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Race and Sex Differences in Pain Sensitivity and Beliefs

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A Dissertation submitted to the Faculty of Health Science, University of the Witwatersrand, Johannesburg, in fulfillment for the degree of Master of Science in Medicine.

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ABSTRACT

Differences in pain perception and beliefs have been demonstrated between races and sexes. Beliefs, social influence, psychological factors, and socioeconomic status have been attributed to these differences in pain. There currently are no data on whether sex and racial differences in pain perception and beliefs exist in the South African population. Therefore in this study I evaluated sex and racial differences in pain perception and pain beliefs within a cohort of black and white Southern African university students.

Sixty-four black and 56 white female students and 44 black and 52 white male students were recruited from the University of Witwatersrand. Cold pain tolerance was assessed using the cold pressor test, and pressure-pain was assessed using a blunt pressure algometer. Pain intensity was measured after both pain tests and pain tolerance was recorded. Psychological variables and socioeconomic status were evaluated using the Pain Catastrophizing Scale; Hopkins Symptoms Checklist-25; Appropriate Pain Behaviour Questionnaire and the Assessment of Socioeconomic Status questionnaire. Univariate analyses were carried out for all variables, for the comparison of black males against black females; white males against white females; white females against black females, and white males against black males. Regression tree analyses were used to determine the correlates of experimental pain tolerance, pain intensity and pain beliefs, to the variables.

Black males and females had a lower tolerance to cold pain ($p = 0.01$; $p < 0.01$) compared to white males and females, as well as greater depression ($p < 0.01$; $p = 0.02$) and pain catastrophizing ($p = 0.03$; $p < 0.01$). In general, females had a lower tolerance to pressure pain ($p < 0.01$; $p < 0.01$), as well as greater anxiety ($p < 0.01$; $p < 0.01$), depression ($p < 0.01$; $p < 0.01$), and pain catastrophizing in black females ($p < 0.01$). There were no differences in rating of pain intensity for the cold or pressure pain stimuli between the sexes and races, except for black females, who reported greater pain intensity during the cold pain test ($p < 0.01$). Males and females were more accepting of females expressing pain than men ($p < 0.01$; $p = 0.04$). In particular, black males felt men should not express pain ($p < 0.01$). Regression analyses revealed that pain beliefs on men; pain tolerance; and cold pain

intensity were correlated with race and sex difference. In conclusion, pain tolerance and sensitivity to experimental pain were affected by both race and sex in this cohort of black and white South African students. Whilst these data need to be verified in patient cohorts, they have important implications for the assessment and management of pain in South Africa.

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DECLARATION

I declare that this dissertation is my own, unaided work. It is being submitted for the Degree of Master of Science in Medicine in the Faculty of Health Sciences, at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

.....

Leeana Aarthi Bagwath Persad

..... day of ....., 2014

I certify that the studies contained in this dissertation have the approval of the Committee for Research in Human Studies of the University of the Witwatersrand, Johannesburg. The ethics approval number is M120648.

Leeana Aarthi Bagwath Persad

.....day of....., 2014

.....	.....
Peter Kamerman (supervisor)	Antonia Wadley (supervisor)
Date.....……..	Date.....……..

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List of Abbreviations

AF	Asian females
AIF	American Indian females
APBQ	Appropriate Pain Behaviour Questionnaire
ASS	Assessment of Socioeconomic Status
BDNF	Brain derived neurotropic factor
BF	Black females
BM	Black males
BMI	Body mass index
CCM	Chinese-Chinese milieu
CECM	Chinese European milieu
CP	Cold pain
CPT	Cold pressor test
HF	Hispanic females
HR	Heart rate
HSCL-25	Hopkins Symptom Checklist-25
IF	Indian females
mRNA	Messenger ribonucleic acid
PCS	Pain Catastrophizing Scale
PP	Pressure-pain
PPT	Pressure-pain test
QOL	Quality of life
SAF	South Asian females
SES	Socioeconomic status
VAS	Visual analogue scale
WF	White females
WM	White males

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CHAPTER 1

INTRODUCTION

1. INTRODUCTION

The term ‘race’ distinguishes the major groups of people corresponding to their ancestry. Race is used to differentiate a population related by blood, common descent or heredity, while ethnicity focuses on the distinction between groups of people based on physical characteristics, biology, culture and behaviour (Edwards *et al,* 2001). In this dissertation I use the terms ‘black’ and ‘white’. Currently in South Africa, ethnic Africans are classified as black; Europeans, Jews and Middle Easterners are classified as white (Mickelsfield *et al*, 2013).

Pain is a multidimensional experience affected by biological, psychological and societal factors (Racine *et al*, 2012b; Hashmi and Davis, 2013). Acute and chronic pain affect quality of life (QOL) (Tsang *et al*, 2008; Dominick *et al*, 2012; Butow and Sharpe, 2013) and can lead to disability and financial hardship from absenteeism at work (Schierhout *et al*, 1993; Campbell *et al*, 2003).

Pain intensity varies significantly between people with the same pain conditions (Morin *et al*, 2000; Gray and Berger, 2007; Boerner *et al*, 2014). This difference may be due to different disease stages. However, when pain stimuli are standardized in experimental pain conditions, reports of pain intensity, unpleasantness and tolerance still vary between individuals (Tashani *et al*, 2010; Forsythe *et al*, 2011). Genetics, sex, race and economics are factors thought to affect one’s perception of pain. Furthermore, sex and race also affect access to healthcare and pain treatment (Green *et al*, 2003; Gray and Berger, 2007).

Although direct epidemiological data are not available, pain is thought to be common in South Africa with the high prevalence of HIV and cancer contributing to this (Beck and Falkson, 2001; Sukati *et al*, 2005; Harding *et al*, 2012; Maree *et al*, 2013). South Africa is an ethnically and culturally diverse country, containing individuals of predominantly black, white, Indian and coloured (mixed race) descent, and has a unique culture both generally and within race groups. Economic status varies significantly within the population, with signified ethnic stratification (Stats SA, 2013). Therefore, research completed in Europe and the United States cannot always be generalized to this country. For pain in clinical conditions to be identified, assessed

and managed appropriately in this country, having a baseline understanding of the differences in pain sensitivity and beliefs between the sexes and races is essential.

In the Introduction chapter I will discuss the evidence for differences in pain sensitivity between the sexes and between the races. In both these sections I will primarily discuss the impact of psychological and socioeconomic factors on the pain experience.

1.2 LITERATURE REVIEW

The following search criteria were used for selecting articles and studies that used physically healthy subjects or those with chronic pain.

The following search engines were used: Science Direct; Pubmed; SCOPUS; SpringerLINK; Wiley Online Library; Google Scholar.

Table 1.1 Key words searched

African; anxiety; cardiovascular; catastrophizing; chronic pain; cold pain; depression; ethnicity; experimental pain; female hormones; gender; pain; pain beliefs; pain genes; pain medication; pain perception; pain intensity; pressure pain; race; sex; socioeconomic status; South Africa; state catastrophizing; trait catastrophizing

1.2.1 SEX AND PAIN

Experimental and clinical studies have consistently shown a higher prevalence of pain (Sanford *et al*, 2002; Tsang *et al*, 2008; Boerner *et al*, 2014) and pain sensitivity (lower pain thresholds and tolerance) (Robinson *et al*, 2001) in women than in men. The principal conditions that could lead to these differences between women and men are examined below.

The association between sex and experimental pain sensitivity is summarised in Table 1.2 Scores were allocated to studies based on criteria questions in Appendix 1, a score closer to 1.00 indicated a good study that met most of the criteria questions.

A score of less than 0.40 is indicative of a poor study and is considered the cutoff point to exclude a study. None of the articles had a poor score and none were excluded. In general, women had a lower pain tolerance and reported greater intensity for experimental pain than did men. These results were most consistent with the cold pressor test (CPT). Despite there being an abundance of evidence indicating that women experience more pain than men, it has been reported that women are prescribed less pain medication (Wandner *et al,* 2011).

Females had a lower cold pain tolerance than men (Rahim-Williams *et al*, 2007) however the sample size of black males (about 21) were much less than that of black females (41), therefore a comparison between black males and females does not have strong statistical power.

Robinson *et al* (2003) compared cold pain sensitivity between men and women allocated in three groups (no goal; 30 seconds; 60 seconds), however each group had 20 men and 20 women, this sample size was not sufficient for power analysis. This study also has a psychosocial component that explores men and women's perception on the expected pain behaviour of their sex, however no sociological tools were used to assess the participant's views on gender roles or beliefs in society, or in pain.

Some studies suggested blood pressure may contribute to differences in pain sensitivity between the sexes (Koltyn *et al*, 1999; Myers *et al*, 2001). However they were not successful and did not include any psychological variables in their study which are evident in sex comparisons (Lei and You, 2012; Racine *et al*, 2012b).

It may be advantageous to assess multiple psychological variables instead of only one. Soetanto *et al* (2006) found females to have a lower pressure-pain tolerance, yet no difference in state and trait anxiety when compared to males. They attributed their sample, for having similar demographic characteristics, as the reason for no difference in anxiety between the sexes but an explanation on this association was lacking.

TABLE 1.2 WOMEN EXHIBIT GREATER EXPERIMENTAL PAIN SENSITIVITY THAN DO MEN

Authors	n	% Female	Country	Ethnicity	Type of pain	Findings	Score (1.00)†
Forsythe *et al*, 2011	155	53.5%	America	61.3%White 38.7% African American	Cold	Women had lower CP tolerance. Women had greater pain intensity.	1.00
Hirsh *et al*, 2008	100	66%	America	46% White 20% Hispanic 17% Asian/ Pacific Islander, 10% African American 7% missing/other	Cold	Women had lower CP tolerance. No difference on pain intensity.	0.91
Jackson *et al*, 2002	112	61.6%	America		Cold	Women had lower CP tolerance. Women had greater pain intensity.	0.82
Jackson *et al*, 2005	91	62.6%	America		Cold	Women had lower CP tolerance. Women had greater pain intensity.	0.86
Jackson, 2007	118	58.4%	Australia	97.5% White	Cold	Women had lower CP tolerance, except for when they were asked to identify uncomfortable sensations.	0.86

Authors	n	% Female	Country	Ethnicity	Type of pain	Findings	Score (1.00)†
Kim *et al*, 2004	617	59.8%	America	55.8% White 21.1% African American 9.6% Hispanic 10.9% Asian American 2.8% mixed race	Cold Heat	Women had lower CP tolerance. Women had greater heat pain intensity.	0.64
Koltyn, 1999	29	48.2%	America		Pressure	Women had lower PP thresholds.	0.64
Myers *et al*, 2001	99	55.5%	America	78.8% White 9.6% Asian-American 7.7% Hispanic 3.8% other	Cold	Women had lower CP tolerance.	0.68
Nayak *et al*, 2000	226	50% 47.7%WF 52.2% IF	America India	47.3% White 52.6% Indian	Cold	Women had lower CP tolerance. No difference on pain intensity	0.91
Quiton and Greenspan, 2008	64	50% 62% WF 13% HF 13% AF 6% SAF 3% BF 3% AIF	America	White Hispanic Asian South Asian Black American Indian	Heat	Women had greater pain intensity.	0.55

Authors	n	% Female	Country	Ethnicity	Type of pain	Findings	Score (1.00)†
Rahim-Williams *et al*, 2007	206	66% BF 43% WF 56% HF	America	30.6% African American 29.6% Hispanic 39.8% White	Heat Ischemic Cold	BF had a lower ischemic and CP tolerance than BM. WF had a lower CP tolerance than WM. No difference for heat pain.	0.59
Robinson *et al*, 2003	120	50%	America		Cold	Women had lower CP tolerance. No difference on intensity.	0.55
Sanford *et al,* 2002	144	54.1%	America		Cold	Women had lower CP tolerance. Women had greater pain intensity.	0.86
Sarlani and Greenspan, 2002	20	50%	America		Mechanical	Women had a lower PP tolerance.	0.68
Sarlani *et al*, 2004	50	50%	America		Mechanical	Women had a lower PP tolerance.	0.73
Soetanto *et al*, 2006	178	50%	Hong Kong	Chinese	Pressure	Women had a lower PP tolerance.	0.64
Thorn *et al*, 2004	219	58.9%	America	84.4%White 10.9% African American 4.5% Hispanic	Cold	Women had lower CP tolerance. Women had greater pain intensity.	0.68

Authors	n	% Female	Country	Ethnicity	Type of pain	Findings	Score (1.00)†
Wise *et al*, 2002	148	58.8%	America		Heat	Women had lower heat tolerance. Women had greater pain intensity.	0.86

WF = white females, BF = black females, HF = Hispanic females, IF = Indian females, AF = Asian females, SAF = South Asian females, AIF = American Indian females, BM = black males, WM = whites males, CP = cold pain, PP = pressure-pain

† Appendices 1 and 2

1.2.1.1 BIOLOGICAL FACTORS AND SEX DIFFERENCES IN PAIN

Physiological variables have been extensively researched as potential reasons for sex differences in pain sensitivity. However, a review of 129 articles found the evidence inconsistent for biological and physiological factors mediating differences in pain perception between the sexes (Racine *et al*, 2012b). The literature regarding physiological factors and pain sensitivity is vast and outside the scope of this dissertation therefore I provide a brief account of the field.

One of the main differences between men and women is exposure to different concentrations of sex hormones. Furthermore, these hormonal concentrations differ across the menstrual cycle and with the taking of oral contraceptives. A review by Aloisi and Fiorenzani (2013) had mixed views on the role of estrogen being analgesic, causing hyperalgesia, or having no effect on acute nociceptive responses. However, studies have shown that estrogen is involved in the development of chronic pain, with an increase in estrogen affecting the development of chronic pain (Aloisi and Fiorenzani, 2013). Kowalczyk *et al* (2010) states that sensory discrimination (the ability to distinguish among various stimulus intensities) can be a measure of sensory sensitivity to differences in painful stimuli and could therefore be a measure of pain sensitivity. Kowalczyk *et al* (2010) found normally menstruating women (not on oral contraceptive) to have a better sensory discrimination to mechanical stimuli during the luteal phase of their menstrual cycle, suggesting that high levels of estradiol and progesterone may have coincided with better sensory discrimination and therefore may influence greater pain sensitivity.

A review of sex differences in hormonal modulation of deep tissue pain by Traub and Ji (2013) proposed that female sex hormones excite spinal, supraspinal and primary afferent neuron activity (ascending nociceptive pathways), leading to differences in pain perception. Aloisi and Fiorenzani (2013) also found the superficial dorsal horn lamina of the spinal cord to have estrogen sensitive neurons, that will increase in activity as levels of estrogen increase. However, the mechanisms and involvement of these processes is uncertain. Furthermore, another review on sex differences by Hashmi and Davis (2013) suggested that women have a greater sensory response to pain that stems from ascending nociceptive pathways, and a greater modulation, or coping response, from the descending modulation pathways.

Other physiological variables such as cortisol secretion and cardiovascular reactivity have been said to predict sex differences in pain experience but the evidence is equivocal. For example, one study showed that when subjected to cold pain (CP), men had a greater CP tolerance and greater post-test salivary cortisol levels when compared to women (Dixon *et al*, 2004) while another study (Bento *et al*, 2010) found no cortisol differences between the sexes when exposed to cold pain. Inconsistencies between pain sensitivity and heart rate (HR) have also been identified. When subjected to heat pain, men had a higher pain tolerance and HR than women (Myers *et al*, 2001; Tousignant-Laflamme *et al*, 2005) yet when participants with and without a family history of hypertension were exposed to CP, no sex differences were found (al' Absi *et al*, 1999).

In summary, women have lower cold and pressure-pain tolerance than do men. Physiological variables such as hormonal differences, cortisol levels and cardiovascular reactivity may contribute to differences in pain sensitivity between the sexes but the evidence is mixed.

1.2.1.2 Psychological factors influencing sex differences

Psychological factors may correlate with differences in pain sensitivity (Keogh, 2006; Lei and You, 2012; Racine *et al*, 2012b). When subjected to a cold and electrical pain stimuli, individuals with greater anxiety had a lower pain tolerance (Keogh and Cochrane, 2002; Tang and Gibson, 2005). With regards to sex, studies have shown that women tend to be more anxious than are men. Womens' greater anxiety was correlated with a lower pain tolerance in musculoskeletal pain (Stubbs *et al*, 2010). And when subjected to a CP stimulus, women had greater anxiety and lower tolerance compared to men (Jones *et al*, 2002; Keogh and Cochrane, 2002; Jones and Zachariae *et al*, 2004; Thompson *et al*, 2008; Thibodeau *et al,* 2013). Thibodeau (2013) also found greater anxiety in women compared to men when exposed to heat pain.

