatic shift to the use of antidepressants, in lieu of hypnotics, for the symptomatic treatment of insomnia," despite a paucity of data regarding their efficacy and the potential for serious side effects. He also reported that insomnia is also a risk factor for the onset of depression, if it persists for one year.

All of the above psychiatric and non psychiatric conditions are common conditions seen on a daily basis at our day hospital, and the literature provides enough evidence for the use of antidepressants in our patients presenting with these conditions.

2.1 BACKGROUND MEDICAL INFORMATION ABOUT MAIN FACTORS IN STUDY

2.1.1 ANXIETY DISORDERS

Anxiety is a subjective feeling of fear and apprehension, accompanied by an overwhelming feeling of impending doom.[34] The symptoms and signs associated with anxiety include many features consisting of affective, cognitive, behavioural and somatic symptoms. The patients often feel a sense of dread or panic causing them to seek to neutralize the distress and to reflect their anxious states by certain responses to it (e.g. avoidance behaviours). They may appear restless, agitated, jittery, with heightened arousal including being hyper-vigilant, distractible, with impaired concentration, and insomnia.[34] The somatic manifestations may mimic many medical conditions in which there is stimulation of the sympathetic nervous system, causing autonomic hyper reactivity and include systemic (fatigue, weakness, insomnia), cardiopulmonary (palpitations, chest pain, dyspnoea, hyperventilation),

gastrointestinal (nausea, vomiting, diarrhoea, dry mouth), urinary (frequency) and neurologic (dizziness, tremulousness, restlessness, near syncope, paraesthesia) symptoms.[34]

2.1.2 DEPRESSION

Clinical depression can be distinguished from transient depressive moods and depressive personality by three main features, the depressive illness being a sustained depression of mood, lasting for weeks or months. The depression is severe enough to interfere with normal daily life and it has a definite onset with a clear, noticeable change from normal to depressive thinking.[33]

A patient who presents with psychological symptoms or signs e.g. sad mood, depressed affect, anxiety, irritability or anger, anhedonia, loss of interest in environment, or activities, decreased libido, social withdrawal, guilt feelings, poor self esteem, self deprecatory thoughts, poor concentration, obsessive thoughts, multiple physical complaints, hypochondrial fears, feelings of hopelessness, recurrent thoughts of death, or psychotic symptoms, should be suspected of being depressed. [32,33,34]

Also, patients who present with neurovegatative symptoms and signs such as sleep disturbances, decreased energy, appetite disturbances, diurnal mood variation, psychomotor retardation or agitation, should be screened for depression.[32,33,34]

2.1.3 INSOMNIA

Insomnia is an experience of inadequate or poor quality sleep characterised by either difficulty falling asleep, difficulty in maintaining sleep, waking up too early in the morning and sleep that is not refreshing, and compromises daytime functioning.[42]

Acute insomnia is a period of sleep difficulty lasting between one night and a few weeks. Chronic insomnia refers to sleep difficulty occurring at least three nights per week for one month or more.[42]

Acute insomnia is often caused by emotional or physical discomfort, such as any significant life stressors, acute illness, environmental disturbances (such as noise, light, and temperature), and jet lag.[42] The disturbance often develops in association with negative conditioning to sleep and the sleep environment. The patient has increased anxiety as it nears sleeping time and often "tries too hard" to fall asleep, further increasing the level of arousal and anxiety and thus further decreasing the ability to sleep. Very often if the acute stressor or disturbance is removed, patients develop a normal sleeping pattern again. In some patients, however, their confidence in the ability to fall asleep, decreases and the patients become more apprehensive about their poor sleeping patterns and may develop chronic insomnia, as well.

Chronic insomnia may be caused by many different causes either acting on their own or in conjunction with other health problems.[42] The hallmark of chronic insomnia is the focused absorption of the patient on the sleep problem itself. Patients with major depression complain of either difficulty in falling asleep or of early morning awakening.

Patients with bipolar mood disorder, in the manic phase have decreased total sleep, but do not experience fatigue when awake. Patients with dysthymia, often report difficulty with falling asleep and not feeling fully rested. Patients with anxiety disorders, frequently have difficulty initiating sleep, when they lie in their beds and are constantly thinking about their anxiety- producing states. Patients with personality disorders, often report insomnia. Active psychosis of any type also produces disturbed sleep. Caffeine and other stimulant xanthines, found in tea, coffee, chocolate or cola drinks, can also cause difficulty with sleep. [31,32,33,34] Numerous medical conditions can cause insomnia. Chronic pain is a well known cause of insomnia. The many causes for delirium can cause sleep difficulty. Patients with cardiopulmonary disease can have symptoms such as orthopnea, paroxysmal nocturnal dyspnoea, or nocturnal angina, keeping them awake at night. Patients with sleep apnoea can also have disrupted sleep. Prostatism, diabetes, urinary tract infections, causing urinary frequency, can also interrupt sleep. Repetitive twitching of the legs, whilst sleeping, (often unrecognized by the patient), called nocturnal myoclonus, is another cause of poor quality sleep.[31,32,33,34] There is also a insomniac state called primary or idiopathic sleep disorder, where patients have objectively verified difficulty falling asleep or maintaining sleep in the absence of any underlying disorder.[31] Some patients may also have a persistent complaint of insomnia, without any objective evidence of a cause.[31]

2.1.4 PAIN

Acute pain is typically associated with acute disease or injury. Its main aim is to warn the patient of tissue damage. It has a well defined temporal onset and its course is usually to subside as healing continues.[53,55]

Chronic pain may appear when an acute pain episode does not resolve in the expected time, or when pain emerges with no definite precipitating factor. It may persist for months or years and serves no biological function.[53,55]

Nociceptive pain is pain primarily due to an injury or inflammation of somatic or visceral tissue.[53]

Nociceptive somatic pain[53] is caused by activation of peripheral and central nociceptors, superficial and deep tissues. It is well localised, aching or gnawing in character e.g. joint pain, myofascial pain, inflammatory and ischaemic pathology.

Nociceptive visceral pain is caused by distortion of viscera, distension of hollow organs, infiltration, organ compression or capsular stretching. It is poorly localized, and often referred to the skin surface, which may be warm and tender. It is squeezing or pressure-like in character and may have associated autonomic symptoms e.g. gallstones, kidney stones, gastric ulcer, bowel obstruction.[53]

Neuropathic pain is caused by injury to the central nervous system.[53] Pain may be referred along the nerve pathway. It may be severe, constant, vice-like with paroxysms of burning or shock-like sensations e.g. diabetic neuropathy, post herpetic neuralgia, phantom limb pain.[53]

2.1.5 SOMATIC PRESENTATION OF A PSYCHIATRIC DISORDER

Somatoform disorders, conversion and dissociative disorders and factitious disorders and malingering are somatic presentations of psychiatric disorders.[34]

Somatoform disorders are conditions in which physical symptoms are present for which no organic or physiological basis can be found and where there are demonstrable underlying psychological factors or conflicts i.e. the physical symptoms are manifestations of underlying psychological distress or disease.[33] There are three types of somatoform disorders viz. somatoform pain disorder, somatisation disorders, and hypochondriasis.[33] Somatoform pain disorder is characterised by the presence of severe and prolonged pain, which is the primary complaint and is not consistent with known neuroanatomic distribution of pain receptors. No organic aetiology is detectable to explain the cause of pain.[33] Somatisation disorders are polysymptomatic disorders in which the patient experiences multiple unexplained symptoms without physical disease and in the context of a disturbed personality.[33] Hypochondriasis is characterised by an unrealistic preoccupation with the fear of having, or belief that one has, a serious disease.[33] Such a patient interprets physical signs or symptoms as evidence to support his or her views.

Factitious disorders are characterised by conscious, deliberate and surreptitious feigning of physical or psychological symptoms to simulate disease. Patients demonstrate an unexplained psychological need to assume the sick role.[34] Malingering is characterised by intentional production of physical or psychological symptoms. This is motivated by identifiable external incentives (e.g. financial compensation or evading the police or criminal proceedings).[34]

Anxiety, depression, insomnia, chronic pain conditions and patients with somatisation, may display common symptoms that may be related and conditions may co-exist, as well. It may be very difficult to differentiate signs and symptoms among the conditions, since they may

occur in all of the above situations. Antidepressants are used to treat patients with these conditions, and were appropriately prescribed for the patients in our study.

3. AIM OF STUDY

The aim of this study is to describe how doctors are prescribing low dose antidepressants at Heideveld Community Health Centre.

4. OBJECTIVES

1. To determine how many patients are being prescribed low dose antidepressants at Heideveld Community Health Centre.
2. To see what sort of dosages are being prescribed as low dose, (e.g. 10mg, 25mg, 50mg, 75mg) most frequently.
3. To see if indications for the use of low dose antidepressants are being recorded.
4. To identify the indications for which low dose antidepressants are being prescribed, where they had been recorded.

5. RESEARCH METHODOLOGY

5.1 STUDY DESIGN

A retrospective descriptive study was done.

5.2 STUDY POPULATION

All patients attending Heideveld Community Health Clinic, for whom low dose antidepressants were being prescribed, by the clinic doctors, during a two week period in 2000. (The study excluded known psychiatric patients).

5.3 SAMPLE SIZE CALCULATION

A pilot study, done at the Heideveld Community Health Clinic, revealed, that 30%, of patients attending our community health clinic were currently on low dose antidepressants. With the assistance of a biostatistician from the University of Cape Town, Community Health department, the sample size required for the study which would give a 95% confidence interval, was calculated to be 500 patients.

5.4 SAMPLING STRATEGY

All folders of patients seen by the five medical officers at Heideveld CHC, over a period of two weeks, were retrieved and reviewed in the study.

A sample of 50 patients a day, using the statistics sheets from the doctors, was selected. (The usual statistics sheets being used by the community health centre, contains only the folder numbers of the patients seen by that particular doctor. Ten patients' folders from each doctor, per day, for five days of the week, for a period of two weeks, were drawn by the reception staff, and kept for the study. By systematic sampling, folders were selected from the statistic

sheets. If a doctor had seen 50 patients for the day, every fifth patient's folder was drawn for the study. If the doctor had seen 40 patients for the day, every fourth folder was drawn, and if the doctor had seen 30 patients for the day, every third folder was drawn, thus selecting the random 10 patients chosen for the study. Folders used were flagged, to avoid using the same folder twice, should a patient be seen more than once during the two week study period. The patients seen at the clinic are seen in no particular order, since the chronic patients and the patients with acute illnesses are all seen together. This ensured a good spread of patients seen, including patients seen at all of the clinics, and thus avoiding bias towards one particular chronic illness.