Additionally women have a higher prevalence of depression (Gerrits *et al*, 2014). Like anxiety, depression has been associated with the risk of developing chronic pain (Roth *et al*, 2005; Stubbs *et al*, 2010). However, these factors may not explain sex differences in pain sensitivity. Keogh and Herdenfeldt (2002) assessed a healthy

cohort using a CP stimulus, but prior to starting the cold exposure, participants were asked to place their hand in a bath of 37°C water to standardize skin temperature at the start of exposure. Results indicated that men had a higher CP tolerance but no difference between anxiety and depression between the sexes was found. In a study using CP and heat pain stimuli, anxiety and depression did not influence sex differences in pain sensitivity or tolerance (Garofalo ***et al***, 2006). In a contrasting study where participants were subjected to an ischemic pain, participants classified as minor depression (Zung Self Rating Depression Scale of $\geq$ 50), had a lower pain tolerance than the control group (without depression) but no sex difference was found in pain tolerance (Piñerva-Suhaibar ***et al***, 1999). However most of the participants in the minor depression group were women (91% female) therefore they did not have the statistical power to make such a statement.

Psychological factors do not occur in isolation. Pain catastrophizing, a maladaptive cognitive style, characterized by feelings of helplessness and creating a negative forecast on future pain events, is often seen in individuals with anxiety and depressed mood (Ellis, 1962; Beck *et al;* 1979; Sullivan *et al*, 2000; Quartana *et al*, 2009). Persistent pain can lead to catastrophizing which influences pain severity (Campbell *et al*, 2003). Pain catastrophizing may influence variance found in experimental pain, for example, in a study by Kristiansen *et al* (2013), low catastrophizers (participants with a Pain Catastrophizing Scale (PCS) score of > 8), were more sensitive to visceral thermal, mechanical stimulation and to CP compared to non-catastrophizers. Catastrophizing was also associated with higher observer ratings of pain behaviour (exhibited by catastrophizers) during a CPT (Sullivan *et al*, 2006). Studies indicate that women catastrophize more than men (Roth *et al*, 2005; Keogh, 2006), and this may be associated with a lower tolerance to cold pain (Thorn *et al*, 2004), therefore this factor may contribute significantly to sex differences in pain sensitivity.

According to Quartana *et al* (2009) “trait catastrophizing” relates to an individual's general tendency to catastrophize while “state catastrophizing” relates to an individual’s catastrophizing in certain circumstances, such as after being exposed to a noxious stimulus. Thorn *et al* (2004) found increased pain rating and lower pain tolerance could be attributed to increased state catastrophizing. State catastrophizing was greater than trait catastrophizing for men and women.

It is well known that anxiety and depression is associated with altered pain perception. Women have greater rates of anxiety and depression and have a tendency to catastrophize more than men do. Pain catastrophizing may not directly affect nociception but may influence one's perception of pain.

1.2.1.3 PAIN BELIEFS BETWEEN THE SEXES

Men and women experience pain differently and are influenced by society to respond differently to pain. There is accumulating evidence that willingness to express pain is influenced by sex, and that expression of pain is more acceptable in women than men (Nayak *et al*, 2000; Robinson *et al*, 2001). Possible reasons maybe differences in biology, perceptions, and a society that treats the sexes differently (Miller and Newton, 2006) as socialization may encourage physical robustness in men and the expression of distress in females, leading to gender differences. Miller and Newton (2006) also put forward differences in: perceptual sensitivity or style, cognitive or emotional ways of dealing with pain, sociology and culture, as sex differences in pain perception.

Jackson *et al* (2002) suggests that self-efficacy, beliefs on one's capability and ability to produce a successful outcome, may mediate the relationship between the sexes and pain perception. Results of this study showed that men had greater physical self-efficacy than women and a greater task specific self-efficacy predicted greater tolerance and lower pain intensity. Therefore one's beliefs on capability and ability may influence one's pain sensitivity.

In a study from Israel, men perceived themselves as less sensitive to, and less willing to report pain. This contrasted with women whom perceived themselves as more sensitive to, and more willing to report pain (Defrin and Eli, 2009; Defrin *et al*, 2011). Similarly, in America, sex accounted for 46% of the variance in willingness to report pain in general, with women being more willing than men (Robinson *et al*, 2001). Additionally, (Robinson *et al*, 2001) reported that men were expected to endure more pain than women.

Studies in America have found gender role expectations of pain to influence and predict greater pain sensitivity in women for temporal summation of a thermal stimuli

and thermal pain (Wise *et al*, 2002; Robinson *et al,* 2004). Yet, gender-specific tolerance expectations for CP stimuli found no differences in pain tolerance, threshold or rating between the sexes (Robinson *et al*, 2003).

Societal pressures are more conducive to the expression of pain by women.

1.2.2 RACE AND PAIN

Studies have shown racial differences in levels of clinical and experimental pain. African Americans had lower tolerance in heat, ischemic, cold pain modalities, and greater severity in chronic pain, when compared to whites. Campbell *et al* (2005) suggest that psychological variables such anxiety, depression, hypervigilence and catastrophizing could influence pain coping and pain responses. While, Forsythe *et al* (2011) found African Americans to have a lower pain tolerance with race explaining differences in catastrophizing.

Table 1.3 summarises published data on racial disparities in pain perception. Scores were calculated as reported in Section 1.2.1 McCracken *et al* (2001) compared chronic pain in black and white patients, with an objective of assessing their adjustment to pain. However, it is not clear how this objective was achieved, as only psychological variables and current pain intensity were tested. The dosage and frequency of medication, and the use of other therapies were not reported. These studies suggest that blacks have a lower CP tolerance, ischemic tolerance and heat pain tolerance compared to whites. Black participants were also found to have greater pain severity in chronic pain compared to whites.

Furthermore, responses to treatment may also differ. Whilst both African-Americans and white chronic pain patients had reduced disability following a multidisciplinary pain programme, African-Americans reported less reduction in pain intensity than did whites (Merry *et al,* 2011). The authors of the study suggested that ethnic minority patients may engage in less self-care activities in response to pain, and this could explain the difference in results between the two groups.

Great disparities have been recorded in access to healthcare for pain conditions and prescription of pain medication between the races. For example, African-American

war veterans diagnosed with chronic pain and with a pain rating score of moderate to high, were being prescribed less opioid medication than white war veterans (Burgess *et al*, 2013). However this disparity is not consistent, Carey *et al* (2010) found similar use of opioids between white and black chronic pain patients.

A study by Mathur *et al* (2014), examined racial disparities in patients in a clinical environment. A cohort of 324 students was assessed on how they would treat and how much empathy they have towards patients' pain, as well as how responsible they thought the patients were for their current pain. Results showed that African-American students were more sensitive than white students to the pain of all (African-American and white) patients. When patient race was shown for *30 milliseconds* (unidentifiable), participants responded more to white patients than African-American patients; when patient race was shown for *seven seconds* (identifiable), participants responded more to African-American patients. The authors reported that racial bias is apparent, but it may be automatic (the effect of patient race is below the level of conscious control) and not deliberate.

TABLE 1.3 BLACKS EXHIBITED A LOWER EXPERIMENTAL PAIN TOLERANCE COMPARED TO WHITES

Authors	n	% Female	Country	Ethnicity	Type of pain	Findings	Score (1.00)†
Campbell *et al*, 2005	120	67.6% BF 47.1% WF	America	52.5% African American 48.3% White	Heat Ischemic Cold	African-Americans had lower heat pain tolerance, ischemic pain tolerance, CP tolerance	0.77
Forsythe *et al*, 2011	155	53.5%	America	38.7% African American 61.3% White	Cold	African-Americans had lower CP tolerance. No difference for pain intensity.	1.00
Green *et al*, 2003	3669	70.3% BF 59.9% WF	America	10% Black American 90% White	Chronic	African-Americans with chronic pain had greater impairment of health status and quality of life.	0.86
Hsieh *et al*, 2011	184	82% WF 73% CCM 62% CECM	Canada	44.5% White 28.2% CCM 27.1% CECM	Cold	Chinese reported greater pain intensity.	0.95
McCracken *et al*, 2001	264	73.7% BF 64.3% WF	America	20.7% Black American 75.3% White 1.8% Hispanic 1.8% Asian 0.4% Other	Chronic	African-Americans had greater pain intensity.	0.68

Authors	n	% Female	Country	Ethnicity	Type of pain	Findings	Score (1.00)†
Nayak *et al*, 2000	226	50% 47.7% WF 52.2% IF	America India	47.3% White 52.6% Indian	Cold	Indians had higher CP tolerance. No difference in pain intensity.	0.91
Rahim-Williams *et al*, 2007	206	66% BF 43% WF 56% HF	America	30.6% African American 29.6% Hispanic 39.8% White	Heat Ischemic Cold	African-Americans had lower ischemic pain tolerance and CP tolerance than Whites. No difference for heat pain.	0.59
Riley *et al*, 2013	191		America	27.7% Blacks 72.2% White	Cold Heat Pressure	African-American had lower CP tolerance and heat pain tolerance. No difference in PP.	0.86

WF = white females, BF = black females, HF = Hispanic females, IF = Indian females, CCM = Chinese-Chinese milieu, CECM = Chinese European milieu, CP = cold pain, PP = pressure-pain

† Appendices 1 and 3

1.2.2.1 BIOLOGICAL FACTORS IN RACE DIFFERENCES IN PAIN

Numerous studies have attributed social influences as contributors to differences in pain perception between races (McCracken *et al*, 2001; Green *et al*, 2003; Rahim-Williams *et al*, 2007; Allen *et al*, 2010; Forsythe *et al*, 2011) but not many have focused on biological factors. Whilst genetics may play a role in differences in pain sensitivity between the races (see next section 1.2.2.2), physiology may also play a part. A review by Edwards *et al* (2001) suggested African-Americans had greater cardiovascular reactivity to noxious stimuli yet, in a healthy cohort Campbell *et al* (2005) African Americans had greater pain sensitivity to ischemic pain, with no difference in blood pressure compared to whites.

1.2.2.2 PAIN GENES

Differences amongst races could be accounted for by genetic factors. Indeed several genetic loci have been identified that affect pain sensitivity (Williams *et al*, 2012). Genes *TRPV1, OPRD1* have been linked to pain threshold (Kim *et al*, 2004), *OPRM1* has been linked to a higher pressure pain threshold and is more frequently identified in white individuals than non-white individuals (Riley *et al*, 2012).

Alleles and haplotypes of *GCH1,* a gene encoding a protein involved in the maintenance and processing of pain, have been associated with reduced pain intensity in some studies, but the results have been mixed. These findings were not reproduced in Southern Africans with HIV-associated sensory neuropathy (Wadley *et al*, 2012; Hendry *et al*, 2013). In the same cohort, haplotypes of *KCNS1* (which encodes a potassium channel) were associated with pain intensity showing an association between a *KCNS1* allele and post amputation pain in Israelis (Hendry *et al*, 2013). The population in South Africa has a unique genetic makeup and so genetic studies need replicating here. Genetic studies can help identify novel signaling and metabolic pathways involved in disease, and pharmacogenetic studies in pain may aid in the development of analgesics.

1.2.2.3 PSYCHOLOGICAL FACTORS INFLUENCING RACE DIFFERENCES

Studies have shown psychological variables that influence pain sensitivity to be more severe in blacks than in whites. Nigerian chronic pain patients had greater anxiety and depression than whites did (Egwu and Nwuga, 2008). African American chronic pain patients had a higher baseline depression score (Merry *et al,* 2011); greater depressive symptoms with greater current pain reporting (Green *et al*, 2004); and greater depressive symptoms with a greater degree of impairment in health status and quality of life (QOL) when compared to white patients (Green *et al*, 2003). Lastly, African American outpatients with Major Depressive Disorder reported more pain complaints than white patients (Husain *et al*, 2007).

When exposed to various experimental pain (Table 1.2), African Americans had a greater pain catastrophizing score than did whites (Campbell *et al*, 2005; Forsythe *et al*, 2011; Riley *et al*, 2013) and they used more coping strategies compared to whites (Hastie *et al*, 2004; Chibnall *et al*, 2005; Allen *et al*, 2010).

African Americans may exhibit greater depression and pain catastrophizing, with lower pain tolerance than whites.

1.2.2.4 SOCIOECONOMIC STATUS AFFECTS PAIN BEHAVIOUR IN RACES

Socioeconomic status (SES) based on education, income and occupation, is a strong indicator of an individual's morbidity and mortality (Winkleby *et al*, 1992). Lower socioeconomic status is associated with greater pain intensity in African Americans compared to whites (Edwards *et al*, 2001; Green and Hart-Johnson, 2012).

A lower SES is found in those with a greater prevalence of pain, and a higher incidence of pain. A survey in Austria assessing SES based on education, income and profession, found SES to be inversely related to the prevalence of pain severity (Dorner *et al,* 2011). Education was the more accurate predictor of pain and unemployed subjects had the highest prevalence of pain. Thomtén *et al* (2012) assessed the role of SES and pain in women with and without pain via two surveys

conducted one year apart. Results identified financial strains and occupational level as risk factors for the incidence of pain.

A greater prevalence of pain maybe found amongst those with a lower SES, possible reasons for this could be a difference in health concerns compared to those with a greater SES. As, Hurre *et al* (2003) found parental SES to negatively affect health-issues, as those with a lower parental SES were more inclined to smoke, have a lower self-esteem, greater BMI and lower physical activity.

There is an association between decreased socioeconomic status and greater pain reporting in African American patients compared to white patients. A lower socioeconomic status might also be linked to greater health disparities.

1.2.2.5 Pain beliefs between races

Another potential cause of differences in pain sensitivity between races is acculturation; the process by which immigrants have to adapt to a new set of cultural norms, beliefs and values. In a study conducted in Canada and Hong Kong, First generation Asian Americans in Canada had a lower CP tolerance than European Americans and a Chinese group in Hong Kong had a lower pain tolerance than the Hong Kong group (Chan *et al*, 2013). The authors hypothesised the process of acculturation to a new country could cause stress to immigrants, which could lead to differences in pain sensitivity. In America, Hispanic dental patients experiencing acculturation also reported greater oral pain compared to those that more frequently spoke English (Riley *et al*, 2008).

Different religious and cultural backgrounds may lead individuals to express pain differently. An example of cultural differences between East and West was demonstrated when students from India and the US were compared. White students felt it more appropriate for men and women to express pain than their Indian counterparts (Nayak *et al*, 2000). Similarly, in a study in Canada, white students had a greater CP tolerance and felt it more appropriate for men and women to express pain, than did Chinese students (Hsieh *et al*, 2011).

Culture influences beliefs about the expression of pain.

1.3 RATIONALE FOR STUDY

There is extensive literature to support differences in pain sensitivity between the sexes (Racine *et al*, 2012a; Racine *et al*, 2012b). However, there is a dearth of evidence in black African populations. Additionally, the effect of sex on pain perception is not independent of other factors such as race and social influence (Figure 1.1). Given the culturally diverse population in South Africa it is important to assess both the effect of sex and race on pain sensitivity in this population. Should this effect of sex and race (on pain sensitivity) be found within a South African population, this might have clinical implications as it highlights to healthcare practitioners an awareness on differences in the experience and reporting of pain by different races and sexes.

The choice of experimental pain test is important in determining sex and race differences. The cold pressor test (CPT) and pressure-pain test have been used extensively in tests of sex and race difference in pain sensitivity, and have proven to be sensitive methods (Racine *et al*, 2012a; Racine *et al*, 2012b).

I have conducted a study in healthy individuals in order to give baseline data for sex and race differences in pain sensitivity in South Africans. Pain is a common comorbidity in prevalent diseases such as HIV and cancer in the South African population and my data may have implications for these populations. A better understanding of pain sensitivity and its influences is vital for the development of culturally-relevant pain management approaches.

My study will focus on some of the psychosocial factors that contribute to the emotional and cognitive framework of nociception and therefore pain perception (Figure 1.1).

1.3.1 Aim and objectives

The aim of the study was to determine whether differences in pain sensitivity and beliefs exist among races and sexes within a South African population.