(We have specific days for the chronic care clinics e.g. Diabetic clinic days on Mondays and Thursdays, hypertension clinic days on Tuesdays and Fridays, and asthmatic clinics on Wednesdays).

There was no way that one would have known whether the patient, whose folder number we had selected, was a chronic clinic patient or a non clinic patient, hence ensuring absence of bias towards patients with chronic illnesses, in the sample selection of patients seen.
Records were reviewed and data was captured on a data capture sheet.
Demographic data: age and gender was recorded.
The dose of the antidepressants per patient was recorded.
The indication for its use was recorded.
Where the indication of its use was not recorded, this was also documented.

5.5 DATA MANAGEMENT

Data was captured, using Epi-info 6, which is a word processing, database and statistical package used in public health.

6. ANALYSIS

Statistical analysis was performed using the Epi-info 6 package and data was analysed with assistance from UCT Department of Biostatistics and the MRC. Descriptive statistics was compiled using frequency tables and graphs.

Bivariate analysis was carried out, using chi square tests and Fisher's exact tests. Numerical data was summarised using either the measures of central tendency or the measures of dispersion. The measures of central tendency incorporated the mean, median (50th percentile) and mode, while the measures of dispersion incorporated the inter-quartile range and the standard deviation. Where the distribution of the data were observed to be symmetric, (normally distributed), the data was summarised, using the means and standard deviation. However, for skewed data, the median and quartiles were used as summary statistics, because median and quartiles are not as easily influenced by extreme values and skewed distributions, as are means and standard deviations.

7. ETHICS

The protocol for my thesis was approved by the University of Cape Town Ethics Committee. My reference number was 199/2001. Access to the folders was secured by obtaining permission from the Community Health Care Organization's superintendent, Dr Edmund Michaels, as well as the Heideveld doctor in charge, Dr Bhanu Daya.

Permission was sought from colleagues at the Heideveld Community Health Centre to use documented information from their consultations, regarding diagnoses and treatment plans.

Only folder numbers were used to flag folders that were used. Complete anonymity of patients was ensured.

Confidentiality was ensured at all times.

There were no outside vested interests or monetary gains to be attained, whilst doing the project.

8. REPORTING OF RESULTS

The reporting of results was addressed to all doctors whose patients were used in the study, as well as all interested parties at the Community Health Centre. Feedback was given to the doctor in charge as well as to the medical superintendent of the Community Health Service Organisations.

9. RESULTS: PRESENTATION

9.1 NUMBER OF PATIENTS ON LOW DOSE TRICYCLIC ANTIDEPRESSANTS

Of the 500 folders reviewed, 153 (30,6%) of the patients were prescribed low dose tricyclic antidepressants at the consultation, during the time that the study took place.

9.2 DEMOGRAPHIC DATA

9.2.1 AGE GROUPS

The patient's ages were categorised in 10 year age intervals.

The youngest of the patients in the study population was 16 years old and the oldest patient was 90 years old.

1 patient was in the age group category 10-19 (0.65%).

10 patients were in the age group category 20-29 (6.54%).

16 patients were in the age group category 30-39 (10.46%).

27 patients were in the age group category 40-49 (17.65%).

51 patients were in the age group category 50-59 (33.33%).

32 patients were in the age group category 60-69 (20.92%).

12 patients were in the age group category 70-79 (7.84%).

3 patients were in the age group category 80-89 (1.96%).

1 patient was in the age group category 90-99 (0.65%).

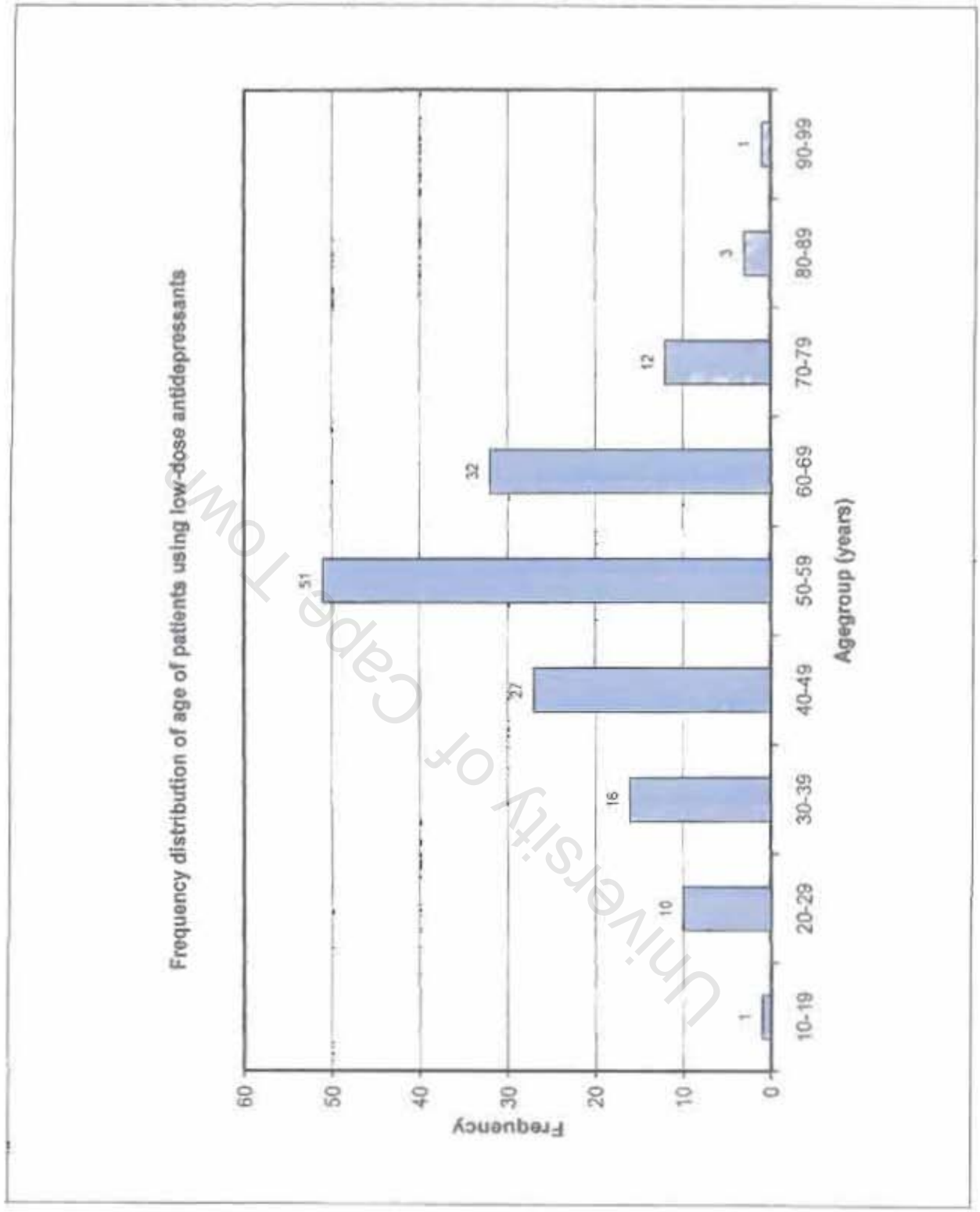


FIGURE 1

9.2.2 GENDER

There were 116 females (76%), and 37 males (24%) in the study.

GENDER AND AGE GROUP OF PATIENTS

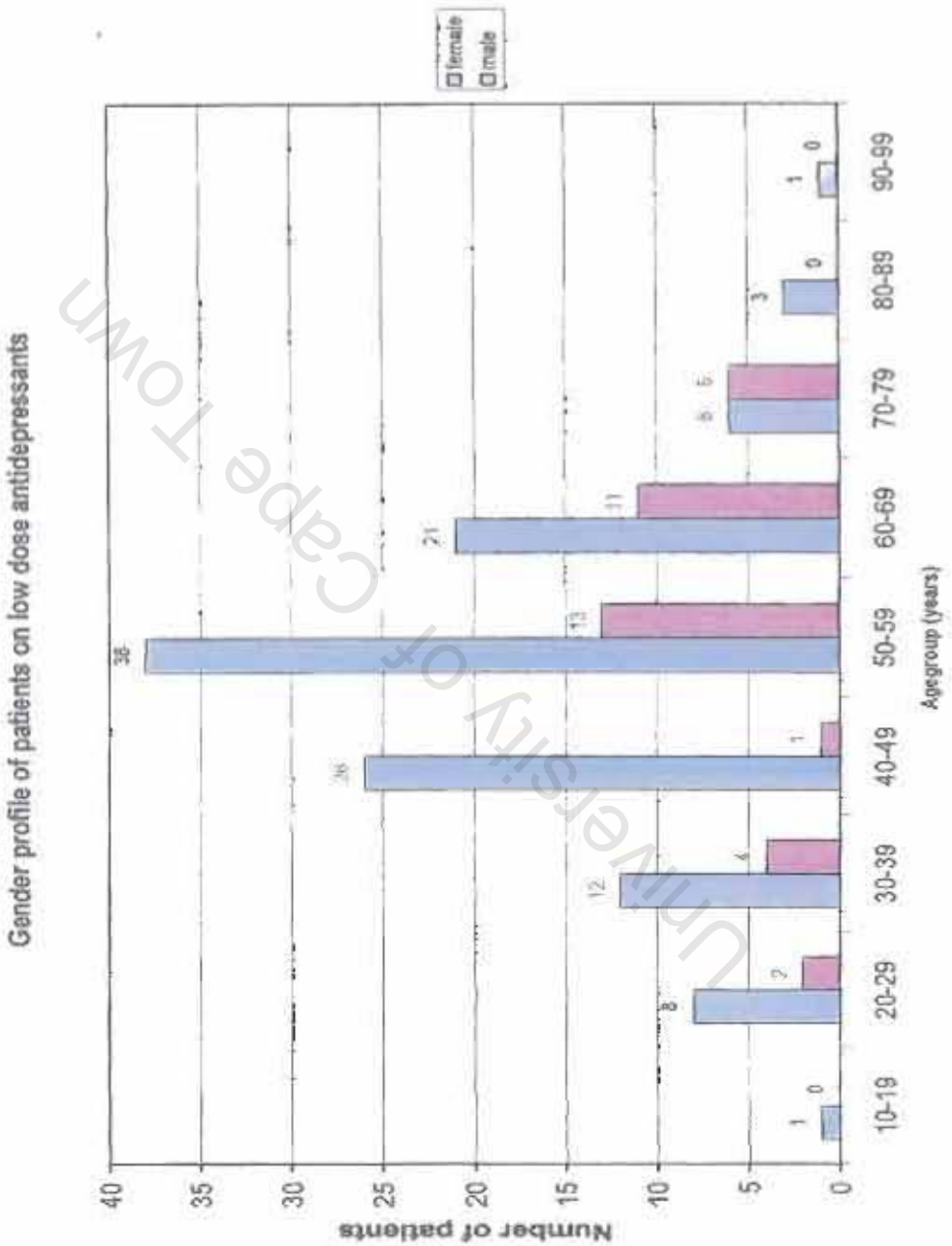


FIGURE 2

9.3 DOSE OF ANTIDEPRESSANTS USED

The minimum dose used was 10mg and the maximum dose used was 75mg of tricyclic antidepressant.