The objectives were:

- To compare pain intensity of, and tolerance to, experimental cold and pressure pain between black and white, and male and female participants
- To compare pain beliefs between black and white, and male and female participants
- To determine if psychosocial factors influence pain intensity and tolerance between the races and the sexes

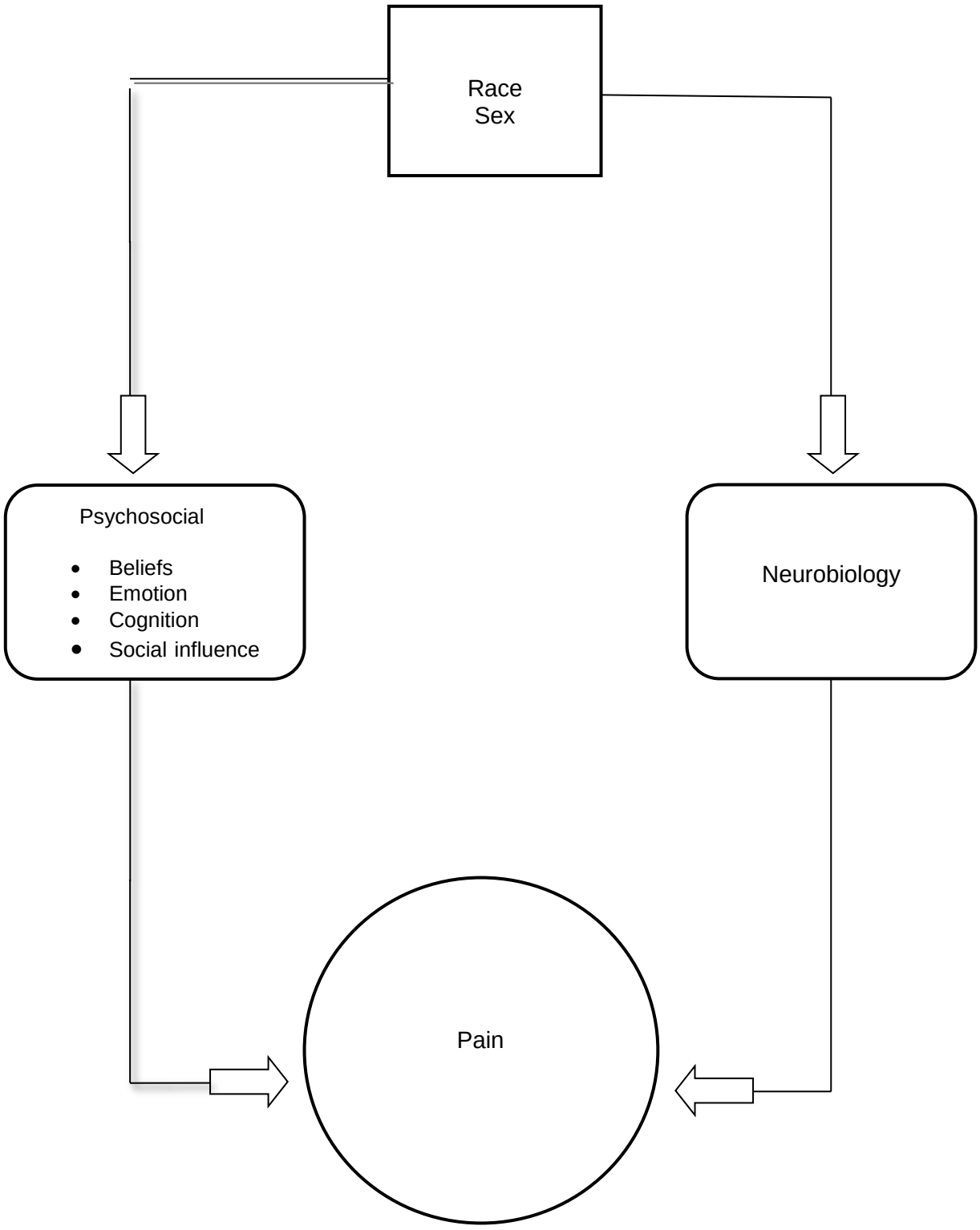

FIGURE 1.1 THE ROLE OF PSYCHOSOCIAL FACTORS ON THE INFLUENCE OF PAIN.

CHAPTER 2

METHODS

2. METHODS

2.1 Study design

The study was a prospective, quantitative study involving 108 black and 108 white students attending the University of the Witwatersrand. Dependent variables assessed were pain tolerance and pain intensity. Independent predictors assessed were psychological variables, socioeconomic status and pain beliefs.

Black and white, second and third year, medical and health sciences students were recruited for the study. The study took place from September 2012 to June 2013, and testing was conducted throughout the day until 17h00.
Several methods of recruitment were used: 1) a general announcement was made at the beginning of student practical classes in the School of Physiology, informing the students of the study and inviting them to participate, and 2) direct one-on-one recruitment, which involved me directly approaching students. Participation was voluntary and students were not obligated to participate. There was no power relationship between investigator and participant, and participants were allowed to withdraw at any time. The study was conducted in a private room situated at the back of the School of Physiology teaching laboratory, and testing took place in the presence of the investigator only.

2.2 Sample

2.2.1 Population

The sample was derived from second and third year physiology students in 2012 and 2013. Table 2.1 indicates the demographic of the sample.

Table 2.1 Demographics of sample population

	2012	2013
Data represented as a percentage (%)		
Female	72	72
Male	28	28
Black		
Black female	28	31
Black male	11	9
White		
White female	22	25
White male	10	10

2.2.2 Exclusion criteria

- Participants under 18 years old
- Females that were pregnant or lactating
- Participants that took any medication that could interfere with pain perception, within four hours of the time of testing

2.2.3 Ethical issues

The University of Witwatersrand Human Research Ethics Committee (Medical) approved the study with clearance certificate number M120648 (Appendix 4). Confidentiality was ensured by separating informed consent (Appendix 5) and personal details from the questionnaires which were identified by assigning each participant a reference number.

2.2.4 Procedure

An overview of the study procedure is illustrated in Figure 2.1. The procedure and what it entailed was explained to interested participants, if they agreed to participate they proceeded to complete the informed consent. Once completed, they were asked to complete six questionnaires (Appendix 7, 8, 9, 10, 11, 12) in the questionnaire booklet, which pertained to general health, psychological variables, pain beliefs and socioeconomic status. After completion of the questionnaires, I proceeded to carry out the pain tests with the cold pain test (CPT) being the first. Here, participants were instructed on the method of the test and ensured that they could withdraw at any

time. Once this was understood the test was carried out, after the test they were allowed to recover and rate their pain intensity. We proceeded to the second pain test only when the participant fully recovered from the cold pain. Once again, they were instructed on the method of the test. Here, they first had a trial test with the algometer to familiarise themselves with its operation, after which, the test was then carried out. On completion of the pressure-pain test, they were asked to rate their pain intensity. Following the tests the participants completed the pain catastrophizing scale (PCS) again.

2.2.5 Sample size

An objective sample size of 41 participants per group had a sufficient effect size. Lan and Lian (2010) compared sample and effect size, for t-tests, a sample size of about 38 is sufficient for an effect size of 0.5. For an ANOVA, a sample size of about 38 is sufficient for an effect size of 0.25; a one-way ANOVA requires a sample size of about 38 for an effect size of 0.6; and a sample size just under 50 is sufficient for an effect size of 0.8. Given an estimated effect size of 0.55 for pain threshold or 0.57 for pain tolerance (Riley *et al*, 1998), 41 subjects per group are necessary to provide adequate power (0.70) to test for this difference.

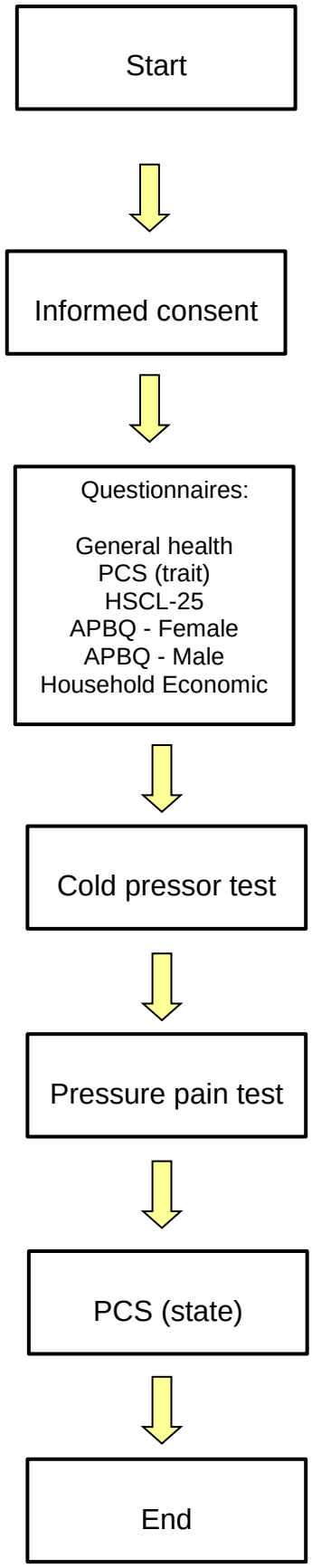

FIGURE 2.1 OVERVIEW OF THE PROCEDURE OF THE STUDY

2.3 QUESTIONNAIRES

The following questionnaires were used in the study.

- General health questionnaire
- Assessment of Socioeconomic Status (ASS)
- Hopkins Symptom Checklist-25 (HSCL-25)
- Appropriate Pain Behaviour Questionnaire (APBQ) - Female
- Appropriate Pain Behaviour Questionnaire (APBQ) - Male
- Pain Catastrophizing Scale (PCS)

2.3.1 General Health Questionnaire

I developed a general health questionnaire, which assessed participants' current health and pain status, and current medication usage (Appendix 7). The general health questionnaire was also used as selection criteria to assess if the participant met the selection criteria, did not have any health conditions that could result in chronic or acute pain and interfere with the experimental pain results and did not use any pain medication within the past four hours that would also interfere with the experimental pain results.

2.3.2 Assessment of socioeconomic status

Socioeconomic status (SES) is primarily measured by assessing education, income and occupation (Winkleby *et al*, 1992). Mainstream SES questionnaires were mostly developed for an American population, which differs economically to our South African population (World Bank, 2012). There is no SES questionnaire developed for a South African population that has a clear numerical scoring system that can be used for statistical analysis. There is a tool developed in a South African population (Barbarin and Khomo, 1997), however the scoring is unclear and some of the material wealth items are out of date as it is 14 years old. The Assessment of Socioeconomic Status (ASS) assesses participants' basic household economic status within the South Africa population (Appendix 8). Areas assessed include the participant's parents' or guardian's education level, employment status, and

ownership of material household items such as refrigerator, television, car, microwave, telephone and washing machine. The six material items were taken from the Living Standards Measures (LSM) 2011. The LSM is a widely used household economic status measure in South Africa, used by the South African Advertising Research Foundation (SAARF) (Schnieder *et al*, 2011) for marketing research. Each of the SES components were catergorised into sub-groups. Education level was catergorised into: none; primary school; high school; and tertiary education. Employment status was catergorised into income (employed or a pensioner) or no income. Ownership of household assets were catergorised into either yes or no.

2.3.3 The Hopkins Symptom Checklist-25

The Hopkins Symptom Checklist (HSCL) is a self-reporting method assessing five psychological symptom dimensions i) somatization; ii) obsessive compulsive behaviour and thought; iii) interpersonal sensitivity; iv) depression and v) anxiety (Derogatis *et al*, 1974). The Hopkins Symptom Checklist-25 (HSCL-25) derived from the widely used HSCL (Derogatis *et al*, 1974), is a 25-item questionnaire that assesses anxiety and depression symptom dimensions (Leiknes *et al,* 2007). It is a shorter version of the HSCL and contains 10 items from the anxiety cluster and 15 items from the depression cluster. I used the HSCL-25 (Appendix 9) because the HSCL-25 is convenient in a large-scale screening, and participants can easily complete the questionnaire within five minutes (Winokur *et al*, 1984), which is well suited as the participants in my study had numerous questionnaires to complete.

Participants were asked to indicate the extent to which they had experienced each of the 25 symptoms within the last week by scoring them on a 4 point Likert scale with (1) not at all to (4) extremely.

The questionnaire contains subsections for anxiety and depression. Scores for the sections are summed and divided by the number of questions (anxiety [10]; depression [15]). Scores more than 1.75 indicated the individual was symptomatic (Derogatis *et al*, 1974; Winokur *et al*, 1984).

The HSCL has consistently high reliability coefficients alpha ranging from 0.84 to 0.87 for the five primary symptom dimensions (Derogatis *et al*, 1974), correlation coefficients of 0.79 for anxiety and 0.73 for depression was also obtained for the HSCL-25 (Winokur *et al*, 1984).

The HSCL-25 is a well-used method of screening for major psychiatric disease in epidemiological studies (Veijola *et al*, 2003). It has been validated as a screening tool for depression in HIV-positive pregnant women (Kaaya *et al*, 2002) and in antenatal clinical patients (Lee *et al*, 2008) in Tanzania. In a South African population, the HSCL-25 displayed a cronbach's alpha of 0.96 in a healthy sample (Kagee, 2005), and in an HIV patient population (Kagee and Martin, 2010). The HSCL-25 can be used as a screening tool in clinical and normative samples.

2.3.4 Appropriate Pain Behaviour Questionnaire

The Appropriate Pain Behaviour Questionnaire (APBQ) is a 14-item questionnaire that measures individual beliefs about the appropriateness of expressing pain in the presence of others. Pain expression includes crying, grimacing, talking about the pain or holding the painful site (Nayak *et al*, 2000). There are two versions of the APBQ: the APBQ-Males (APBQ-M) (Appendix 10), which assess whether the individual finds men expressing pain to be appropriate and the APBQ-Females (APBQ-F) (Appendix 11), which assess whether the individual finds women expressing pain to be appropriate (Nayak *et al*, 2000). The APBQ proved to be reliable, the APBQ-M and APBQ-F had reliability analysis coefficient alphas of 0.89 and 0.85 respectively in the U.S sample and 0.80 and 0.74 in the Indian Sample (Nayak *et al*, 2000). The questionnaire asks similar questions to that in the GREP (Robinson *et al*, 2001), indicating strong convergent validity in the construct.

All participants were asked to complete both the APBQ-M and APBQ-F, to determine if there was a difference in their beliefs about the appropriateness of pain expression between men and women. Participants were asked to indicate the extent to which they agreed with each of the 14 statements by scoring them on the 7-point Likert scale from (1) strongly disagree to (7) strongly agree. Scores were determined by the following calculation (Figure 2.2):

The scoring method in Nayak *et al* (2000) lacked clarity. It summed all the questions to give a final score, the greater the score, the more accepting the participant was of expressing pain behaviour. There was no “neutral” marker for the scores, and a marker for behavior being perceived as unacceptable was not clear. The only known scoring method for the APBQ was in Nayak *et al* (2000) and Hsieh *et al* (2011), who both scored it the same way. I modified the scoring so it was more interpretable, with appropriateness being assigned to a polarity (positive or negative) rather than a total score. I allocated all questions that deem the behaviour acceptable, to the A-Score, and all questions that deem the behaviour unacceptable, to the I-Score. The number of questions that contribute to the A-Score and I-Score were uneven, so the questions were evenly weighted (summed and divided by the respective number of questions in each category), equalizing the weight of each question in each category. The A-score was then subtracted from the I-Score to give a final score with polarity and with “0” being the neutral marker. This makes it easier to identify whether the individual considered the stated behaviour as acceptable or not.

Six statements reflecting an aversion to pain expression were summed and divided by the number of questions (six) to give the I-Score, ranging from 6 to 42. Eight statements indicating a willingness to express pain were summed and divided by the number of questions (eight) to give the A-Score, ranging from 8 to 56. The A-Score was then subtracted from the I-Score to give a final score ranging from -6 to +6. A negative value meant the I-Score was higher than the A-Score and hence overall pain expression was considered ‘inappropriate’. Conversely, a positive score indicated pain expression was considered ‘appropriate’ and a value close to zero meant the individual had a neutral view on pain expression for men and women. This calculation for scoring was used for both the APBQ-M and APBQ-F.

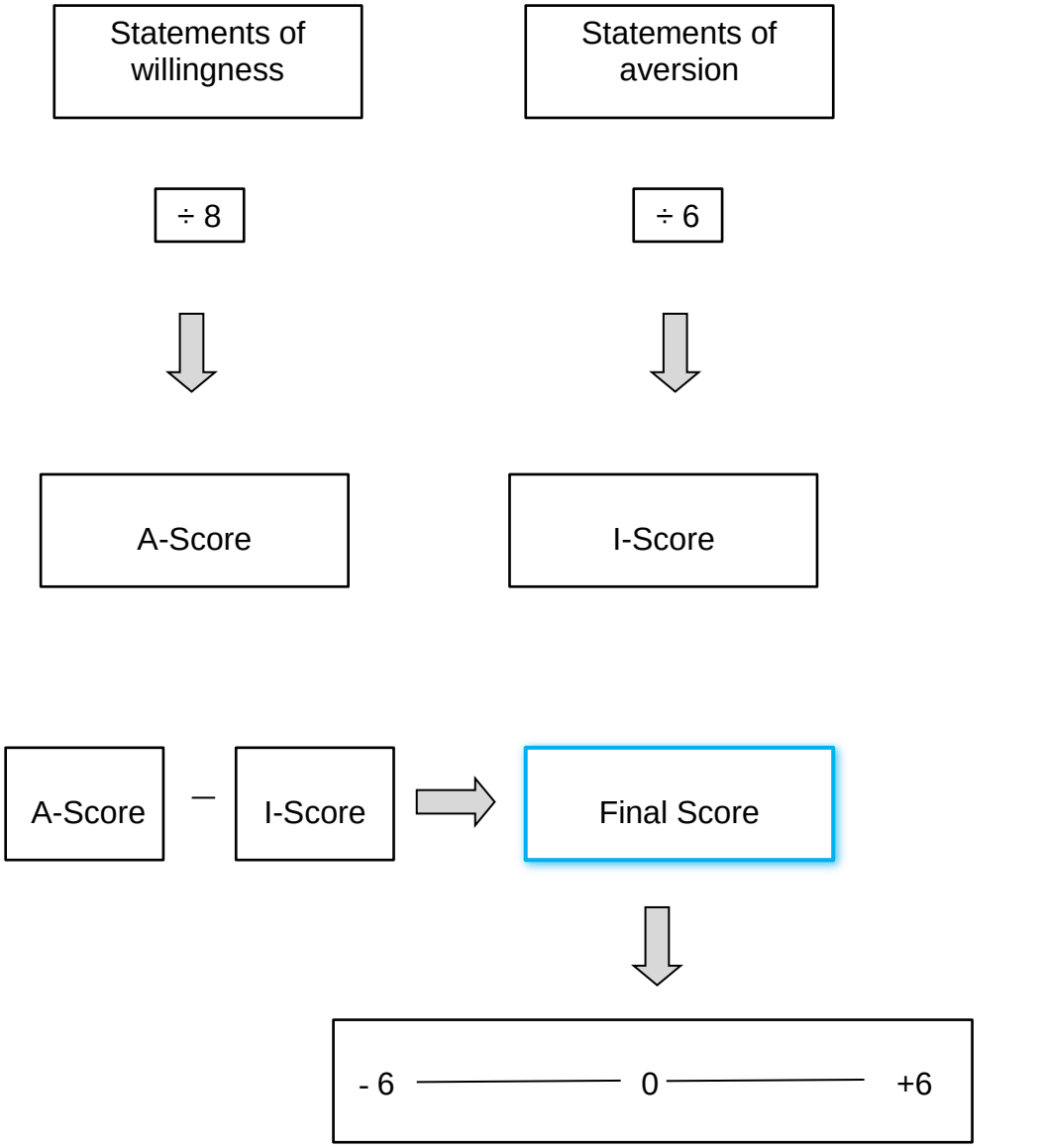

FIGURE 2.2 CALCULATION OF APPROPRIATE PAIN BEHAVIOUR QUESTIONNAIRE SCORES

2.3.5 Pain Catastrophizing Scale

The Pain Catastrophizing Scale (PCS, Appendix 12) is a 13-item questionnaire which measures catastrophic thinking related to pain. Pain catastrophizing is the tendency to intensify the threat value of a painful stimulus and the inability to impede pain related thoughts before, during, or after exposure to a painful stimulus, contributing to feelings of helplessness (Quartana *et al*, 2009). The PCS assesses three domains: rumination, magnification and helplessness felt about exposure to pain and is therefore a broader assessment than other measures such as the Coping Strategies Questionnaire (CSQ) (Quartana *et al*, 2009).

The PCS is one of the most commonly used instruments to measure pain catastrophizing and has been adapted for different cultures, including South Africa with the South African Pain Catastrophizing Scale (SA-PCS) (Morris *et al*, 2012). However, in comparison to the adapted versions, the original English PCS is considered a more valid and reliable measure of catastrophizing (Morris *et al*, 2012), with alpha coefficients of 0.87 for rumination, 0.60 for magnification and 0.79 for helplessness and Chronbach's alpha for the total PCS of 0.90 (Sullivan & Bishop, 1995) and was therefore used here.

The PCS requires the participant to reflect on a past painful experience and then indicate the extent to which they experienced each of the 13 thoughts or feelings by scoring them on a 5 point Likert Scale with (0) not at all to (4) all the time. The total score of the PCS is a summation of the 13 items, with a score ranging from 0-52 (Sullivan, 2005). A score of more than 24 indicates a high level of catastrophizing (Morris *et al*, 2012).

Participants were asked to complete the PCS prior to the pain tests, to assess their trait catastrophizing. After both pain tests were completed, participants were asked to repeat the PCS to assess their state catastrophizing. Trait catastrophizing reflects the participant's current notion on catastrophizing, while state catastrophizing reflects the participant's notion on catastrophizing after being exposed to a noxious stimulus (Quartana *et al*, 2009).

2.4 PAIN TESTS

2.4.1 Cold pressor test

The cold pressor test (CPT) is frequently used as a form of experimental pain. It requires the participant to submerge their hand or limb in a bath of cold water for as long as the participant can endure (tolerance) or until the test was terminated. During a CPT a dull, aching pain is perceived and other physiological responses such as increased systolic and diastolic pressure (Ferracuti *et al*, 1994). The CPT has proven to be a reliable indicator of pain perception and pain sensation (Wolff, 1951; Mitchell *et al*, 2004).

Testing took place in the presence of the investigator only. A dish was filled with tap water and ice. The temperature of the water was monitored with a mercury bulb thermometer. A consistent temperature of 5°C was maintained by routinely stirring and adding more ice when necessary. The temperature was recorded before and after the test. Participants were instructed to place their dominant hand in the cold water for as long as they could endure (Figure 2.3). The time was recorded giving a pain tolerance score. If participants did not remove their hand before five minutes the test was terminated to prevent tissue damage (Weisenberg and Tepper, 1995). The hand had to be submerged in the middle of the dish and not touch the base of the dish, as this would increase the temperature of the hand and affect the true tolerance. The participants were not informed of the duration of the test or on the temperature of the water so pain ratings or tolerance times were not affected (Weisenberg and Tepper, 1995) After the CPT, participants were asked to rate the pain intensity felt on a visual analogue scale (VAS), ranging from a score of 0 to 100.



FIGURE 2.3 THE COLD PRESSOR TEST

Participants were allowed a ten minute recovery period before proceeding to the pressure-pain test (PPT). The recovery period fluctuated depending on the individual. They were allowed to proceed to the next pain test only if sensation had returned to their dominant hand indicating that any discomfort had passed and would not influence their pain perception in the non-dominant hand for the next pain test.

2.4.2 Pressure-pain test

Pressure-pain (PP) tolerance was measured using a pressure algometer (Somedic, Sweden; Figure 2.4). The algometer was calibrated each day using the calibration weight before data was collected. PP was applied on the nail bed of the index finger of the non-dominant hand. A $1cm^2$ probe was used with a maximum pressure of 1500kPa.

During the recovery period, the PPT procedure was explained to the participant. The participant was assured that it was a blunt pressure-pain test and no other pain stimuli would be used. A trial test was first carried out with the participant on their

middle finger, to ensure they were familiar with the procedure and how to halt the test.

For the test procedure the algometer was placed on the nail bed of the index finger. A force was slowly exerted at a constant rate. When the participant could not tolerate any more pressure, they pressed the ‘stop’ button and simultaneously said ‘stop’ and I released the algometer trigger ending the test. Tolerance was defined as the ‘most pressure that you can take’. If the participant did not reach tolerance at 1500kPa, this pressure was considered their tolerance. After the PPT, participants were asked to rate the intensity of the pain by rating it on a VAS ranging from 0 to 100. After both pain tests and VAS were completed, the participant was asked to complete the PCS again.



FIGURE 2.4 THE PRESSURE ALGOMETER

2.4.3 Visual Analogue Scale

The visual analogue scale (VAS) (Appendix 13) is a graphical representation of pain intensity, it is a straight line, 100mm long, with one end of the line labeled ‘No pain’ and the other end ‘The worst pain imaginable’ indicating two divergent ends of the rating scale. Once each pain test was completed the participant was asked to rate

the pain intensity perceived, on the VAS ranging from “No pain” (0) to “The worst pain imaginable” (100).

The VAS is a sensitive measure of pain intensity. It has a true zero, and shows linear scaling over the mild to moderate pain range, it is ten centimeters in length when printed. It is able to detect slight differences in change of sensory pain intensity with minimal invasion (Katz and Melzack, 1999). Price *et al* (1983) found the VAS to be a reliable and valid assessment for pain measurement in chronic pain and experimental heat pain. A between session reliability of 0.97 was produced for the experimental heat pain. In a rating scale verbal descriptions may not have the same meaning to everyone, which is why the VAS is preferred over a verbal rating scale (Rundshagen *et al*, 1999). Scrimshaw and Maher (2001) also preferred the use of the VAS rather than the McGill Pain Questionnaire is assessing changes in clinical trials and practice.

2.5 Data analysis

Statistical analysis was carried out using GraphPad Prism version 4 for Windows, (GraphPad Software, San Diego, California, USA). Fisher’s exact tests and the random forest analyses were carried out using R version 3.0.2. Descriptive statistics were used to assess demographic characteristics, data are shown as mean (SD) unless otherwise specified. Variables such as age and body mass index (BMI) were further assessed with Kruskal Wallis tests.

Univariate analyses were carried out for all variables and demographic groups. The following tests all compared black males against black females; white females against black females; white males against black males; and white males against white females.

The Mann Whitney test was used to compare the unpaired, non-parametric data: socioeconomic status from the ASS; anxiety scores from the HSCL-25, depression from the HSCL-25, APBQ-F scores, APBQ-M scores, Trait PCS scores, State PCS scores, CP tolerances scores, PP tolerance scores, VAS CPT scores, VAS PPT scores. P-values of < 0.05 indicated a difference between the two groups. For the

APBQ-F and APBQ-M Bonferroni correction was allowed and p-values of < 0.025 indicated a statistically significant difference between the two groups.

Wilcoxon signed rank test was used for comparing the APBQ-F and APBQ-M. It compared the individual's score for the APBQ-F and APBQ-M. Bonferroni correction was made and a p-value of 0.0166 indicated a difference between the two scores for the same individual.

Fisher's exact test was used to analyse each of the SES components (education, employment and household assets) with post hoc analysis for all participants.

Regression tree analysis was used to model the predictors of pain sensitivity, for cold pain and pressure-pain. The random forest method of regression tree analysis was used to identify informative variables for pain sensitivity (cold tolerance and intensity; pressure-pain tolerance and intensity) and pain beliefs. All random forest analyses were run under four different conditions (different resampling number – 500 and 2000, and different random seeds to initiate the modeling) to establish the stability of the models. Variables were judged to be informative if their importance value was above the absolute value of the lowest negative-scoring variable.

CHAPTER 3

RESULTS

3. RESULTS

3.1 Cohort characteristics

One hundred and eight black students (males = 44; females = 64) with 14 (1) years of education and 108 white students (males = 52; females = 56) with 14 (1) years of education participated in the study. Participants were all in good health and had not used any pain medication within the last four hours from the time of testing. 1 (2%) Black female and 26 (46%) white females were on oral contraceptive, and 15 (24%) black females and 8 (14%) white females had dysmenorrhea.

Table 3.1 describes the demographic characteristics of all participants, as well as black and white men, and black and white women separately. Participants had a mean age of 20.47 (1.98) with no statistical difference in age or years of education. However, BMI comparisons were statistically significant ($p < 0.01$), for white males (who had greater BMI scores) than did white females.

English was the most frequently spoken home language by white participants while isiZulu was the most frequently spoken home language by black participants, followed by Sotho and Xhosa (Table 3.1).

TABLE 3.1 DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS INDICATED THAT ENGLISH AND ZULU WERE THE FREQUENTLY SPOKEN HOME LANGUAGES

Variable	All	Male		Female		P-value
		Black	White	Black	White	
Age [years: mean (SD)]	20.5 (1.97)	20.93 (2.86)	20.59 (1.64)	20.10 (1.11)	20.40 (2.10)	p = 0.32; KW Statistic = 3.52
Height [meters: mean (SD)]	1.69 (0.11)	1.72 (0.09)	1.81 (0.07)	1.61 (0.08)	1.66 (0.07)	
Mass [kilograms: mean (SD)]	68 (13.74)	66.81 (9.49)	79.50 (11.09)	63.85 (13.70)	63.16 (12.63)	
BMI [kg/m²: mean (SD)]	23.66 (3.83)	22.85 (2.91)	24.34 (3.06)*	24.47 (4.90)	22.81 (3.77)*	p = 0.01*; KW Statistic = 11.32
Years of education [years: mean (SD)]	14.40 (1.02)	14.60 (1.37)	14.52 (1.02)	14.20 (0.54)	14.34 (1.12)	p = 0.17; KW Statistic = 5.01
Home language (%)						
English		11%	85%	5%	77%	
Afrikaans		0%	10%	0%	16%	
isiZulu		25%	0%	20%	0%	
Sotho		21%	0%	14%	0%	
Xhosa		9%	0%	14%	0%	
Other		29%	4%	45%	5%	
Omitted		5%	1%	2%	2%	
		100%	100%	100%	100%	

* Significance at $p < 0.05$

Age, BMI and years of education comparisons were carried out using a One-way ANOVA Kruskal-Wallis test

3.2 Assessment of Socioeconomic Status

Assessment of Socioeconomic Status (ASS) scores illustrated that black males had a lower socioeconomic status (SES) than white males ($p < 0.01$) furthermore black females had a lower SES than white females ($p < 0.01$) (Table 3.2). Overall, black participants had a lower SES than white participants.

TABLE 3.2 PARTICIPANTS' ASSESSMENT OF SOCIOECONOMIC STATUS SCORES

Parent/Guardian's education level	**None**	**Primary school**	**High school**	**Tertiary level**	**P-value**
Black males (n = 44)*	0	5	8	28	p = 0.03*****
White males (n = 52)*	0	0	8	41	Post hoc analysis was unable to detect
Black females (n = 64)*	0	2	8	53	where the differences where.
White females (n = 56)	0	0	6	50	
† Missing data: black males = 3; white males = 3;					
black females = 1					
Parent/Guardian's employment level	**Income**	**No income**			
Black males (n = 44)	38	6			p = 0.05
White males (n = 52)*	49	1			
Black females (n = 64)	56	8			
White females (n = 56)	54	2			
† Missing data: white males = 2					
Household Assets					
Refrigerator	**Yes**	**No**			
Black males (n = 44)*	41	2			p = 0.12
White males (n = 52)*	50	0			
Black females (n = 64)	64	0			
White females (n = 56)	55	1			
† Missing data: black males = 1; white males = 2					
Television	**Yes**	**No**			
Black males (n = 44)*	39	4			p = 0.40
White males (n = 52)*	49	1			
Black females (n = 64)	62	2			
White females (n = 56)	53	3			
† Missing data: black males = 1; white males = 2					

Telephone	**Yes**	**No**			
Black males (n = 44)*	27	16			p < 0.01*****
White males (n = 52)*	47	3			Post-hoc indicates BM < WM and BF < WF
Black females (n = 64)	40	24			
White females (n = 56)	50	6			
† Missing data: black males = 1; white males = 2					
Car	**Yes**	**No**			
Black males (n = 44)*	28	15			p < 0.01*****
White males (n = 52)*	50	0			Post-hoc indicates BM < WM and BF < WF
Black females (n = 64)	50	14			
White females (n = 56)	55	1			
† Missing data: black males = 1; white males = 2					
Washing machine	**Yes**	**No**			
Black males (n = 44)*	29	14			p <0.01*****
White males (n = 52)*	50	0			Post-hoc indicates BM < WM and BF < WF
Black females (n = 64)	53	11			
White females (n = 56)	55	1			
† Missing data: black males = 1; white males = 2					
Microwave	**Yes**	**No**			
Black males (n = 44)*	35	8			p < 0.01*****
White males (n = 52)*	50	0			Post hoc indicates BM < WM
Black females (n = 64)	59	5			
White females (n = 56)	55	1			
† Missing data: black males = 1; white males = 2					

3.3 PAIN TESTS

COLD PRESSOR TEST

Cold pain tolerance

Table 3.3 Cold pain tolerance results

CPT	Black female	Black male	White female	White male	P-value
Median (IQR)	41 (29-62)	57 (41-300)	111 (39-300)	300 (70-300)	
Black male vs.Black female					p < 0.01; Mann U = 791
White female vs.Black female					p < 0.01; Mann U = 997,5
White male vs. Black male					p = 0.01; Mann U = 769,5
White male vs.White female					p = 0.02; Mann U = 1036

Black males did tolerate the cold water longer than black females ($p < 0.01$), as did white females ($p < 0.01$) as 39% of white females reached the cut-off time compared to merely 6% of black females (Table 3.3). White males were able to tolerate the cold water significantly longer than black males ($p = 0.01$), and white females ($p = 0.02$) (Table 3.3). Indeed, 57% of white males reached the cut-off time of 300 seconds compared to 39% of black males. Thus males tended to have greater CP tolerance than females, and whites tended to have greater tolerances than blacks.