The doses used per age group were as follows:

Table 1: Antidepressant dose profile amongst agegroups

Agegroup	Dose (mg)						Total number of patients
	10	12.5	20	25	50	75	
10-19	1	0	0	0	0	0	1
20-29	6	0	0	0	3	1	10
30-39	6	0	0	8	1	1	16
40-49	6	0	0	16	2	3	27
50-59	24	1	0	18	5	3	51
60-69	10	0	1	17	2	2	32
70-79	5	0	0	4	3	0	12
80-89	1	0	0	0	2	0	3
90-99	1	0	0	0	0	0	1

FIGURE 3

The median dose of tricyclic used was 25mg.

The highest frequency of low dose antidepressant use was in the 50-59 year age group category. (Figure 3)

The highest frequency for both sexes for the use of low dose antidepressant was in the 50-59 year age group category. (Figure 3)

9.4 REASONS FOR ANTIDEPRESSANT USAGE

9.4.1 DOCUMENTATION OF REASONS

44% of the folders had one reason for the use of antidepressants recorded.

29% of the folders had two reasons recorded.

10% of the folders had three reasons recorded.

17% of the folders had no reason recorded.

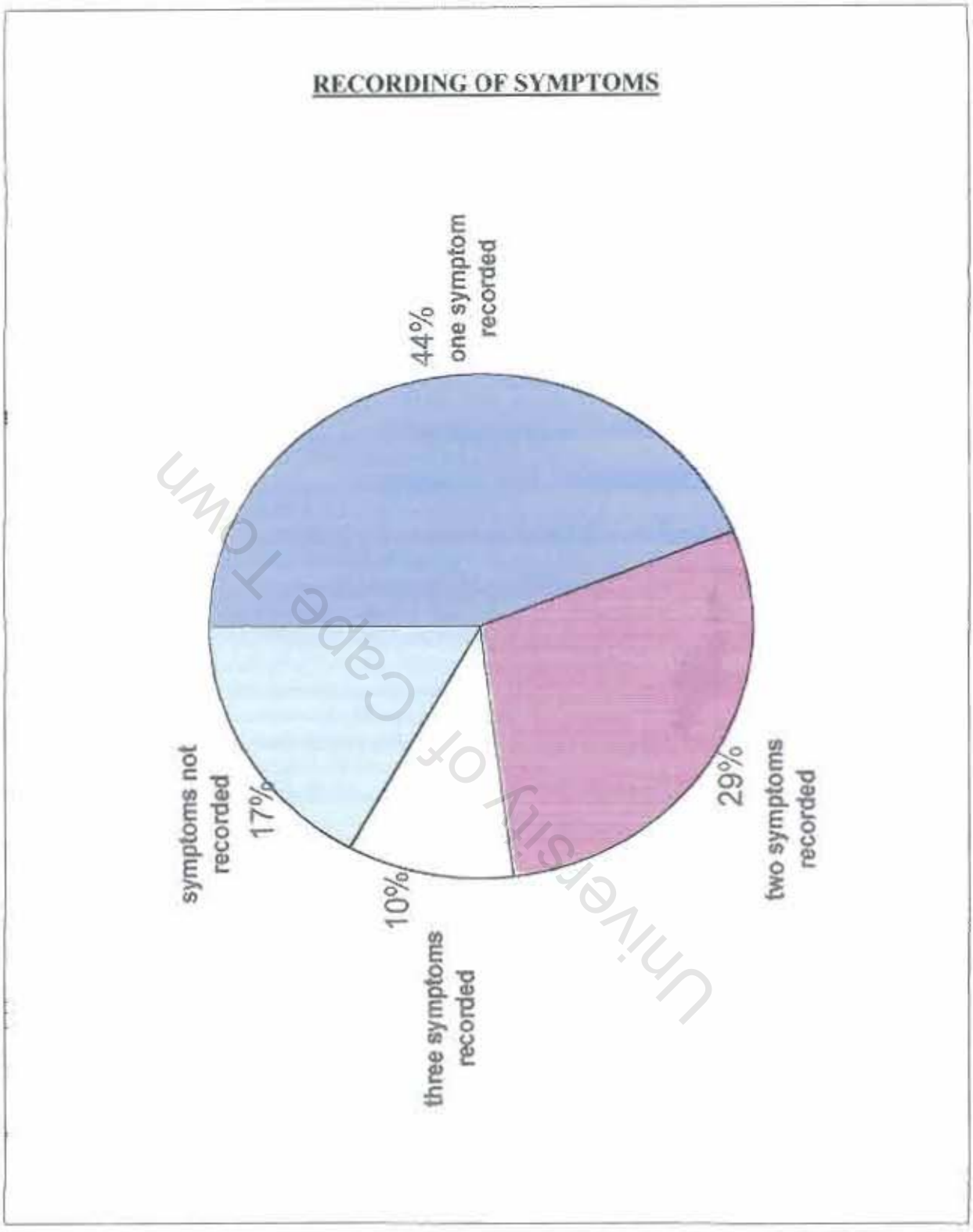


FIGURE 4

9.4.2 REASONS RECORDED

Of the 83% (153) of the folders that reasons were recorded,

28% (43) had insomnia

20% (31) had headaches

14% (18) had stress

18% (21) had anxiety

8.5% (13) had fibromyalgia or complaints of muscular pains

6.5% (10) had complained of chest pain

5.9% (9) had osteoarthritis

5.2% (8) had complained of general body pains

5.2% (8) had neuropathy

3.9% (6) had chronic lower backache

2.6% (4) had depression

2.6% (4) had been in bereavement

2.6% (4) had complained of abdominal pain

2.6% (4) had complained of chronic leg pain

1.96% (3) had complained of dizziness

1.96% (3) had complained of chronic pain (related to old fractures)

1.96% (3) had urinary incontinence

1.3% (2) had complained of tiredness

0.65% (1) had been complaining of menopausal symptoms

0.65% (1) had post herpetic neuralgia

0.65% (1) had myelopathy

0.65% (1) had phantom limb pain

0.65% (1) had complained of an unexplained "funny" taste in the mouth

0.65% (1) had peripheral vascular disease

0.65% (1) had synovitis

0.65% (1) had complained of palpitations

Of the above recorded symptoms, 16 (of the above categories) can be included in the chronic pain syndromes (i.e. headaches, fibromyalgia, chest pain, general body aches, neuropathy, osteoarthritis, chronic lower backache, chronic pain at old fracture sites, post herpetic neuralgia, myelopathy, phantom limb pain, "funny" tastes, peripheral vascular disease, synovitis, chronic leg pain, abdominal pain).

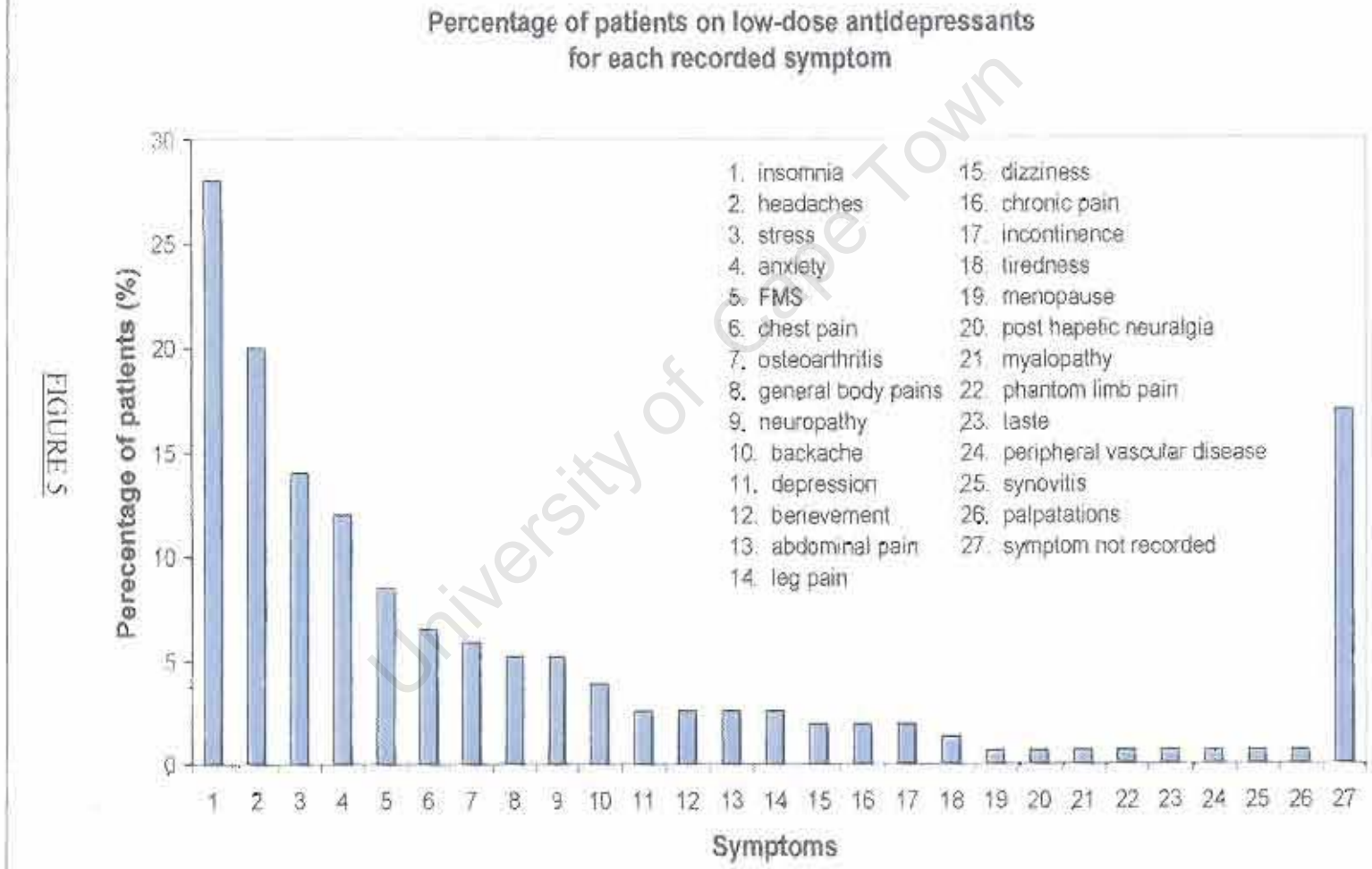
5 of the symptoms can be classified as being either of psychiatric or psychological nature (i.e. insomnia, anxiety, stress, depression, bereavement).