Cold pain intensity

Table 3.4 Cold pain intensity results

	Black female	**Black male**	**White female**	**White male**	**p-value**
Median (IQR)	62 (43-72)	54 (37-75)	52 (26-68)	58 (36-69)	
Black male vs. Black female					p = 0.47; Mann U = 1250
White female vs. Black female					p < 0.01; Mann U = 1235
White male vs. Black male					p = 0.44; Mann U = 1017
White male vs. White female					p = 0.49; Mann U = 1293

Maximum pain intensity of the CPT was measured using visual analogue scales (VAS) scores. Black males had a similar median CP intensity of 53.50/100 compared to black females 61.50/100, no difference was found between black participants(p = 0.47); white males had a median CP intensity of 58.00/100 compared to 52.00/100 for white females (p = 0.49), no difference was found between white participants (Figure 3.2 panels a and b). However, black females had a greater cold pain intensity than white females (p = 0.01), and no significant difference was found between the males (p = 0.46) (Table 3.4). Thus maximum pain intensity in the CPT was similar across race and sex, except for black females which reported significantly greater pain at tolerance.

PRESSURE-PAIN TEST

Pressure-pain tolerance

Table 3.5 Pressure-pain tolerance results

	Black female	**Black male**	**White female**	**White male**	**p-value**
Median (IQR)	685 (545-859)	976 (1101-710)	655 (557-710)	915 (792-1134)	
Black male vs. Black female					p < 0.01; Mann U = 699
White female vs. Black female					p = 0.92; Mann U = 1687
White male vs. Black male					p = 0.75; Mann U =1079
White male vs. White female					p < 0.01; Mann U = 528

Females had a lower pressure pain test (PPT) compared to men. Black males had a significantly higher pressure-pain (PP) tolerance compared to black females ($p < 0.01$), with a median PP tolerance of 976kPa and 984.50kPa for black females (Table 3.5). White males had a significantly higher PP tolerance compared to white females ($p < 0.01$) with a median PP tolerance of 915kPa compared to 655kPa for white females (Table 3.5). No significant difference was found in pressure pain tolerance between black and white females ($p = 0.92$) and between black and white males ($p = 0.75$) (Table 3.5). Thus, in general females had a lower PP tolerance than men did.

Pressure-pain intensity

Table 3.6 Pressure-pain intensity results

	Black female	**Black male**	**White female**	**White male**	**P-value**
Median (IQR)	52 (34-66)	58 (41-71)	51 (35-68)	55 (40-69)	
Black male vs. Black female					p = 0.19; Mann U = 1159
White female vs. Black female					p = 0.95; Mann U = 1694
White male vs. Black male					p = 0.61; Mann U = 1053
White male vs. White female					p = 0.41; Mann U = 1272

Pain intensity of the PPT was measured using VAS scores. Black males had a median PP intensity of 57.50/100 compared to 52/100 for black females, no difference in PP tolerance was found between black participants (p = 0.19) (Table 3.6). White males had a median PP intensity of 55/100, compared to 51/100 for white females, no difference in PP tolerance was found between black participants (p = 0.41) (Table 3.6). Furthermore no differences were found in pressure pain intensity between female (p = 0.95) and male participants (p = 0.61) (Table 3.6). Thus, there were no significant differences in maximum PP intensity between the sexes or race groups.

3.4 Pain beliefs

APPROPRIATE PAIN BEHAVIOUR QUESTIONNAIRE (APBQ)

APBQ-Female

Table 3.7 Appropriate Pain Behaviour Questionnaire-Female Scores

	Black female	**Black male**	**White female**	**White male**	**p-value**
Median (IQR)	2.8 (1.3-4.4)	3.6 (2.8-4.7)	3.3 (2.8-4.7)	4.2 (2.0-5.3)	
Black male vs. Black female					p = 0.42; Mann U = 1248
White female vs. Black female					p = 0.18; Mann U = 1538
White male vs. Black male					p = 0.33; Mann U = 811
White male vs. White female					p = 0.54; Mann U = 1118

Results for the APBQ-Female scores questions on average are shown in Table 3.7. Participants found it appropriate for women to express pain and no differences were found between groups. Black males had a median APBQ-F score of 3.58 compared to 3.17 for black females; no difference was found between black participants (p = 0.42) (Table 3.7). White males had a median APBQ-F score of 3.92 compared to 3.63 for females; no difference was found between white participants (p = 0.54) (Table 3.7). No difference in APBQ-F scores were found between black and white female (p = 0.18) and male (p = 0.33) participants (Table 3.7).

APBQ-Male

Table 3.8 Appropriate Pain Behaviour Questionnaire - Male Scores

	Black female	**Black male**	**White female**	**White male**	**p-value**
Median (IQR)	2.5 (1.1-4.1)	0.3 (-1.8-4.2)	3.0 (1.4-4.7)	2.2 (0.6-3.8)	
Black male vs. Black female					$p < 0.01$; Mann U = 542
White female vs. Black female					$p = 0.42$; Mann U = 1322
White male vs. Black male					$p < 0.01$; Mann U = 609
White male vs. White female					$p = 0.04$; Mann U = 1020

Results of the APBQ-Male questions on average, are shown in Table 3.8. Females were more accepting of men expressing pain than males and white males were more accepting of men expressing pain than black males. Black males had a median APBQ-M score of 0.38 compared to 3.04 for black females, black females were more accepting of men expressing pain compared to black males ($p < 0.01$) (Table 3.8). White males had a mean APBQ-M score of 2.13 compared to 3.08 of white females, white females were more accepting of men expressing pain compared to white males ($p = 0.04$) (Table 3.8). No difference was found between the female participants ($p = 0.42$), however white males were more accepting than black males of pain expression ($p < 0.01$) (Table 3.8).

Table 3.9 Individual Appropriate Pain Behaviour Questionnaire Scores

APBQ-F vs. APBQ-M	Black female	Black male	White female	White male
P-value	0.88	<0.01	0.34	0.03
Sum of signed ranks (W)	-14.00	199.00	75.00	116.00

Wilcoxon signed rank tests were then carried out for APBQ-Female and APBQ-Male scores of the same individual (Table 3.9). Due to multiple comparisons being made, a Bonferroni correction adjusted the p-values to <0.0125. Black females found pain expression acceptable for men and women showed no significant differences $p = 0.88$. Black males were more accepting of pain expression in women than men $p < 0.01$. White males were more accepting of pain expression in women than men $p = 0.03$. White females found pain expression acceptable for men and women $p = 0.34$.

3.5 PSYCHOSOCIAL FACTORS

ANXIETY

Table 3.10 Anxiety Results

	Black female	Black male	White female	White male	p-value
Median (IQR)	1.7 (1.4-2.2)	1.4 (1.1-1.6)	1.6 (1.4-2.1)	1.4 (1.3-1.5)	
Black male vs. Black female					p < 0.01; Mann U = 796
White female vs. Black female					p = 0.50; Mann U = 1664
White male vs. Black male					p = 0.40; Mann U = 1008
White male vs. White female					p < 0.01; Mann U = 833

Participants completed the Hopkins Symptoms Checklist-25 (HSCL-25), of which a sub-scale assessed anxiety. A score of more than 1.75 indicated the individual had clinically significant symptoms of anxiety. Results showed that female participants were more anxious their male counterparts but, on average, no group had a level of anxiety greater than 1.75.Black males had a median anxiety score of 1.35, compared to 1.70 for black females, black females were significantly more anxious than black males (p = <0.01) (Table 3.10). White males had a median anxiety score of 1.41 compared to 1.72 for white females, white females were more anxious than white males (p < 0.01) (Table 3.10). Black females were more anxious than white females (p = 0.05) (Table 3.10). However, no significant difference was found between male participants (p = 0.40) (Table 3.10).

DEPRESSION

Table 3.11 Depression Results

	Black female	Black male	White female	White male	p-value
Median (IQR)	1.7 (1.2-1.6)	1.3 (1.4-2.1)	1.2 (1.1-1.3)	1.5 (1.3-1.9)	
Black male vs. Black female					$p < 0.01$; Mann U = 781
White female vs. Black female					$p = 0.02$; Mann U = 1356
White male vs. Black male					$p < 0.01$; Mann U = 766,5
White male vs. White female					$p < 0.01$; Mann U = 671,5

Participants completed the Hopkins Symptoms Checklist-25 (HSCL-25), of which a sub-scale assessed depression. A score of more than 1.75 indicated the individual had clinically significant symptoms of depression. Results showed that females were more depressed than males and, black males were more depressed than white males (Table 3.11) on average, no group had a level of depression greater than 1.75. Black males had a median depression score of 1.30, compared to 1.70 for black females, black females had greater depressive symptoms than black males ($p < 0.01$) (Table 3.11). White males had a mean depression score of 1.20 compared to 1.47 for white females, white females had greater depressive symptoms than white males ($p < 0.01$) (Table 3.11). Black participants had greater depressive symptoms than their race counterparts; black females had greater depressive symptoms than white females ($p = 0.02$), and black males had greater depressive symptoms than white males ($p < 0.01$) (Table 3.11).

PAIN CATASTROPHIZING

Pain catastrophizing - Trait

Table 3.12 Trait catastrophizing scores

	Black female	**Black male**	**White female**	**White male**	**p-value**
Median (IQR)	22 (10-22)	15 (13-30)	12 (5-18)	11 (7-18)	
Black male vs. Black female					$p < 0.01$; Mann U = 907,5
White female vs. Black female					$p < 0.01$; Mann U = 968
White male vs. Black male					$p = 0.03$; Mann U = 851
White male vs. White female					$p = 0.32$; Mann U = 1294

Trait catastrophizing was assessed by measuring pain catastrophizing scale (PCS) scores *before* the pain tests (Table 3.12). A score of more than 24 indicated a high level of catastrophizing; no group had a level of greater than 24 on average. Results indicated that black participants catastrophize more than their white counterparts. Black males had median PCS score of 15 compared to 22 for black females, black females catastrophized more than black males ($p < 0.01$) (Table 3.12). White males had a mean PCS score of 11 compared to 12 for white females, no difference was found between the white participants ($p = 0.32$) (Table 3.12). Black females catastrophized more than white females ($p < 0.01$) and black males catastrophized more than white males ($p = 0.03$) (Table 3.12).

Pain Catastrophizing – State

Table 3.13 State catastrophizing scores

	Black female	Black male	White female	White male	p-value
Median (IQR)	21 (12-31)	16 (8-23)	9 (5-16)	10 (4-15)	
Black male vs. Black female					p = 0.02; Mann U = 948,5
White female vs. Black female					p < 0.01; Mann U = 889,5
White male vs. Black male					p = 0.01; Mann U = 751,5
White male vs. White female					p = 0.67; Mann U = 1308

State catastrophizing was measuring PCS scores *after* the pain tests were conducted (Table 3.13). A score of more than 24 indicated a high level of catastrophizing; no group had a level greater than 24 on average. Results showed that black participant's catastrophized more than their white counterparts. Black males had a median PCS score of 16 compared to 21 for black females, black females catastrophized more than black males (p = 0.02) (Table 3.13). White males had a mean PCS score of 10 compared to 9 for white female, no difference was found between white participants (p = 0.67) (Table 3.13). Black females catastrophized more than white females (p < 0.01) and black males catastrophized more than white males (p = 0.01) (Table 3.13).

A comparison of median trait and state pain catastrophizing scores are shown in (Figures 3.1; 3.12; 3.3; 3.4). Participants had a similar level of catastrophizing for both trait and state catastrophizing, no groups had a level greater than 24 on average. Median scores of state pain catastrophizing were lower than that of trait catastrophizing for all groups.

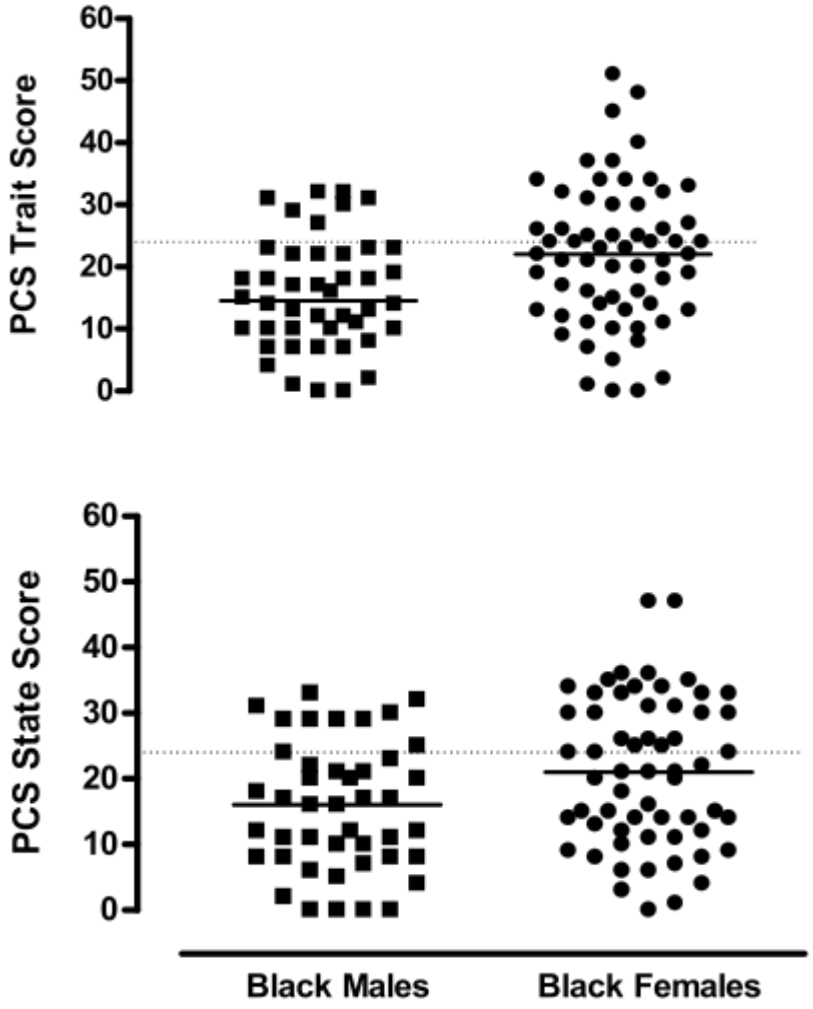

FIGURE 3.1 COMPARISON OF MEDIAN TRAIT AND STATE CATASTROPHIZING SCORES FOR BLACK MALES AND FEMALES. VALUES ABOVE THE DASHED LINE INDICATE HIGH LEVELS OF CATASTROPHIZING. A) BLACK FEMALES HAD A GREATER TRAIT CATASTROPHIZING THAN DID BLACK MALES ($P < 0.01$), B) BLACK FEMALES HAD GREATER CATASTROPHIZING THAN BLACK MALES ($P = 0.02$).

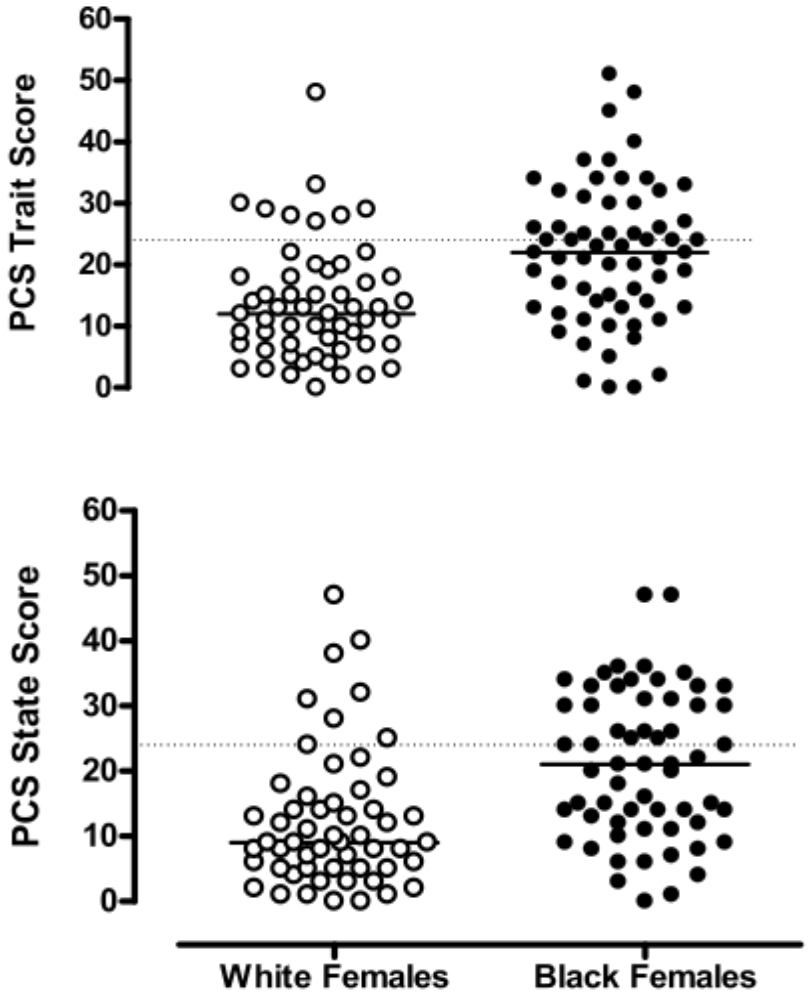

FIGURE 3.2 COMPARISON OF MEDIAN TRAIT AND STATE CATASTROPHIZING SCORES FOR WHITE AND BLACK FEMALES. VALUES ABOVE THE DASHED LINE INDICATE HIGH LEVELS OF CATASTROPHIZING. A) BLACK FEMALES HAD A GREATER TRAIT CATASTROPHIZING THAN DID WHITE FEMALES ($P < 0.01$), B) BLACK FEMALES HAD A GREATER CATASTROPHIZING THAN WHITE FEMALES ($P < 0.01$).

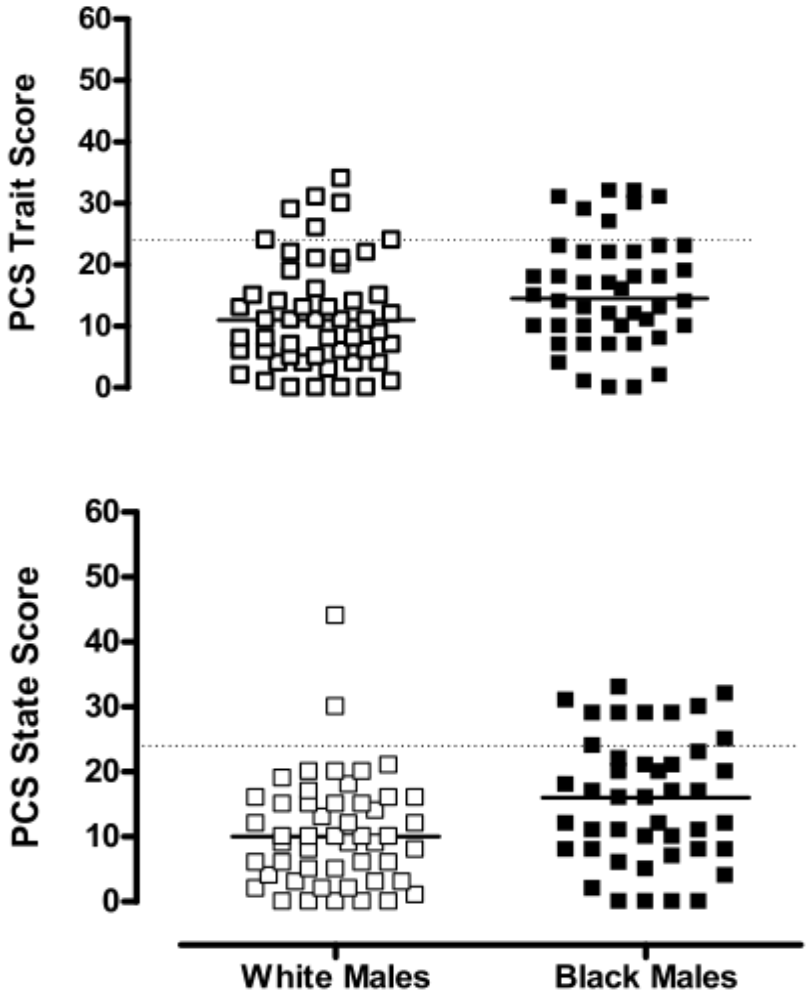

FIGURE 3.3 COMPARISON OF MEDIAN TRAIT AND STATE CATASTROPHIZING SCORES FOR WHITE AND BLACK MALES. VALUES ABOVE THE DASHED LINE INDICATE HIGH LEVELS OF CATASTROPHIZING. A) BLACK MALES HAD GREATER TRAIT CATASTROPHIZING THAN DID WHITE MALES ($P = 0.03$). B) BLACK MALES HAD A GREATER CATASTROPHIZING THAN DID WHITE MALES ($P = 0.01$).

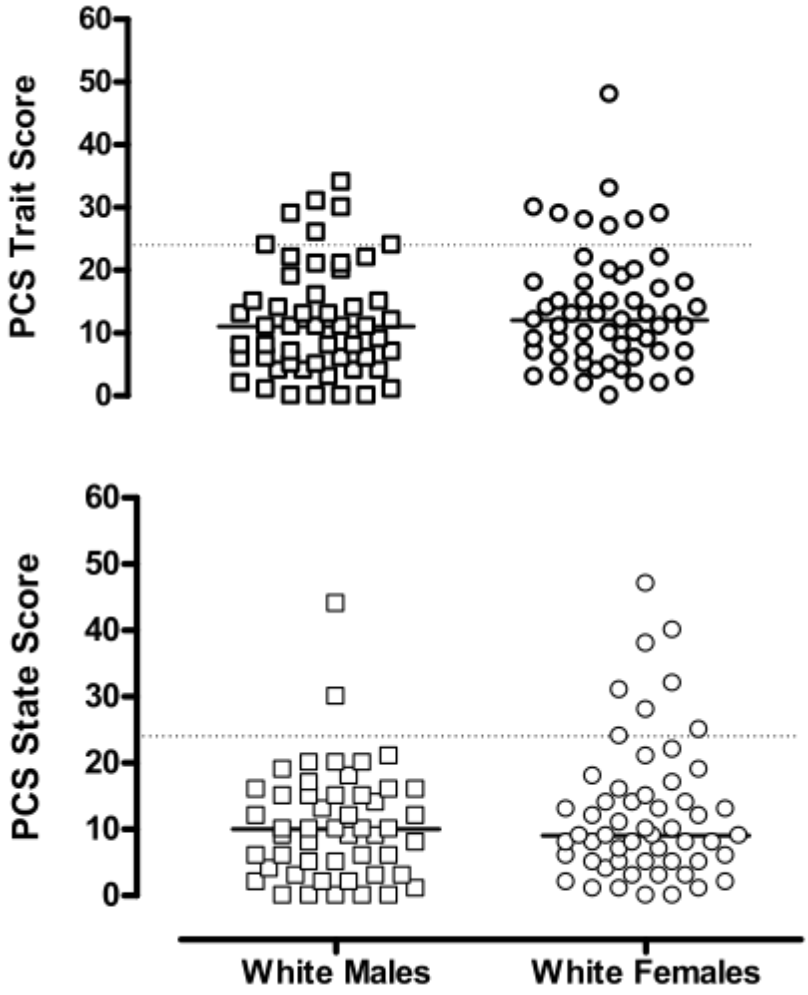

FIGURE 3.4 COMPARISON OF MEDIAN TRAIT AND STATE CATASTROPHIZING SCORES FOR WHITE MALES AND FEMALES. VALUES ABOVE THE DASHED LINE INDICATE HIGH LEVELS OF CATASTROPHIZING. A) WHITE MALES AND FEMALES HAD NO SIGNIFICANT DIFFERENCES IN TRAIT CATASTROPHIZING ($P = 0.32$), B) WHITE MALES AND FEMALES HAD NO SIGNIFICANT DIFFERENCES IN CATASTROPHIZING ($P = 0.67$).

3.6 Regression Tree Analyses

Regression tree analyses were carried out to determine predictors of pain sensitivity and beliefs. Random forest plots determined possible important predictors (variables), those located above the dotted line, in red, were an important predictor for that outcome. If a predictor appeared in multiple samples, it is assumed to be important, as opposed to appearing in just one sample.

Random forest plots for cold pain tolerance are indicated in Figure 3.5.

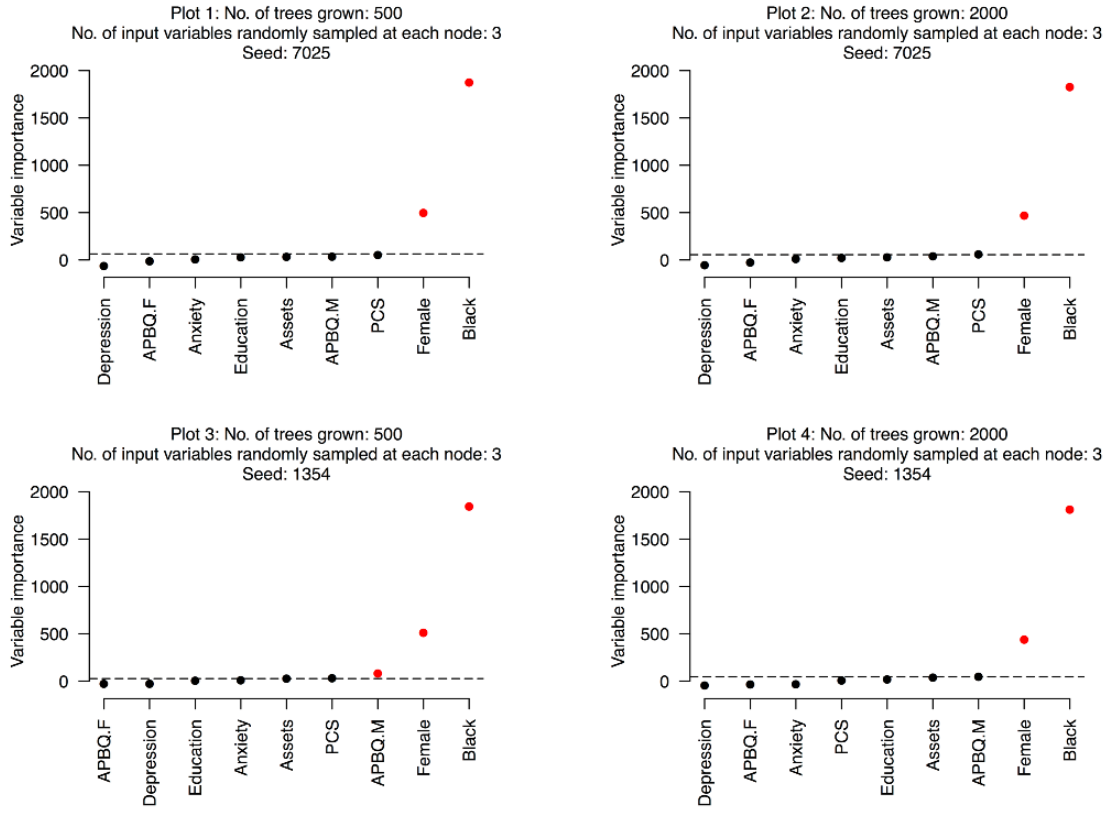

Figure 3.5 Random forest plot for cold pain tolerance.

Race and sex were identified as important variables in cold pain tolerance. APBQ-M score was identified as an important factor in only one of the models and therefore was not taken as an important predictor. Variables that best predicted an association to low cold pain tolerance were race and sex. Being black and being female was

associated with having a lower cold pain tolerance as compared to being white and being male.

Figure 3.6 indicates the random forest plots for pressure-pain tolerance.

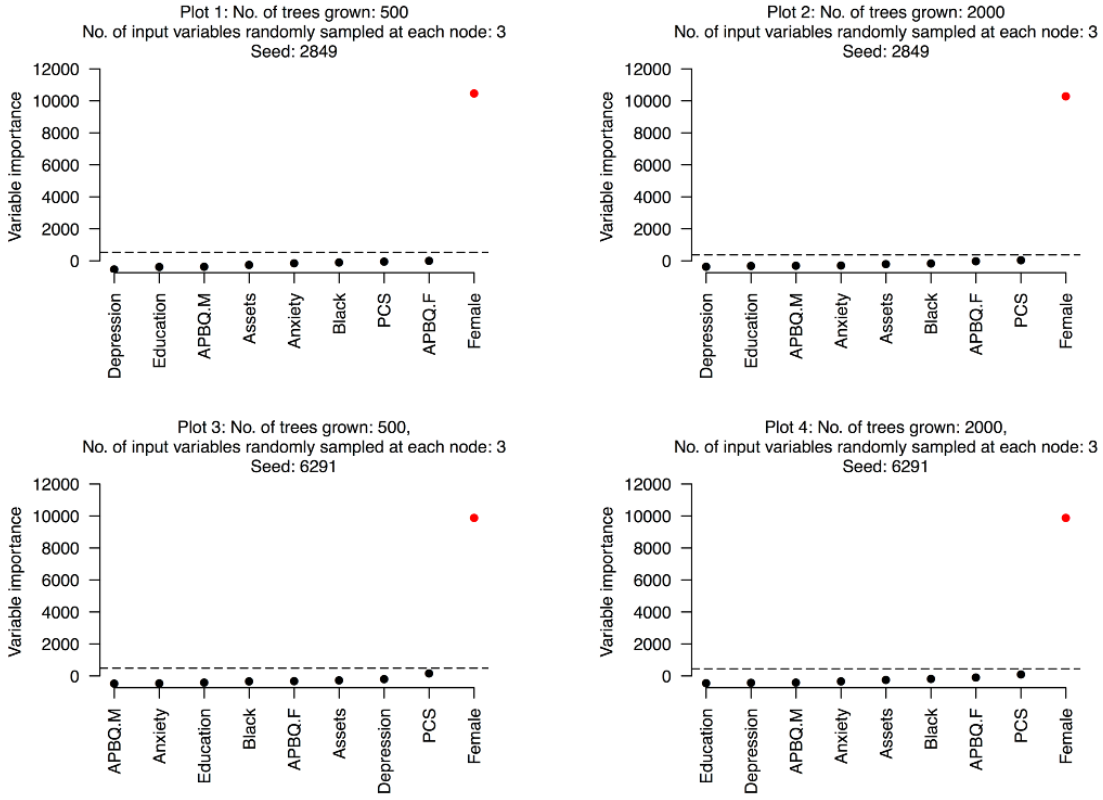

FIGURE 3.6 RANDOM FOREST PLOT FOR PRESSURE-PAIN TOLERANCE.

Sex was identified as the only important predictor variable in pressure-pain tolerance. Being female was associated with increased probability of having a low pressure-pain tolerance when compared to being male.

Random forest plots for cold pain intensity are indicates in Figure 3.7.

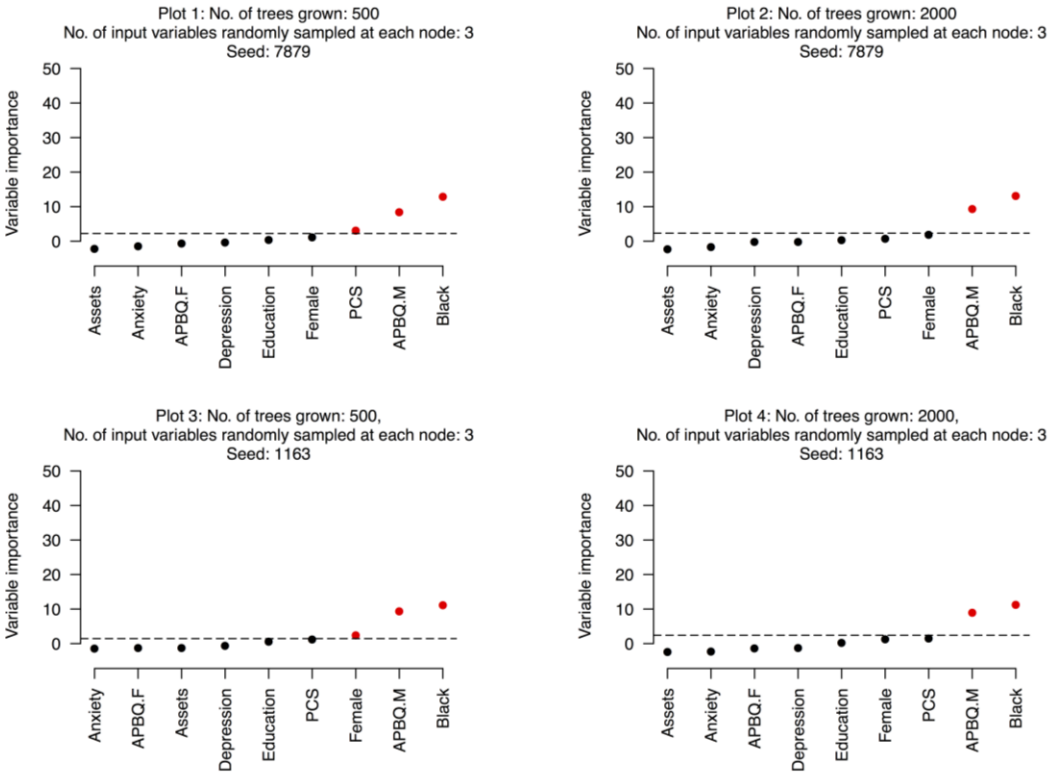

FIGURE 3.7 RANDOM FOREST PLOT OF COLD PAIN INTENSITY.