The other 5 i.e. dizziness, urinary incontinence, tiredness, menopause related symptoms and palpitations were classified as "others."

Where two or three symptoms were recorded, there was an overlap of the above categories.

There were no indications in the folders as to the possible reasons for the usage of antidepressants in 17% of the folders.

FIGURE 5



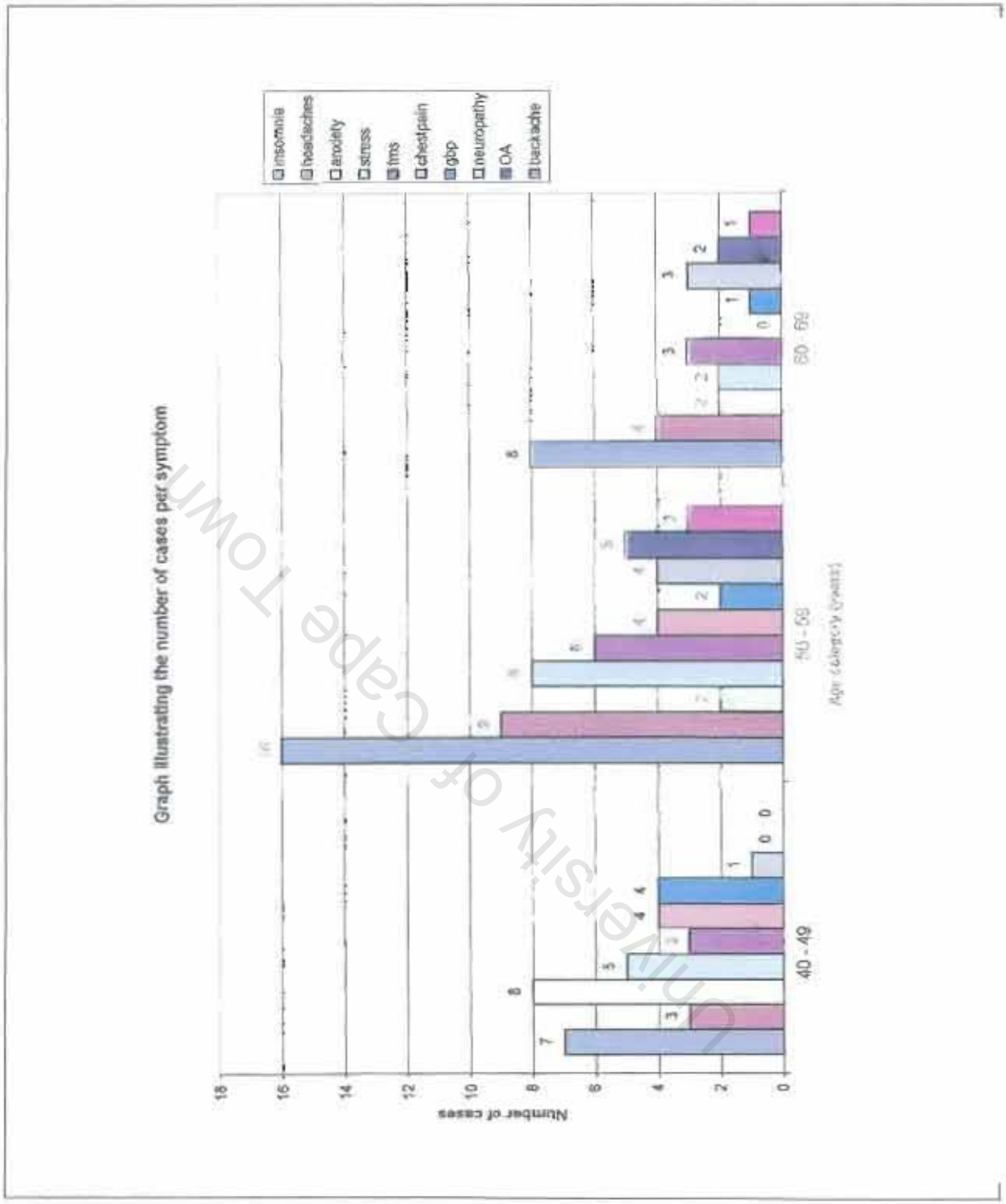


FIGURE 6

(GRAPH ILLUSTRATING THE MOST COMMON AGE GROUP CATEGORIES)

9.4.3 RELATIONSHIPS BETWEEN SYMPTOMS DOCUMENTED

The relationships between the following chronic pain symptoms and psychological/psychiatric symptoms (stress, anxiety, insomnia) were analysed, where there were more than six symptoms in the category recorded i.e. headaches, fibromyalgia, chest pain, general body aches, neuropathy and osteoarthritis.

INSOMNIA

There was a significant association with headaches (p=0.05).

There was no significant association with fibromyalgia syndrome (p=0.07).

There was no association with chest pain.

There was no association with general body aches.

There was no association with neuropathy.

There was no significant association with osteoarthritis (p=0.45).

ANXIETY

There was no significant association with fibromyalgia syndrome (p=1).

There was no significant association with headaches (p=0.76).

There was no significant association with chest pain (p=0.31).

There was no significant association with general body pains (p=1).

There was no association with neuropathy.

There was no association with osteoarthritis.

STRESS

There was no significant association with fibromyalgia syndrome (p=0.21).

There was no significant association with headaches (p=0.31).

There was no significant association with chest pain (p=0.63).

There was no significant association with general body aches (p=1).

There was no association with neuropathy.

There was no association with osteoarthritis.

Although there was no statistical significance, (besides headaches and insomnia) amongst the factors above, the clinical significance is well known, and there is an association with all the factors as mentioned in the section titled "Background medical information about main factors in study" (See literature review).[31, 32, 33, 34]

10. SUMMARY OF FINDINGS

Basically, our objectives were achieved:

Objective 1: To determine how many patients were prescribed low dose antidepressants:

30,6% of the patients, in our study at Heideveld Community Health Clinic, were prescribed low dose antidepressants.

Objective 2: To see what sort of doses were being prescribed as low dose antidepressants, most frequently:

See Figure 3

Minimum dose used was 10mg and the maximum dose used was 75mg of tricyclic antidepressant.

Objective 3: To see if indications for the use of low dose antidepressants are being recorded:

83% of the folders had reasons recorded.

17% of the folders had no reason recorded.

Objective 4: To identify the indications for the use of low dose antidepressants:

See Figure 5

Basically, the reasons for the use of low dose antidepressants were for chronic pain syndromes, somatic symptoms, insomnia, and for psychological or psychiatric reasons (anxiety or depression related symptoms).

11. DISCUSSION

Amitriptyline has often been described as a "wonder" drug by consultants, when we present our difficult patients to them. If no known cause of a particular symptom presentation can be found, usually after extensive investigations, consultants have advised: "Try some Amitriptyline. See if it will help." In most of the cases, in their experience, this has proved to be true, and the antidepressant has helped. Another consultant favouring Amitriptyline, for these patients, suggested that Amitriptyline should be added to our drinking water, since he was sure it would cure many of the modern ailments, in our primary health care setting.

For the purposes of our study, we considered a low dose, to be 10-75mg of tricyclic antidepressant, as discussed with our consultant psychiatrist in the South African setting. Anything higher than 75mg, is considered full antidepressant dose.[84]

The first three objectives achieved were peculiar to the Heideveld Community Health Centre only.

It is also noted that the findings of tricyclic antidepressant prescriptions in 30% of the files reviewed in the pilot study closely matched the 30.6% found in the definitive study.

As found in previous studies [2,4,5], doctors often do not record psychiatric diagnosis when prescribing psychotropic medication. My study also lacked a diagnosis in 17% of the folders reviewed. It is likely that the reasons for not recording a diagnosis, in my study, would

closely resemble Broadhead's[4] findings which were "inadequate evaluation by the physicians, a lack of proper physician training, a lack of vocabulary for describing recognised psychological distress in patients, poor record keeping in general or physician's reluctance to record a mental disorder as the diagnosis".

As can be seen by our findings, there was widespread use of low dose antidepressants for the various conditions listed. According to the literature review these conditions are known to respond to low dose antidepressants. In our study we assumed that doctors had made the correct diagnosis and that they were prescribing low dose antidepressants for the appropriate conditions, therefore one could state that the low dose antidepressants were used appropriately at our community health centre.

11.1 THE USE OF TRICYCLIC ANTIDEPRESSANTS IN TREATING ANXIETY

As can be seen in above symptoms and signs listed for anxiety recorded in our study there were symptoms like insomnia, fatigue, weakness, palpitations, chest pain, dry mouth (causing possible "funny taste" recorded in our study) and dizziness, all symptoms that could have been part of anxiety states. Very often the patient presented with only the one symptom, e.g. palpitations, a symptom of the cardiovascular disease. Depending on the medical officer's approach and history taking technique, an anxiety state could have been completely missed and one could have over-investigated that particular patient, looking for a particular medical condition, which could have caused his or her palpitations. This could be extremely costly, (ECG's, laboratory testing, referral to a cardiologist, etc) as well as very frustrating for

both the patient and the doctor, especially if no conclusion is reached. Taking a full medical history, including a psychosocial history, could get the doctor to home in to the actual diagnosis quicker, with much more satisfaction for both the patient and the doctor.[80,85,86]

The actual first presentation to the practitioner could have been the very first opportunity, as well as possibly the only opportunity, that the patient had to present their problem to the doctor, in some cases. It would have been very unfortunate for the patient, if the patient left the rooms without feeling "heard" by the doctor, and also for the doctor, who could have missed an opportunity to really get to know his patient, and get the patient to have "opened up" to the doctor. Alternatively, the patient feeling "not heard" would go around "doctor shopping" again, until he did get some relief from some doctor, who may have been more sensitive to the patient's needs or more thorough with the history taking. It is extremely important, though that the doctor does not miss an important medical condition that could be responsible or otherwise co-exist with the underlying anxiety disorder. Therefore the necessary baseline tests have to be performed, to rule out any medical conditions, before treating the patient only for the anxiety disorder that he presents with. It is also important to classify the type of anxiety disorder that the patient may have presented with. From our study, the type of anxiety disorder that the patient presented with was usually not documented. The medical officers may well have been of the condition they were dealing with, when they treated the patient for an anxiety disorder, but to another doctor who would follow up that patient, the patient would probably have to repeat his or her story to the next doctor again. In many of our patients, the reasons for their anxiety states had caused great discomfort already (e.g. violence, rape, domestic conflict, etc.), and having to repeat the story

to another doctor, is a further anxiety- provoking and traumatic experience in the majority of cases. The nature of the episode may have been another reason for the doctor's poor record-keeping or maintaining patient confidentiality, by not recording the exact anxiety diagnosis, in our study. The reason for the patient's anxiety state is a very important part of the records, which was not very well documented in our records. Was the patient treated for a generalised anxiety disorder? Did the patient suffer from a panic disorder? Did the patient have a simple or social phobia? Was the patient someone suffering from an obsessive compulsive disorder? Could it have been a post traumatic stress disorder, causing the anxiety? Did the patient have a possible adjustment disorder with an anxious mood? Could the patients have been abusing anxiolytics, alcohol, benzodiazepines, or any other sedating agent, which could have reflected an underlying anxiety disorder?