Important predictor variables for cold pain intensity were APBQ-M score and race. PCS and sex (being female) were each identified as significant predictors in one model each, and therefore they were not considered as important variables. Being black and having a greater APBQ-M score increased the probability of reporting greater cold pain intensity, as compared to being white and having low APBQ-M scores.

Figure 3.8 indicates the random forest plots for pressure-pain intensity.

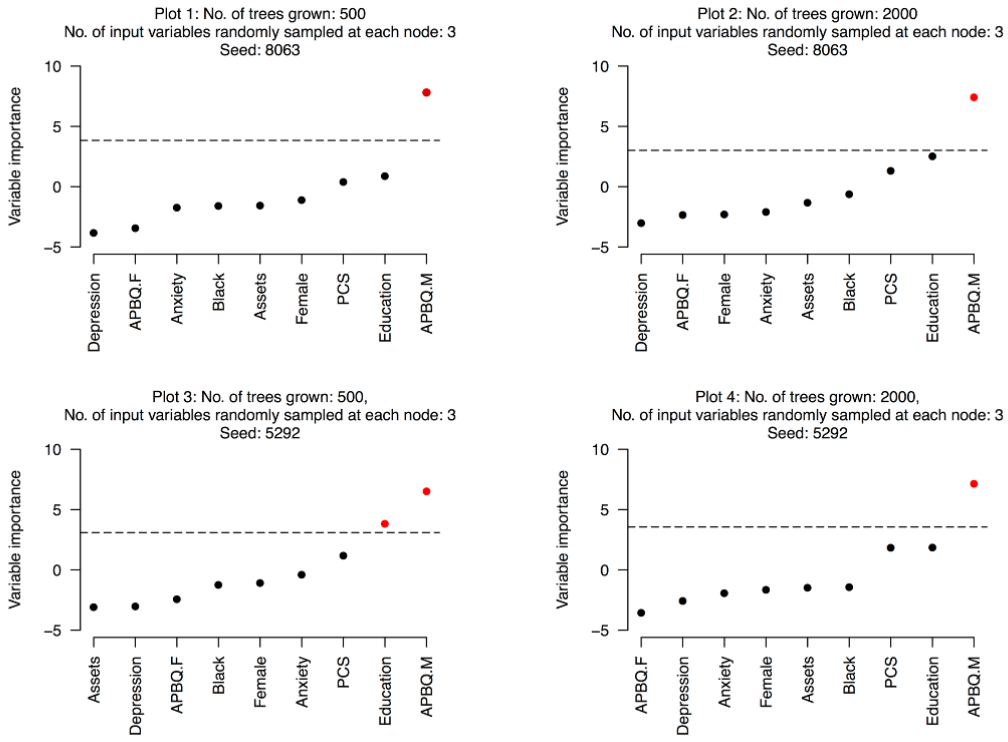

FIGURE 3.8 RANDOM FOREST PLOT OF PRESSURE-PAIN INTENSITY.

APBQ-M score was the only important predicator for pressure-pain intensity. Education was identified as a significant predictor in only one sample, and therefore it was not considered an important predictor. It is notable that greater APBQ-M score was associated with greater pressure-pain intensity.

Appropriate Pain Behaviour Questionnaire-Females random forest plots are indicated in Figure 3.9.

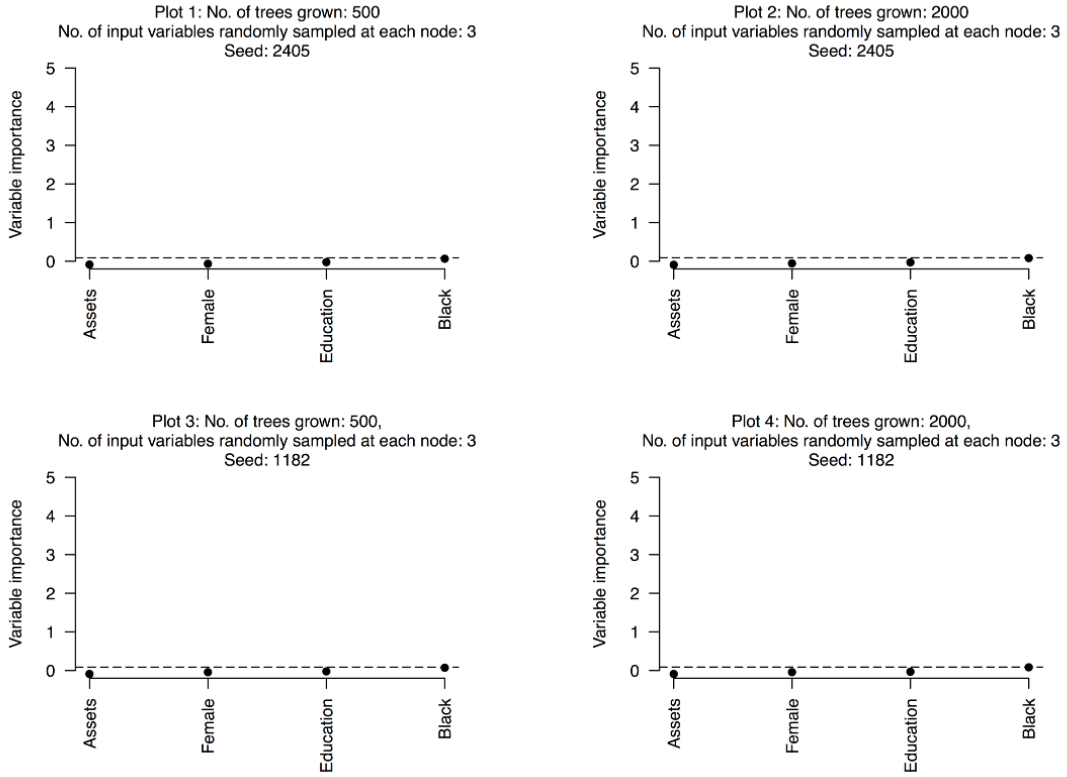

FIGURE 3.9 RANDOM FOREST PLOT OF APPROPRIATE PAIN BEHAVIOUR QUESTIONNAIRE-FEMALES.

There were no important predictors of APBQ-F score.

Figure 3.10 indicated the Appropriate Pain Behaviour Questionnaire-Males random forest plots.

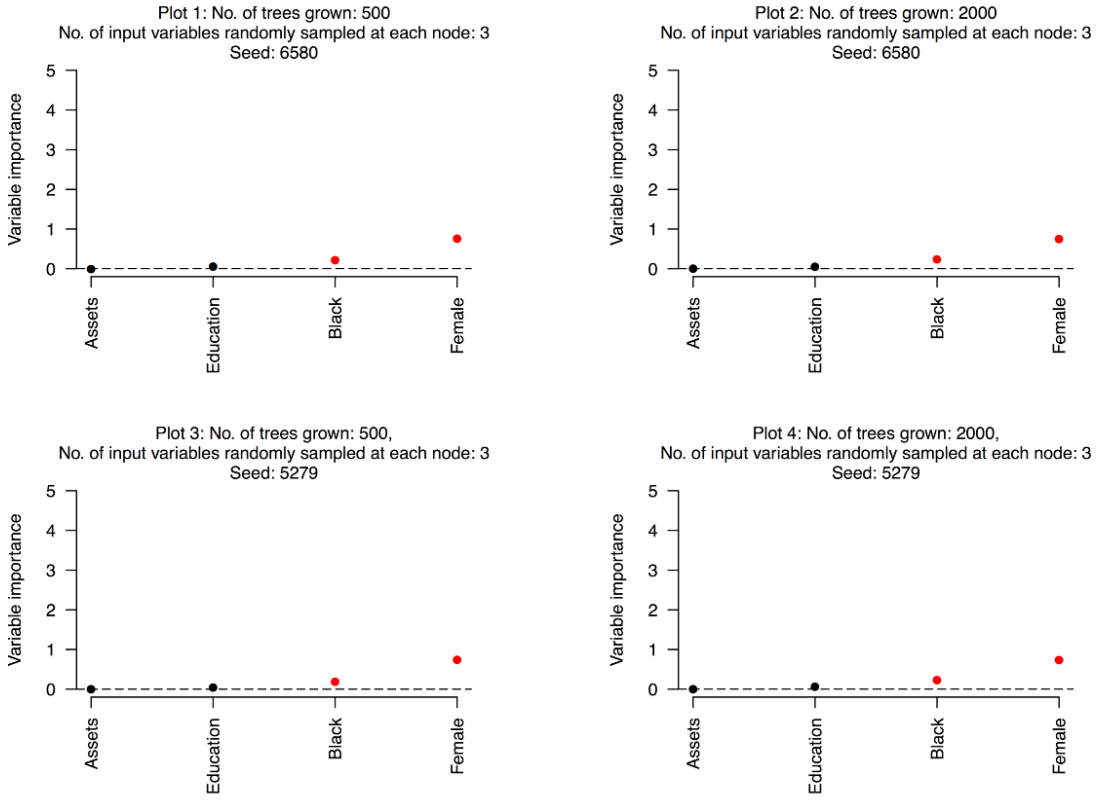

FIGURE 3.10 RANDOM FOREST PLOT OF APPROPRIATE PAIN BEHAVIOUR QUESTIONNAIRE-MALES.

Sex and race were the only important predictors of APBQ-M score, however the race variable is located only slightly above the dotted line. Therefore being female may indicate a probability to greater APBQ-M score, as compared to being male with lower APBQ-M scores.

A summary of significant univariate analyses are shown in Table 3.14. Race and sex were the most prominent significant variables resulting in differences in pain sensitivity, pain beliefs about men and psychological variables. Black participants had a lower cold pain tolerance, and greater trait and state pain catastrophizing compared to white participants. Greater trait and state pain catastrophizing were found in black females when compared to black males. Black females also had

greater cold pain intensity than white females. Black males had a greater level of depression than white males. Males had greater cold pain and pressure-pain tolerance compared to females. Greater APBQ-M scores were found in females, as well as greater levels of anxiety and depression as compared to males.

3.7. Summary of results

A summary of significant univariate analyses are indicated in Table 3.14. Table 3.15 shows the results of the regression tree analyses.

Table 3.14 Summary of Significant Univariate Analyses

Variable	Outcomes		
Cold pain tolerance	Males > Females	Black males > black females	White males > white females
	Whites > blacks	White males > black males	White females > black females
Cold pain intensity	Black > whites	Black females > white females	
Pressure-pain tolerance	Males > Females	Black males > black females	White males > white females
APBQ-M scores (expression of pain seen as appropriate)	Females > males	Black females > black males	White females > white males
	Whites > blacks	White males > black males	
Anxiety	Females > males	Black females > black males	White females > white males
Depression	Females > males	Black females > black males	White females > white males
	Black > whites	Black males > white males	
Pain catastrophizing - trait	Females > males	Black females > black males	
	Black > whites	Black females > white females	Black males > white males
Pain catastrophizing - state	Females > males	Black females > black males	
	Black > whites	Black females > white females	Black males > white males

A summary of regression analyses is shown in Table 3.15. Results indicated that race and sex were important variables in correlation to low cold pain tolerance, and greater APBQ-M scores. Race was an important predictor in cold pain intensity, and so was sex in pressure-pain tolerance. Greater APBQ-M scores (found in females) were a possible predictor of greater cold pain and pressure-pain intensity. PCS and education were not possible predictors of cold pain and pressure-pain intensity as they were located on and slightly above the dotted line in random forest plots (Figure 3.7 and Figure 3.8).

Table 3.15 Summary of Significant Regression Analyses

	Important predictors
Low cold pain tolerance	Black; female
Greater cold pain intensity	Black; APBQ-M; PCS
Low pressure-pain tolerance	Female
Greater pressure-pain intensity	APBQ-M; Education
APBQ-F	None
APBQ-M	(Accepting of men expressing pain) Black; female

CHAPTER 4

DISCUSSION

4. DISCUSSION

This was the first study to investigate sex and race differences in pain sensitivity and beliefs in a South African population. I found that tolerance to cold pain differed between the races and sexes, while tolerance of pressure-pain only differed between the sexes. Cold pain intensity was greater in black, than white females. Females also had greater levels of anxiety and depression when compared to males, and black males had a greater level of depression than white males. Black participants had greater trait and state catastrophizing compared to white participants, and black females had greater trait and state catastrophizing compared to black males. A lower socioeconomic status was found in black participants when compared to white counterparts. The expression of pain behaviour in men was least accepted by males compared to female participants. Furthermore, black males were least accepting of men expressing pain behaviour than white males.

4.1 SEX DIFFERENCES IN PAIN SENSITIVITY

Pain tolerance

In my study, women had lower tolerance to both the cold pain and pressure-pain than men did. Regression analyses revealed sex (being female) as a predictor for low cold pain and pressure-pain tolerance. This phenomenon has been found in studies using the cold pressor test (CPT) and pressure-pain test (PPT) conducted in different countries and in women of different ages (Sanford *et al*, 2002; Kowalczyk *et al*, 2010; Tashani *et al*, 2010; Forsythe *et al*, 2011; Hashmi and Davis, 2013).

Stefani *et al* (2012) proposes that in healthy participants, brain derived neurotrophic factor (BDNF) may be related to sex differences in pressure-pain sensitivity. They found a higher level of BDNF serum associated with higher pain thresholds for pressure-pain and heat pain in females, yet the inverse was found in males, suggesting that estrogen may regulate BDNF mRNA in areas associated with nociceptive sensory processing (hippocampus, cerebral-cortex, spinal cord).

Ellermeier and Westphal (1995) suggest that a difference in pressure-pain tolerance between the sexes could be due to differences in body measures and sizes.

Pain intensity

Some studies have reported that women experience greater pain intensity than men do in response to chronic and experimental pain (Roth *et al*, 2005; Traub and Ji, 2013), however I found no sex differences for cold and pressure-pain intensity. This lack of difference in maximum pain intensity between men and women in my study, together with greater cold and pressure-pain tolerance in men than women, indicates that the ability to withstand more pain was not the reason for greater pain tolerance in men in my study. Even though men and women reported similar pain intensity, men were able to tolerate it for longer, or it took longer for men to get to the same pain intensity level as women. Hirsh *et al* (2008), Nayak *et al* (2000) and Robinson *et al* (2003) also found no difference in pain intensity between the sexes for cold pain. Sarlani *et al* (2002; 2004) found women to report greater pain intensity than men for pressure-pain, however they both assessed temporal summation of mechanical pain and not a single exposure to pressure-pain as in my study. An individual's previous exposure to painful stimuli, may affect their pain intensity ratings, as those with a greater pain history tend to exhibit a lower pain tolerance (Rollman *et al,* 1979; Rollman *et al*, 2004), and in my young cohort (having a mean age of 20.7) the women might not have had many painful experiences such as childbirth.

Psychological variables

Levels of anxiety and depression were greater in women than the men in my study. Women had greater anxiety, and lower cold and pressure-pain tolerance than did the men, this finding has also been found in American women with musculoskeletal pain (Stubbs *et al*, 2010). Women also had greater depression and a lower cold and pressure-pain tolerance compared to the men in my study, coinciding with American women with chronic pain (Roth *et al*, 2005). My findings are similar to those of Roth *et al* (2005); Stubbs *et al* (2010), black females had a mean depression and anxiety score of 1.84; 1.80 respectively, white females had a mean score of depression and anxiety score of 1.62; 1.72 respectively; a score of more than 1.75 reflects the

individual is symptomatic. This lends support to the body of evidence that links greater anxiety and depression to greater pain (Racine *et al*, 2012b), and that the greater depression and anxiety experienced by women in my study may at least particularly explain the lower pain tolerance levels compared to the male participants.