Sullivan[52] reports that anxiety disorders are found at a rate greater in patients with chronic pain, than in the general population. Panic disorders and generalised anxiety disorders were reported to be most common. He stated that patients with panic disorder often presented to the doctors with chronic migraine, headaches or chest pain, for investigation.

All these factors causing symptoms in our patients, could have been probable causes for a label of "anxiety", resulting in receiving treatment with low dose antidepressants.

It is important to know these factors and be aware of them when treating patients with their anxiety conditions.

11.2 THE USE OF TRICYCLIC ANTIDEPRESSANTS IN TREATING DEPRESSION

In our daily practice at the community health centre, there are so many patients with several psychosocial stressors that it is not uncommon for our patients to present with depression, or transient depressive states. It is thus important to screen for depression, when a patient presents with signs or symptoms of a depressive state. In my experience many of the patients at our community health centre, presented with chronic dysthymic disorders, due to their chronic exposure to poor life circumstances (poverty, unemployment, financial problems, inadequate housing, sanitation, gangster-ridden areas, substance abuse, violence, etc.).

Dysthymia and major depression can coexist, and must be distinguished from each other, and treated adequately. In patients with dysthymia, their symptoms are less severe than in major depression and neurovegatative features are fewer.[32] This could also be another reason for the use of low dose antidepressants prescribed, to assist with symptom management. (In the diagnosis of "depression", made by the medical officers in our study, no distinction was made as to the type of depression diagnosed. Was the patient just transiently depressed, and symptomatic tricyclic antidepressant was prescribed, or was a major depression being treated, just starting off with low dose tricyclic antidepressant? The answer was not obvious from the notes recorded). Yet again, co-morbid disorders frequently exist, and must be recognised. Van Balkom et al[47]in their study, stated that about one third of an elderly population with phobic disorders and generalised anxiety disorder also had major depression. He also found that patients with co-morbid anxiety and depression had more severe psychiatric complaints. Roberts et al[69] reported that in previous research, it was shown that women, the less educated, the unmarried, those with

health and disability problems, those with more negative life events, those with less social support, and greater isolation" were found to be more at risk for depression. Our study had a preponderance of females. The other factors are common to patients attending the hospital. Could this have been a factor causing depression in our patients? Sullivan[52] reported that major depression is the most important and prevalent psychiatric diagnosis found in association with chronic pain. He reports that prevalence of major depression in the general population is 3-5% but prevalence in a chronic pain clinic setting, is approximately 30%. He also reported that these depression episodes tend to be recurrent. In the chronic pain sufferers, in our study, it is not known how many patients were really depressed as well. Arnold et al [54] in their study, reviewed studies that examined lifetime prevalence rates of psychiatric disorders in patients with fibromyalgia and found elevated rates of major depression amongst them. Also, studies of family history of psychiatric illness in patients with fibromyalgia, reported elevated rates of depression in first degree relatives. They stated that fibromyalgia had an estimated lifetime prevalence of approximately 2% in community studies, and that it was at least twice as common as rheumatoid arthritis and is also a major public health concern. "Fibromyalgia, general body pains, muscular aches" are common symptoms reported in our records. Whether they were associated with depression is not known in our study. Van Hook[68] reported a lack of time, stigma about depression and perceptions that the primary care providers were not interested in their concerns, were amongst some of the barriers to the open discussion of depression in primary care. In their study, 32% of patients did not want information about their depression recorded in their folders. It is possible that patients had requested that their information also not be recorded, in our study patients, leading to presumed poor record keeping notes for other viewers of records. The severity of the depression, where noted, was also not obvious from the

notes, in our study. Very often neither the features of depression were recorded nor how the diagnosis was obtained in our study. Did the patient volunteer the symptoms or was it a gut feeling by the doctor, once the patient had presented his case? Did the doctor screen properly for depression? Why did the doctor use the low dose antidepressant in these cases? The answers were not clear from the records.

11.3 THE USE OR TRICYCLIC ANTIDEPRESSANTS IN TREATING INSOMNIA

From the literature review we gathered that up to a third of patients seen in the primary health care setting experienced occasional difficulties in sleeping, and up to 10 percent had chronic sleep problems. It was also noted that the prevalence of insomnia increased in age and was more common in females, the elderly, those with chronic illnesses and those with anxiety and depressive disorders.

The causes for insomnia in our study were not clear from our record keeping at Heideveld Community Health Centre. (This was not an aim of our study, thus reasons for insomnia were not sought, but it poses an important question for future study). From patients seen at our health centre, the causes may be numerous.

Psychiatric causes are believed to be the underlying disorder in more than half of all patients complaining of insomnia.[32] Proper history-taking and screening for psychiatric diseases can give the reasons for many causes of insomnia. Simon et al[41] in their study showed that there was a considerable overlap between depression and insomnia. They stated that depression was a

"powerful predictor of disability and health care utilization" but that insomnia appeared to make an "independent contribution". Walsh[40] also stated that insomnia is a risk factor for new onset depression when it persisted for one year. In my experience, patients with psychiatric causes of insomnia, patients with personality disorders and patients with chronic medical conditions causing insomnia, are all seen on a daily basis at our community health centre, and it is important to screen for these diseases when the patients present with insomnia as a symptom. Patients with substance or alcohol abuse often also report sleep problems. Sedatives or alcohol induce sedation, but causes shallow, fragmented and non- restorative sleep, if used on a regular, long term basis.[32] Sedatives and alcohol depress respiratory function which can also cause poor quality sleep.[32] Tolerance can occur with certain sedatives, prompting increased dosages and reuse of the drugs, causing a vicious cycle.[32]Substance abuse is very common in our setting. Alcohol abuse is rife on the Cape Flats. Alcohol abuse is the cause of many patients' distress when presenting with psychiatric, or psychologic, or even medical, conditions. It is a factor that crops up in the majority of cases and plays an important role in the patient's underlying anxiety or depression, or conflict state at our community health centre. Stimulant drugs, such as amphetamines, activating antidepressants, or that contained in decongestants or slimming agents, can also cause insomnia.[32] "Tik", an amphetamine derivative, is currently being abused by many children on the Cape Flats. Some use it for its stimulant effects, and some (mainly females) are abusing it for its slimming properties. Insomnia is an important symptom of substance abuse and should be explored in the history. We see all categories of these causes of insomnia in the patients at our health centre but, in our study, the underlying reasons for the patient's insomniac states were not documented. Where there were two or more symptoms documented e.g. chronic pain and depression, both could have been the cause for the patient's

insomnia. The use of tricyclic antidepressants would be acceptable in all three conditions, except that higher doses are used in the patients that were also depressed. Mertz and Fess[43] report that patients with fibromyalgia and chronic fatigue syndrome and a large proportion of patients with functional bowel disease complain of "frequent nocturnal awakenings and non-regenerative sleep." Interestingly enough, they report that sleep disturbance is more common in patients with functional dyspepsia, than with irritable bowel syndrome. It is not known what the patient's diagnosis was in the category of "abdominal pain," in our study. Could the antidepressants have been prescribed for chronic pain or was it prescribed for sleep disturbances possibly related to it? It is not known, in our study, whether the patients had volunteered insomnia as a symptom, or if it was elicited by the doctor in the history taking. The World Health Organization Psychological problems in General Health Care survey stated that insomnia amongst primary care patients was associated with significant increases in functional impairment and days of disability due to illness.[41] The National Heart, lung, and blood institute working group on insomnia, in their study[42] reported that psychiatric disorders account for less than 50% of causes of insomnia. Problems encountered during the day such as chronic pain, immobility, difficulty breathing, dementia, hormonal changes associated with pregnancy, perimenopause and menopause may also cause insomnia. They also found that more than half of patients, who believed they suffered from chronic insomnia had never discussed the problem with a doctor. They reported that insomnia is seldom the main reason for an office visit They suggested direct inquiry into a sleep history, in the routine review of systems, in history taking, to enhance detecting patients with insomnia.. They report that sleep disturbance is a "reliable indicator of psychological ill health, physical ill health or both." Therefore in patients who report sleep disturbances, this signals the need for further investigation. This is important in our

setting, since due to possible time constraints, the patient may not have the time to volunteer insomnia as a complaint during the consultation and an important signal like insomnia, could be missed. Shapiro[22] reports that "teaching about sleep and sleep disorders, in most medical schools is inadequate" and that "most doctors have the same unsubstantiated belief about sleep problems as their patients e.g. many think that all sleep problems are secondary to illness, psychological distress or psychiatric disorder." A study they reviewed showed that the average doctor asks less than three questions about insomnia before planning treatment, whereas there are many important questions that should be asked about onset of sleep, length of sleep and the patient's daytime performance. (Due to inadequacy of record keeping, it was not possible to report on questions asked and doctor's approach to insomnia, in our study, even if this is an aim for future study).

11.4 THE USE OF TRICYCLIC ANTIDEPRESSANTS IN TREATING CHRONIC PAIN

In our study, terms such as "general body pains" chronic "abdominal pain", or "chest pain" were very non-specific. It is not clear if these were genuine physical symptoms (still unexplained, still to be investigated, or vague presentations of an underlying medical disorder), or if they were part of somatic presentations of a psychiatric disorder. On the other hand, phantom limb pain, post herpetic neuralgia, fibromyalgia are examples of definite chronic pain entities, which are responsive to tricyclic antidepressants. As in Broadhead's study[4], the diagnosis clusters within the tricyclic responsive categories, were low back pain diseases and syndromes, peptic disease, fibrositis, myalgia, arthralgia, headaches, peripheral neuropathy, rheumatoid disease, and irritable bowel disease. He stated that most of these diagnoses are not purely non-

psychiatric and may often be accompanied by an Axis 1 diagnosis such as a "psychological factor affecting a physical condition". This could very well be the case in some of our diagnoses, as well. Many of our patients often have many psychological factors together with their medical illnesses. Bill O' Neill[82] reports that for most patients, physical pain is only one of several symptoms they present with. Pain relief should be seen as "part of a comprehensive pattern of care encompassing the physical, psychological, social and spiritual aspects of suffering." Physical aspects of pain cannot be treated in isolation from other aspects, nor can patients' anxieties be effectively addressed when patients are suffering physically. The need for a multidisciplinary team approach is necessary to alleviate this suffering. It is not known, in some of the cases, whether other health care officials such as the social worker, physiotherapist, or psychiatrist were consulted in our study. This could have happened but the referral of the patient to the health official was not documented in our records. Reis et al[59] reported that 5-10% of individuals with acute episodes of lower backache develop a chronic condition. Lower back pain is the single most common cause of limitation of activity in patients younger than 45 years, according to them. Patients are often not satisfied with the care they receive for lower back pain and clinicians find it one of the most difficult and unrewarding aspects of clinical medicine.[59] Their study documented that chronic lower back pain is a "biopsychosocial condition in which psychosocial and patient-centred variables play a role in predicting the clinical course". In their study of chronic pain sufferers, they identified 7% of patients with depression, 37% with a family history of chronic pain, 36% lacked family support during the pain episode, and 8% of family members and 9% of work colleagues expressed their doubts about the severity of their symptoms. They suggested that the patient-doctor agreement on sick leave days, overall satisfaction with their first office visit for the episode, patients coping style and delegitimisation

of chronic lower back pain by the family, are factors that emphasised the biopsychosocial and patient centred models of care, which should be implemented by primary care doctors. Schmader[60] stated that the outcome of chronic pain included fatigue, sleep disturbance, anorexia, depression, social withdrawal, impaired activities of daily living and profound lowering of quality of life. These factors are commonly seen in our setting, and yet again the factors such as disturbed sleep, depression fatigue and chronic pain were factors common in our study. Anderson[74] reports that patients suffering from their chronic pain resulted in exhibition of pain behaviours such as abnormal physical positioning, talking about their pain, multiple doctor visits, unemployment, excessive bed rest, limping, wincing, or crying. They may be faced with many other stressors besides the physical ones such as vocational, financial, or marital stressors. These stressors are quite common in our Heideveld community centre, and it is not unusual for the patients to present with all three and more stressors added to their physical ailments. He suggested that the easiest thing for the patient suffering from chronic pain, is to "retreat into a world of illness that is acceptable to all", for it is the "sick person who has respectable disability" and not the "person who cannot cope with his daily living." He suggested that the doctors having difficulty treating patients with chronic pain, view the patients' environment and psychosocial causes of chronic pain as "real," then they would be able to understand their pain as being "real" in the absence of a definitive diagnosis. Sullivan[52] reported that substance abuse may arise in conjunction with the chronic pain problems, or it may precede it. He stated that substance abuse impedes rehabilitation and needs to be addressed aggressively. Substance abuse is quite common in patients attending our clinic, but it was not ascertained, in our study, if it was indeed a factor in our chronic pain sufferers. In the study done by Hoss[19] they were also uncertain if their patients with chronic pain had pain secondary to underlying psychiatric

conditions such as anxiety, dysthymia, somatisation or whether these psychiatric problems were unrelated or caused by their chronic pain. Diane Hoss[19] states that a psychiatric cause or overlay has been reported in patients with chronic pain syndrome and that many of the chronic pain syndromes were initially thought to represent a psychiatric disorder only, but she stresses that one should exercise caution when reviewing data describing a personality profile or a psychiatric disorder, and not be clouded by it, in treating patients with this condition. Leland[53] in their study of older patients stated that symptoms of chronic pain, anxiety and depression are often associated and may intensify each other. This could be a reason for the overlap of symptoms reported in our data as well.

Feinmann[61] states that there is still some dispute as to whether the tricyclics exert their effects via analgesic or antidepressant pathways. She states that the complex association between pain and depression has created some confusion and that pain has been classified as a symptom of "masked or atypical depression" or even a "depressive equivalent."

Stauffer[55] reviewed the neurophysiologic similarities between chronic pain and depression. Both of these are accompanied by sleep disturbances and manifests with somatic symptoms, making the distinctions difficult. Our medical officers may be aware of these similarities, and thus be treating all of these with initially low dose tricyclics, possibly planning to review and increase doses of antidepressants used on follow up visits.

Richeimer[3] concluded that tricyclic antidepressants were commonly used in low to intermediate doses, even in situations where there were "neither side effects nor optimal clinical response in his chronic pain clinic patients. From reviewing studies done, they formed a clinical impression that tricyclic antidepressants doses are rarely maximised in treating chronic pain disorders.

Godfrey[6] stated that it was important to remember that there is a one to three week delay in

achieving the maximum sleep modification at any given dose, therefore increasing or decreasing dosages should not be done too rapidly.

Egbunike[58] stated that it is important to differentiate the indication for treatment, since the dosage range for analgesia may be much lower than that needed for the antidepressant effect. He also reported that the patients with depression may report more profound side effects associated with tricyclics. Our medical officers may have been exercising caution in certain cases, where low dose tricyclics were prescribed, in our study.

Interestingly enough, in Broadhead's study[4] he also found that primary care doctors paralleled specialist's prescribing habits for prescribing tricyclic antidepressants for certain conditions (e.g. those of neurologists for low back pain, fibrositis, headache and peripheral neuropathy, or those of gastroenterologists for irritable bowel disease). The specialist's patients were more likely to have received antidepressants, since their patients are selected and referred and may already have failed other treatments, prior to their having received the antidepressants. The doses of antidepressants used, were not recorded in their study. It would have been interesting to have found the dosages used by specialists for their patients, to see if they also used low doses or higher doses of antidepressants.

Erskine et al[57] in the opening statement of his article, said that "chronic pain is undoubtedly the worst taught, least understood and most neglected subject in modern medicine", despite the fact that "pain relief is one of the most therapeutic goals of the medical doctor."

11.5 THE USE OF TRICYCLIC ANTIDEPRESSANTS IN TREATING SOMATOFORM DISORDERS

Patients at our community health centre, often present with numerous somatic complaints. Many of these can be part of a true medical or psychiatric disorder as well. An organic or physiological disorder must be excluded, before labelling a patient as having a somatoform disorder. There are clear guidelines established for this disorder.

From the literature review, studies had shown that somatoform disorders produce significant impairment in patients functioning and quality of life and are associated with increased health care cost and services. Somatoform disorders were found to be common in females in the elderly, in patients with poor social support and also in patients with chronic physical disorders. This situation is well recognised in our hospital setting. Our study had a female predominance. (Our hospital notably sees more female patients, elderly patients and patients with poor social circumstances on a daily basis as well. Reasons for this were not evaluated in our study).

Medical illnesses causing somatisation and depression are also more common in older people therefore a clear understanding of the prevalence and association of somatisation among older people is needed. It can be time intensive when gathering sufficient information from the patient and medical records to ascertain that a physical explanation for somatic complaints in these patients is unlikely, when establishing the presence or absence of a somatoform disorder. In our setting, time is often limited due to vast numbers that the clinic sees and shortage of staff.

Diagnostic efficiency is a major issue at our clinic, but according to Kroenke[71], it is a major issue in general primary care as well. Interestingly enough, he states that the primary care doctor's gut feeling about a symptom being medically unexplained, is quite good and that few patients with symptoms initially judged to be somatoform were later found to have occult serious diseases at follow up visits. Leserman et al[70] in his study, states that many different types of stressors contributed to poor health outcome. These included "traumas and losses, such as sexual and physical abuse, death or illness in a close family member, turmoil in one's childhood home and recent negative stressful events." Jo Roberts[69] reported that somatisation and medical problems were common in victims of childhood sexual abuse. Common problems included insomnia, gastrointestinal problems, obesity, chronic pain, headaches and somatisation. In a study reviewed by her, she reported that 84% of survivors of abuse were never asked about the abuse. The researcher concluded, in her article that most survivors wanted to be asked about previous abuse, about problems encountered during examination and to have their discomfort noted and attended to. Bridges and Goldberg et al[66] also stated that a "disturbed early family environment characterised by an unstable upbringing, psychosocial problems in siblings, a poor relationship between parents and a lack of maternal affection or oversolicitious maternal behaviour," could also result in patients presenting with somatisation in primary care. Patients suffering any of these could present to the primary health centre frequently with numerous somatic complaints, in their quest for help. Direct query into psychosocial circumstances is important to elicit reasons for patients' presentation, when they present with unexplained somatic symptoms. These traumatic and unpleasant circumstances, get presented to us on a daily basis, and are common encounters to the majority of our patients. Bridges and Goldberg et al[66] also stated that somatisation has many disadvantages including the risk of it

becoming chronic and difficult to treat, and therefore these findings should not "distract attention away from the importance of family doctors improving their detection of somatisation disorders and learning how to manage them more effectively". This could be quite common in our patients as well, although this was not assessed in our study. McDaniel[72] stated that every physical symptom has "some biologic, some psychologic, and often some social component to it." Therefore, a doctor needs to be able to address each of these in a balanced and integrated way without fixating inappropriately on any one component of the symptom and therefore they also advocate a "biopsychosocial approach that would break the vicious circle that doctors and patients can be drawn into and leads to successful management."

Included in the somatising patients who presents with somatic complaints that are among the most frustrating encounters that present to primary care, are anxious or depressed patients (or both), hypochondriacs, chronic pain patients and malingers. They have to be carefully evaluated and managed appropriately.

Low dose Imipramine is one of the drugs used to treat nocturnal enuresis[84]. From discussions with colleagues at the community health centre, our medical officers frequently prescribe it for nocturnal enuresis, when the need arises. However, it was interesting to note that nocturnal enuresis was not one of the conditions recorded when prescribing low dose antidepressants in my study.

It is interesting to note that in the information package inserts,[87,88] that the use of Amitriptyline and Imipramine is indicated only for "endogenous depression, mild tranquilising and sedative

properties helpful in alleviating anxiety or agitation that often accompanies depression, Parkinsonism, chronic alcoholism and behavioural disorders in children." Should the manufacturers not be including the many other non-psychiatric conditions that respond to low dose antidepressants amongst the indications for antidepressants in the information package inserts as well?

12. LIMITATIONS OF THE STUDY

I chose to do a retrospective study, for my project. Howie[83] states that "retrospective research analyses material which is already available and has not been collected with the aims of the specific project in mind." It can easily survey very large quantities of information and can cover greater periods of time than in prospective studies. He reports that information is, however, rarely of "definable or standard quality and its accuracy may thus be very difficult to judge." He also states that information obtained is often capable of showing associations between factors studied, but cannot comment on the nature of such associations. I found this to be the case with my study.

I had reviewed 500 folders (a fairly large sample size) over a two week period and managed to retrieve the information sought. As Howie[83] stated, in terms of accuracy, a major assumption was made that the prescribing doctors had indeed made the correct diagnosis in my study. The main limitation of the study was the perceived poor or inadequate record-keeping, by the medical officers, whose notes in the folders were used for the purposes of the study. Quite a

large proportion (17%) of the patients had no diagnosis recorded, thus some of the reasons for the use of low dose antidepressants are not known.

There was an overlap of symptoms as the indications for the use of low dose antidepressants, and it is not clear from the notes alone, for which of the symptoms the low dose antidepressant was prescribed e.g. chronic pain and insomnia. Both respond to low dose antidepressants, but the actual reason for it being prescribed by the doctor is not known. Where for examples, depression and insomnia had co-existed, it is not clear why the doctor then prescribed low dose antidepressants, which is inappropriate for depression.

I was unable to ascertain whether follow-up visits were scheduled to monitor side effects, or for steady increases in dose. The latter would be unlikely since usually a month's supply of the dose of the antidepressants was boarded on the medication script. (I did not actually document the duration of the prescription, for the purposes of the study, although, it would have been useful, for following up the possible treatment of depression in some of the patients).

Compliance with medication and patient satisfaction with medication was not known either. Did the use of low dose antidepressant medication benefit our own Heideveld Community Health Centre population of patients with their multiple intrinsic and extrinsic sources of problems, which could be unique only to our area of patients, and not likened to studies overseas? This question needs to be addressed in subsequent studies in the same cohort of patients.

13. THE NEED FOR FUTURE RESEARCH

From our literature search, we can be satisfied that the use of low dose antidepressants was appropriate for use in patients with chronic pain symptoms. It is not known whether our own patients were compliant with the medication and whether their symptoms were actually relieved with their use. This needs to be explored further.

Likewise, insomnia is successfully treated with low dose antidepressants, but it is not known why so many of our patients needed antidepressants. It is also not known whether they were compliant with the medication, and whether they also needed low dose antidepressants for underlying depression, anxiety or chronic pain symptoms.

Was depression under-treated at our facility? This is another question that I identified. Depression needs to be adequately treated with proper, higher doses of antidepressants. However, in our setting, many of our patients suffer from symptoms that could cause anxiety or temporary depression or reactive depression that warrants the use of antidepressants. With their follow up visits, their symptoms could have resolved, depending on their situational state. Were they truly depressed at the time of their visits? What were their presenting complaints to the doctor at their visit? Did the doctor screen for depression? Did the doctor delve into their reasons for their insomnia or chronic pain? Did the patient come back for the follow up visits? Were dosages appropriately increased in patients that were truly depressed, if it was confirmed at follow up visits? Were patients with depression treated by the medical officers or were they

referred to the psychiatrists? How many of the 30,6 % of our patients that were prescribed low dose antidepressants were actually missed depression cases?

Of the patients that did not have a diagnosis recorded, it is not known why they were using low dose antidepressants. It would have been a valuable exercise to find out from either the doctor or the patient, why the low dose antidepressant was prescribed.

It would be interesting to find out from the doctors the reasons for their poor record keeping? Why was a diagnosis not recorded for 17% of the patients receiving low dose antidepressants? Was it a genuine error of omission, in not recording the diagnosis? Or was it similar to studies done elsewhere, as gathered in our literature search. Was depression being under diagnosed or under treated for any other reason? Were doctors "scared" of using full dose antidepressants for fear of side effects or any other reason? Did doctors screen for depression in patients who presented with physical symptoms, chronic pain or insomnia? Were doctors happy with their consultations? Were they referring appropriately to other health workers where needed to assist them with patient care? Did they feel that they were using low dose antidepressants appropriately? Did they feel that they were prescribing the antidepressant instead of dealing with the patients' possible underlying stressors, e.g. chronic pain, instead of depression, insomnia instead of the chronic pain or domestic stressors, which could cause depression in the patient?

It would be interesting to find out from the patients what they thought the antidepressant was used for, if their symptoms were relieved by the use of it, whether they were compliant with it,

side effects experienced with the low dose antidepressants, and whether they needed higher doses on follow up visits. Did the patients think that they were depressed at the time of the visit? Did they feel the doctor missed a possible depression at their visit? Were they satisfied with the consultation? Were they adequately counselled or referred for counselling where they needed it? Did they feel that the low dose antidepressant was prescribed (like the physiotherapist in the beginning of the study suggested), to solve their problem, instead of counselling them because of time restrictions? In cases where this was indeed the case as well (perhaps in the cases where no diagnoses were recorded), was adequate referral made to the appropriate authorities e.g. social worker, home carers, etc., to assist them with their problems?

All these questions arose which were not part of the aims for this study, (thus remain unanswered), but could provide valuable material to us for future studies.

14. RECOMMENDATIONS

1. Doctors must practice good note taking. Diagnosis must be recorded in folders. It is not only essential for study purposes but also for follow up, especially in areas such as the community health centres, where continuity of care cannot be assured, because of the high turnover of patients. Discussing adequate and appropriate record keeping should be included in both the undergraduate and postgraduate teachings in Family medicine. Regular audits on record keeping should be carried out, in order to ensure compliance with good record keeping.
During my study, it was quite difficult to retrieve information from our folders because of poor record keeping, and impossible in 17% of study subjects to ascertain a diagnosis.

2. Targeting patients with insomnia is the next important recommendation I would suggest. Insomnia was the main indication for the patients using low dose antidepressants. Finding out why there are so many patients who suffer from insomnia at our clinic, would be an interesting and meaningful study. An attempt should be made to identify the underlying reasons for insomnia, in our area, and the surrounding neighbouring areas, served by our clinic. (None of the folders had any idea of the type of insomnia experienced by patients, nor was there any mention of a good sleep history being taken). Doing a study to see how insomnia in general is being treated at our community health centre, would also be a valuable exercise. Finding out about what the patients have been told regarding insomnia and also if the patients who suffer from insomnia have been given appropriate sleep hygiene instructions would be important. Ascertain whether antidepressants are just being dished out to patients with insomnia as a complaint, or are appropriate attempts being made to correct underlying stressors, underlying medical conditions, etc.

3. Screening for depression is one of the main recommendations emanating from this study. As could be seen from our findings, there is a real possibility that depression could have been missed in patients presenting with any of the complaints, all valid, and appropriately treated with antidepressants, but higher doses of antidepressants would then be necessary. Ensure adequate follow up for these patients and ensure appropriate referral for assistance from other members of the health team e.g. social worker, psychiatrist, health care workers, etc.

4. Doctors should check to see that chronic pain is being adequately managed. Finding out whether patients have adequate pain relief and whether they are compliant with their treatment, would be a valuable exercise in our patients. Confirming whether doses being used are adequate to give reasonable pain relief could be a part of the study. Ensuring that a multidisciplinary team approach towards their care is set in place, and that there is easy access to all partners involved. Assisting carers by briefing them about the chronicity of the condition, its treatment, etc. and ensuring that there is care for the carers available would be another recommendation.

5. Target 51-59 year old patients at our day hospital. Finding out what is happening to this age group, and identifying the reason behind the need for an increased prescription rate in prescribing low dose antidepressants, in this age group, as can be seen in Figure 3. Determining whether there is some underlying problem in the area, whether it be physical, environmental, domestic, or financial problems, etc., that may give rise to either an increase in anxiety, depression, insomnia, and increased chronic pain in patients with such afflictions that would warrant low dose antidepressant medication, as an aid, and ensuring that patients' health needs are being met adequately by our clinic.

15. CONCLUSION

In our study we showed that low dose tricyclic antidepressants were appropriately used for the conditions known to respond to it, i.e. non-psychiatric indications, as well as for its psychiatric indications, in our patients at Heideveld Community Health Centre.

The study highlighted areas that could form the basis for future research. Hopefully, medical officers would practice better record keeping and thus also improve communication, and

continuity of care. By paying attention to points of interest that followed from this study, medical officers could also improve on overall care of patients attending Heideveld Community Health Centre with psychiatric conditions, insomnia, chronic pain and somatoform disorders.

16. ARTICLE OF INTEREST

A recent article in the Cape Argus Monday August 9 2004, caught my attention. The headlines read that Prozac, an antidepressant, was found in Britain's water. The article mentioned that Prozac was used in such large quantities, that it could be found travelling through the sewerage network and ended up being recycled back into the water system. The same article reported that since 1991 there has been a 166% increase in prescriptions for antidepressants in England (up to 24 million a year). Another recent study, reported in the article mentioned that four out of five general practitioners admitted to over-prescribing antidepressants. The reasons for this were not mentioned. (Our study could share a common topic of interest, recording reasons for use of antidepressants, in other areas of the world as well).

I wonder what the consultant (in our introduction) who suggested putting Amitriptyline in our drinking water would have said in response to this article!

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87. Trepiline information package insert (Appendix A).

88. Ethipramine information package insert (Appendix B).

APPENDIX A: TREPILINE PACKAGE INSERT

SCHEDULING STATUS: [B6]

PROPRIETARY NAME (AND DOSAGE FORM):

TREPILINE®-10 TABLETS
TREPILINE®-25 TABLETS

COMPOSITION:
Each tablet contains 10 mg (25 mg) of Amitriptyline HCl.

PHARMACOLOGICAL CLASSIFICATION:
A 1.2 Psychoanaleptics.

PHARMACOLOGICAL ACTION:
Amitriptyline inhibits the membrane pump mechanism responsible for re-uptake of noradrenaline into adrenergic neurons. Pharmacologically this action may potentiate or prolong sympathetic activity, since re-uptake of noradrenaline is important physiologically in terminating its transmitting actions. This interference with re-uptake of noradrenaline is believed by some to underline the antidepressant activity of amitriptyline. The precise mechanism of action in man has not yet been confirmed. It is not a monoamine oxidase inhibitor and it does not act primarily by stimulation of the central nervous system.

INDICATIONS:
Amitriptyline is a tricyclic antidepressant used in the treatment of patients with endogenous depression. It also possesses mild tranquillising and sedative properties which is helpful in alleviating anxiety or agitation that often accompanies depression. It has been used with benefit in depression of long or short duration. All patients do not respond to the same degree. Some may respond in 4 to 10 days while others may require up to 30 days to obtain benefit. Lack of response may occur occasionally.

CONTRA-INDICATIONS:
Amitriptyline is contra-indicated in patients who have shown prior hypersensitivity to it.
It should not be given concomitantly with a monoamine oxidase inhibiting compound. Hyperpyretic crises, severe convulsions and deaths have occured in patients receiving tricyclic antidepressant and monoamine oxidase inhibiting drugs simultaneously. When it is desired to substitute amitriptyline for a monoamine oxidase inhibitor, a minimum of 14 days should be allowed to elapse after the latter is discontinued. Amitriptyline should then be initiated cautiously with gradual increases in doses until optimum response is achieved.
Amitriptyline is not recommended for use during the acute recovery phase following myocardial infarction because it has been reported to produce arrythmias, sinus tachycardia and prolongation of the conduction time.
Amitriptyline should not be administered concurrently with antihypertensive medicine, particularly adrenergic blocking agents such as Guanethidine.
Safe use of amitriptyline during pregnancy and lactation has not been established.
Amitriptyline should not be given to children under 12 years of age.

WARNING:
This medicine should at all times be kept out of reach of children, as even small doses may be fatal to them.
Drowsiness is often experienced at the start of amitriptyline therapy and patients if affected should not drive or operate machinery.

DOSAGE AND DIRECTIONS FOR USE:
Adults: Initially 75 mg to 150 mg daily in divided doses.
Maintenance dose is 50 mg to 100 mg daily in divided doses.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:
Many side-effects of amitriptyline are caused by its anticholinergic actions. These include dry mouth, sour or metallic taste, constipation which may lead to paralytic ileus, urinary retention, pupillary dilatation with blurred vision and disturbances in visual accommodation, palpitations, tachycardia and impotence.
Other adverse effects include drowsiness (but sometimes nervousness and insomnia may occur), headache, peripheral neuropathy, tremor, orthostatic hypotension, hypertension, dizziness, sweating, weakness and fatigue, ataxia, epileptiform seizures, extrapyramidal symptoms including speech difficulties, tinnitus, stomatitis and gastric irritation with nausea and vomiting. Confusion or delirium may occur, particularly in the elderly. Anorexia with mass loss, or mass gain may occur. Allergic skin reactions and photosensitisation have been reported and, less frequently, cholestatic jaundice and blood disorders, including eosinophilia, bone-marrow depression, thrombocytopenia, leucopenia and agranulocytosis.
Amitriptyline has an adverse effect on the myocardium and can cause conduction defects and cardiac arrhythmias: an increased risk of sudden death has been suspected in cardiac patients receiving tricyclic antidepressants. Thus amitriptyline should be used with caution in patients with cardiovascular disease and should be avoided in the immediate recovery phase after myocardial infarction and in patients with heart block.
Endocrine effects include changes in libido, interference with sexual function, gynaecomastia and breast enlargement, and galactorrhoea. Changes in blood sugar concentrations may also occur and, less frequently, inappropriate secretion of antidiuretic hormone.
Caution should be observed with patients suffering from a depressive phase of manic depressive psychosis, as occasionally mania can be precipitated in such patients. Withdraw the drug if the depression turns into a manic phase. Patients with suicidal tendencies should be carefully supervised during treatment.
The presser effects of the direct-acting sympathomimetic agents, adrenaline and noradrenaline, are enhanced by amitriptyline, and local anaesthetics containing these vasoconstrictors should be avoided as hypertensive reactions may occur. When possible, treatment should be discontinued several days before elective surgery. The hypotensive effect of certain antihypertensive agents may be reduced.
The use of amitriptyline in patients suffering from acute forms of porphyria, especially variegate porphyria and to a lesser extent acute intermittent porphyria and hereditary coproporphyria, is contentious, and thus Trepiline should be used with caution in these patients.
Amitriptyline should also be used with caution in patients with hyperthyroidism or with impaired liver function, and in those with a history of epilepsy, untreated narrow-angle glaucoma, urinary retention, prostatic hypertrophy, or constipation.
Central nervous system depressants including alcohol and anticholinergic agents can have their effects increased by amitriptyline.

NOTE: Elderly patients are more prone to all these effects, and therapy should be initiated at lower than standard doses in the elderly.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Symptoms of overdosage are excitement and restlessness with marked anticholinergic effects, including dryness of the mouth, dilated pupils, tachycardia, urinary retention, and intestinal stasis. Severe symptoms include unconsciousness, convulsions and myoclonus, hyperreflexia, hypotension, and respiratory and cardiac depression, with life-threatening cardiac arrhythmias that may recur some days after apparent recovery.
Treatment is symptomatic and supportive.

IDENTIFICATION:
10 mg – Pale blue, shallow, biconvex, film-coated tablets.
25 mg – Yellow, shallow, biconvex, film-coated tablets.

PRESENTATION:
10 mg – Securitainers of 100 and 500 tablets.
25 mg – Securitainers of 100 and 500 tablets.

STORAGE INSTRUCTIONS:
Store below 25°C
Protect from light and moisture.
KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBERS:
10 mg Tablets J/1.2/219
25 mg Tablets J/1.2/220

NAME AND BUSINESS ADDRESS OF APPLICANT:
Pharmacare Limited
7 Fairclough Road
PORT ELIZABETH
6001

DATE OF PUBLICATION OF THIS PACKAGE INSERT: 12 May 1978

6875
A & S PRINTERS

APPENDIX B: ETHIPRAMINE PACKAGE INSERT

SCHEDULING STATUS: S5
PROPRIETARY NAME (AND DOSAGE FORM):

ETHIPRAMINE 10 mg TABLETS
ETHIPRAMINE 25 mg TABLETS

Each tablet contains:
Imipramine hydrochloride 10 mg
Imipramine hydrochloride 25 mg
PHARMACOLOGICAL CLASSIFICATION:
A 1.2 Psychoanaleptics (antidepressants)
PHARMACOLOGICAL ACTION:
ETHIPRAMINE (Imipramine hydrochloride) is a tricyclic antidepressant with weak anticholinergic and antihistaminic actions.
INDICATIONS:
Endogenous depression, Parkinsonism, chronic alcoholism, behavioural disorders in children.
CONTRA-INDICATIONS:
The acute phase of myocardial infarction.
Administration is not advised during the first trimester of pregnancy unless there are compelling reasons for its use.
WARNINGS:
This medicine should at all times be kept out of reach of children, as even small doses may be fatal to them.
DOSAGE AND DIRECTIONS FOR USE:
Usual dosage:
75 to 150 mg daily in divided doses or as prescribed
Elderly patients:
Not more than 10 to 30 mg per day
Children:
6 to 12 years: 25 mg at bedtime
Over 12 years: 50 mg at bedtime
SIDE-EFFECTS AND SPECIAL PRECAUTIONS:
Peripheral anticholinergic side-effects:
Dry mouth, constipation, urinary retention and pupillary dilation with blurred vision and changes in visual accommodation.
If these effects are severe, the medication should be withdrawn.
Central nervous system side-effects:
Drowsiness, excessive sedation, disorientation, agitation, insomnia and restlessness.
Note:
All these side-effects occur more commonly in elderly patients, hence therapy should be initiated at lower than normal dosages in these cases.
Precautions:
1. Patients are advised that the use of this medicine may lead to impaired decision-making and hence the driving of motor vehicles, climbing of dangerous heights or operation of dangerous machinery, etc. should be avoided for several days after initiation of therapy.
2. In the depressive phase of manic depressive psychoses, its use may precipitate mania or hypomania, in which case the drug should be immediately withdrawn.
3. In elderly *male patients with prostatism it may precipitate urinary retention.*
4. In cardiac disease, regular cardiological and electrographic examinations are advised, as it may occasionally produce tachycardia, dysrhythmias, orthostatic hypotension, blood pressure disturbances and electrocardiographic abnormalities.
5. Epilepsy and narrow angle glaucoma may be aggravated.
6. The risks of central nervous system depression are increased when it is taken in conjunction with other central nervous system depressants, e.g. alcohol and barbiturates. It should not be given together with MAOI or within 2 weeks of such treatment. (The abovementioned drugs may only be given in conjunction with a tricyclic antidepressant if dosages are very carefully monitored, preferably in hospital). The pressor effects of adrenaline and noradrenaline are enhanced and the use of local anaesthetics containing these should be avoided. Simultaneous administration of anticholinergic agents may be dangerous. The hypotensive effects of certain antihypertensive agents may be reduced.
7. If allergic skin reactions occur the drug should be withdrawn.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Overdosage and poisoning may result in central nervous system depression, excitation, severe anticholinergic effects and cardiotoxicity which may be characterised by the following signs and symptoms: drowsiness, restlessness, ataxia, stupor, coma, pyrexia, palpitations, tachycardia, cardiac arrhythmias, hypotension and, in severe cases, respiratory depression.
Epileptiform seizures may occur. Mixed poisoning with central nervous system depressants is not uncommon.
Treatment includes emptying of the stomach by aspiration and lavage.
Diazepam should be given i.v. or paraldehyde i.m. to control convulsions. Fluid intake should be maintained by infusions of electrolyte solutions. Respiration may need to be assisted and corticosteroids administered.
Cardiac irregularities should be corrected.
IDENTIFICATION:
10 mg: Yellow shiny, sugar-coated tablet
25 mg: Orange, sugar-coated tablet
PRESENTATION:
10 mg: 50', 100', 250', 500', 1 000', 5 000'
25 mg: 50', 100', 250', 500', 1 000', 5 000'
STORAGE INSTRUCTIONS:
Store below 25 °C and protect from light.
KEEP OUT OF REACH OF CHILDREN.
REFERENCE NUMBER:
10 mg: B695 (Act 101/1965)
25 mg: B694 (Act 101/1965)
NAME AND BUSINESS ADDRESS OF APPLICANT:
PHARMACARE LIMITED
Building 12
Healthcare Park
Woodlands Drive
Woodmead
Sandton
2148
DATE OF PUBLICATION OF THIS PACKAGE INSERT: 20 November 1969
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