Previous studies have found that women catastrophize more than men (Roth *et al*, 2005; Keogh 2006; Racine *et al*, 2012b). In my study black females catastrophized more than both black men and white females. This may explain the lower cold and pressure-pain tolerance in black females compared to black males. No difference was found between "trait" and "state" catastrophizing between white participants. This is in contrast to Hirsh *et al* (2008) who proposed that pain tolerance differences between the sexes are mediated by "trait" and "state" catastrophizing.

Another psychological factor that could explain sex differences in experimental pain is primary pain appraisals (one's initial reasoning on whether a circumstance is stressful or not), represented by "threat/harm" or "challenge" (the ability to cope perceived as greater than the danger of the situation) pain appraisals. Forsythe *et al* (2011) found women have a lower "challenge" pain appraisal than men, coinciding with a lower cold pain tolerance, therefore women may perceive the experimental pain as more challenging than do men.

Pain beliefs

Society influences gender roles in pain. Women and men in my study found expression of pain more acceptable in women than men, which is consistent with studies from America and India (Nayak *et al*, 2000; Robinson *et al*, 2001). In America and Israel, men are perceived as less sensitive to pain, less willing to report pain, and more enduring of pain in contrast to women (Defrin *et al*, 2009; Defrin *et al*, 2011; Wandner *et al*, 2012). In my cohort, sex was a predictor of pain beliefs in men. Men found pain expression in men less acceptable than women did, this may explain the greater cold and pressure-pain tolerance. Similarly, a study assessing pain beliefs in experimental pain has also shown an association between stereotypical gender behaviour, and heat pain tolerance (Defrin *et al*, 2009). Therefore pain beliefs may impact pain perception.

4.2 Race differences in pain sensitivity

Pain tolerance

I found that blacks had a lower cold pain tolerance than their sex-matched white counterparts. Furthermore, regression analyses revealed race as a predictor of cold pain tolerance. This phenomenon has also been shown in US studies comparing African-Americans and whites (Kim *et al*, 2004; Campbell *et al*, 2005; Klatzkin *et al*, 2007; Forsythe *et al*, 2011).

Blunt pressure and ice-cold water elicit a painful response, via the same spinothalamic pathway and A-delta and C nerve fibers (Backonja *et al*, 2013), yet only tolerance to cold pain is consistently affected by race (Campbell *et al*, 2005; Rahim-Williams *et al*, 2007; Forsythe *et al*, 2011, Riley *et al*, 2013). This difference may be explained by physiological factors. Numerous studies have shown individuals of African descent to have greater cardiovascular reactivity (heart rate, blood pressure) in general (Yusuf *et al*, 2001; Opie and Seedat 2005; Maseko *et al*, 2011). Exposure to noxious stimuli increases cardiovascular reactivity in African-Americans (Edwards *et al*, 2001), but cardiovascular reactivity has only been demonstrated in response to cold pain (due to sympathetic activation) and not pressure-pain (Roatta *et al,* 1998; Mohn *et al*, 2012).

In my study, 39% of white females reached tolerance in the cold pain test compared to 7% of black females, whereas 46% of white females were on oral contraceptive compared to a mere 2% of black females. Estrogen levels may affect experimental pain perception, a sub-analysis of women on oral contraceptive was not carried out, as the role of estrogen in pain perception was not one of the objectives of the study. However, controlling for estrogen variance in experimental pain studies is a recommendation for future studies.

Pain intensity

Studies have shown African-Americans report a greater pain intensity in response to chronic pain compared to whites (Carey *et al*, 2010; Merry *et al*, 2011), but no

comparison was made between the sexes in the African-American group. I found no difference in pain intensity between the races in response to pressure pain but when I examined differences between the two races according to sex, black females reported greater pain intensity compared to white females for cold pain, but not black males compared to white males. However, regression tree analysis showed that race is a predictor of cold pain intensity, indicating a possible race and sex interaction in pain perception.

Psychological variables

Psychological reasons have also been used to explain racial differences in pain sensitivity to cold pain. Studies analyzing psychological contributions to chronic pain differences between races, state blacks have greater depression and anxiety scores compared to whites (McCracken *et al*, 2001; Green *et al*, 2003; Egwu and Nwuga, 2008; Caldwell *et al*, 2009; Merry *et al*, 2011). I found blacks to have a similar anxiety level to whites but scored higher on the depression scale, and this was associated with a lower cold pain tolerance. When Klatzkin *et al* (2007) compared cold pain tolerance in healthy African-American and white women, with and without prior histories of a mood disorder, women with a prior history of mood disorders had a greater tolerance than did their race counterparts without a prior history of mood disorders. Within the group with a prior history of mood disorders, white women had a greater pain tolerance than African-American women, indicating that irrespective of psychological functioning, race affects cold pain sensitivity.

Several studies have reported that African-Americans catastrophize more than whites do, and they have a lower experimental pain tolerance (Campbell *et al*, 2005; Forsythe *et al*, 2011; Riley *et al*, 2013). I found Black South Africans catastrophized more than their white counterparts, for both “trait” and “state” catastrophizing, however, their scores were below clinical significance (a score of 30 or greater) (Sullivan, 1995). Additionally this greater catastrophizing maybe associated with greater depression and cold pain sensitivity. Indeed, higher catastrophizing may also be a reason for the higher pain intensity reported by black females in cold pain (Campbell *et al*, 2003; Rhudy *et al*, 2009).

Forsythe *et al* (2011) found African-Americans to have a lower “threat/harm” pain appraisal than whites, coinciding with a lower cold pain tolerance. Therefore African-Americans may perceive the experimental pain as more threatening or damaging than do whites.

Pain beliefs

Using the Appropriate Pain Behaviour Questionnaire (APBQ) Nayak *et al* (2000) and Hsieh *et al* (2011) reported that Indian and Chinese participants (irrespective of sex), were less willing to express pain than whites. In my study, whilst there was no difference between black and white females, white males were relatively more accepting of pain expression in men than black males were. Regression analyses showed that pain beliefs were not an important factor in predicting cold pain tolerance. However, this is the first study to use the APBQ in an African population.

Socioeconomic status

It has been observed that African-Americans have a lower socioeconomic status than whites, and it is associated with greater chronic pain intensity (Edwards *et al*, 2001; Green and Hart-Johnson, 2012). I also found blacks to have a lower socioeconomic status than whites as well as a lower cold pain tolerance, and in black female’s greater cold pain intensity. However, socioeconomic status was not a predictor of cold pain tolerance or intensity (Figure 3.5; 3.7).

A low socioeconomic status maybe associated with greater depression. Depression was more prevalent in women with a lower socioeconomic status compared to a higher socioeconomic status, and depression was more prevalent in black than white women (Gazmararian *et al*, 1995; Kosidou *et al*, 2011). I found a lower socioeconomic status and greater depression in black participants compared to white participants.

Although the socioeconomic status questionnaire has not been validated, a review by Shavers (2007) indicated that studies assessing socioeconomic status and health disparities have inconsistent results. Reasons for this could be a lack of precision

and reliability of measures, difficulty with the collection of individual socioeconomic status data, a poor correlation between individual measures and inaccurate interpretation of study results. Differences of socioeconomic status measures are observed in Dorner *et al* (2011) that measured socioeconomic status based on education, income and profession; while Thomtén *et al* (2012) measured socioeconomic status based on education, occupation and financial strains.

4.3 LIMITATIONS

A possible limitation of my study was the small sample size, especially the cohort of black males which only included 44 individuals. Despite the small sample size, we had sufficient power to detect statistical significance between the groups, but some of my findings may reflect type II statistical error. The sex of the experimenter has been noted to affect pain reporting, with men reporting and demonstrating a lower pain response in the presence of a female experimenter and women reporting a lower pain response in the presence of a male experimenter (Levine and Simone, 1991; Defrin *et al*, 2011; Vigil and Coulombe, 2011). Women on oral contraceptive were not excluded from the study, however, pain tolerance and intensity have not been shown to be affected by these medications (Racine *et al*, 2012b).

4.4 FUTURE RESEARCH

My study was based on experimental pain. One should repeat the experiment in a clinical pain population to gain a better understanding of where differences detected under experimental conditions translate into real-world differences. Participants are aware that experimental pain will stop on command, therefore exploring pain appraisals (challenge and threat/harm) in future research will be beneficial in understanding the levels of challenge appraisal in men and women. There were different cultures within the race groups (eg. Zulu, Sotho, Xhosa) so one could divide the groups and repeat the experiment to examine if different cultures within the same race group affects pain intensity and tolerance. I only assessed three psychosocial factors: depression, anxiety and pain catastrophizing, I did not assess coping strategies. African-Americans reportedly use more coping strategies when exposed to pain (Hastie *et al*, 2004; Chibnall *et al*, 2005; Allen *et al*, 2010). It would be useful to know whether this was the case in South Africans too and whether it associated

with pain intensity and tolerance. Previous pain experience should be assessed as it might impact current pain tolerance. It may also present insight on how well an individual manages their pain.

4.5 Conclusion

Sex and race differences in pain tolerance and intensity were evident in this cohort of South African university students. Despite cultural differences, results were similar to those found in African-Americans. Psychosocial factors which are common to both South Africans and African-Americans such as lower socioeconomic status may be the cause but further research is needed.

The clinical implications of my findings are that awareness of these differences in pain sensitivity needs to be raised with healthcare professionals. Black patients are under treated for pain compared to whites (Wandner *et al*, 2012; Burgess *et al*, 2013) despite black females potentially experiencing greater pain intensity. Furthermore as black males may be less prepared to exhibit pain behaviour, their pain may go undetected and therefore untreated. Further research in a clinical pain population is required, however my study provides strong baseline data and is an essential starting point for future research.

CHAPTER 5

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Standard Assessment Criteria

Questions were scored depending on the degree to which the criteria were met. Scores were allocated as “Yes” = 2, “Partial” = 1 and “No” = 0. Questions that were not applicable to a certain study design were excluded and marked “N/A”. To calculate the summary score, the total number of scores are added up and divided by the total number of questions answered (i.e excluding the ones marked as “N/A”). Table 1 shows scores by two reviewers, for two separate samples of quantitative studies. Scores ranged from 0.40 to 0.93, but there was no clarity on an exclusion score, however with 0.40 being the lowest score one can assume that a study with a score lower than 0.40 should not be included. In my study design, questions 5, 6 and 7 (Table 2) were not applicable and were marked as “N/A”.

Table 1. Inter-rater agreement for overall scores of quantitative studies

	First Sample		Second Sample	
Research paper	Rater 1	Rater 2	Rater 1	Rater 2
1	0.44	0.56	0.73	0.73
2	0.86	0.90	0.73	0.77
3	0.73	0.73	0.59	0.73
4	0.89	0.89	0.55	0.55
5	0.89	0.93	0.50	0.45
6	0.68	0.80	0.82	0.86
7	0.55	0.60	0.68	0.73
8	0.90	0.85	0.90	0.80
9	0.82	0.80	0.73	0.77
10	0.82	0.90	0.50	0.60
11	-	-	0.40	0.40

Criteria questions for evaluation of quantitative studies †

1. Question/objective sufficiently described?
2. Study design evident and appropriate?
3. Method of subject/comparison group selection or source of information/input variables described and appropriate?
4. Subject (and comparison group, if applicable) characteristics sufficiently described?
5. If interventional and random allocation was possible, was it described? (N/A)
6. If interventional and blinding of investigators was possible, was it reported? (N/A)
7. If interventional and blinding of subjects was possible, was it reported? (N/A)
8. Outcome (and if applicable) exposure measure (s) well defined and robust to measurement/ misclassification bias? Means of assessment reported?
9. Sample size appropriate?
10. Analytical methods described/justified and sufficient?
11. Some estimate of variance is reported for the main results?
12. Controlling for confounding?
13. Results reported in sufficient detail?
14. Conclusions supported by the results?
Summary score (1)

† Criteria as per Kmet *et al*, 2004

Assessment of the quality of papers used in Table 1.2

Authors	Criteria Questions†											Score (1.00)
	1.	2.	3.	4.	8.	9.	10.	11.	12.	13.	14.	
Forsythe *et al*, 2011	2	2	2	2	2	2	2	2	2	2	2	1.00
Hirsh *et al*, 2008	2	2	2	1	2	2	2	2	2	1	2	0.91
Jackson *et al*, 2002	2	2	2	1	1	2	1	2	2	1	2	0.82
Jackson *et al*, 2005	2	2	2	1	1	1	2	2	2	2	2	0.86
Jackson, 2007	2	1	2	2	1	1	2	2	2	2	2	0.86
Kim *et al*, 2004	2	1	2	2	0	2	1	1	1	1	1	0.64
Koltyn, 1999	2	1	2	1	2	0	1	0	2	1	2	0.64
Myers *et al*, 2001	1	1	2	2	2	2	1	0	2	1	1	0.68
Nayak *et al*, 2000	2	2	2	2	1	2	1	2	2	2	2	0.91
Quiton and Greenspan, 2008	1	1	1	2	1	0	1	2	1	1	1	0.55
Rahim-Williams *et al*, 2007	2	1	1	2	1	0	1	0	2	1	2	0.59
Robinson *et al*, 2003	2	1	2	1	1	0	1	0	2	1	1	0.55
Sanford, *et al* 2002	2	2	1	2	1	2	2	2	1	2	2	0.86
Sarlani and Greenspan, 2002	2	1	2	2	1	0	1	2	2	1	1	0.68
Sarlani *et al*, 2004	1	2	2	2	1	0	1	2	2	1	2	0.73
Soetanto *et al*, 2006	2	1	2	1	1	2	1	0	2	1	1	0.64
Thorn *et al*, 2004	2	2	2	1	1	2	1	0	2	1	1	0.68
Wise *et al*, 2002	2	2	2	1	1	2	2	2	2	1	2	0.86

† Criteria and scoring as per Kmet *et al*, 2004

APPENDIX 3

Assessment of the quality of papers used in Table 1.3

Authors	Criteria Questions†											Score (1.00)
	1.	2.	3.	4.	8.	9.	10.	11.	12.	13.	14.	
Campbell *et al*, 2005	2	2	2	2	1	2	1	1	1	1	2	0.77
Forsythe *et al*, 2011	2	2	2	2	2	2	2	2	2	2	2	1.00
Green *et al*, 2003	2	2	2	2	2	2	1	0	2	2	2	0.86
Hsieh *et al*, 2011	2	2	1	2	2	2	2	2	2	2	2	0.95
McCracken *et al*, 2001	1	1	2	1	1	2	2	1	2	1	1	0.68
Nayak *et al*, 2000	2	2	2	2	1	2	1	2	2	2	2	0.91
Rahim-Williams *et al*, 2007	2	1	1	2	1	0	1	0	2	1	2	0.59
Riley *et al*, 2013	2	1	2	2	1	2	2	2	2	1	2	0.86

† Criteria and scoring as per Kmet *et al*, 2004

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Leena AB Persad

CLEARANCE CERTIFICATE	**M120648**
PROJECT	Race and Sex Differences in Pain Sensitivity and Beliefs
INVESTIGATORS	Ms Leena AB Persad.
DEPARTMENT	School of Physiology
DATE CONSIDERED	29/08/2012
DECISION OF THE COMMITTEE*	Approved Non-Genetics Component

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 14/09/2012 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Dr Peter Kamerman

DECLARATION OF INVESTIGATOR(S)
To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

CONSENT FORM

Race and sex differences in pain sensitivity and beliefs

I, _____, have read the information sheet regarding the research project entitled “Race and sex differences in pain sensitivity and beliefs”. I understand that I shall undergo a cold pressor pain test and a pressure pain test. I shall have to complete seven questionnaires.

I hereby give my full consent to participate in this study knowing that I may experience pain and discomfort. I am aware that participation in this study is completely voluntary and that I may withdraw from the study at any time without prejudice to me.

_____ _____

Signed (participant) Date

_____ _____

Information Sheet

Race and sex differences in pain sensitivity and beliefs

Good day,

My name is Leeana Persad, I am an MSc student at the School of Physiology at Wits University. You are invited to participate in a study I am conducting that investigates the differences in pain sensitivity and pain beliefs between races and sexes. The study comprises of questionnaires and two tests of pain sensitivity.

Women report more pain than men yet are prescribed less pain medication. African American individuals have shown a lower pain tolerance than their White counterparts. Such evidence suggests that sex and race/ethnicity/culture could influence pain sensitivity and beliefs. Yet currently there is no data on whether sex and racial differences in pain perception and beliefs exist in the South African population. Thus, we wish to assess sex and racial differences in pain sensitivity (using two tests of sensitivity) and pain beliefs (using questionnaires) in Black, White, Indian and Coloured South Africans. A better understanding of these pain differences could lead to improved pain management for different races and the sexes.

This information leaflet is to help you decide if you want to participate in the study. Before you agree to participate you must understand what is involved:

The study will take place in a room at the second year teaching labs, 6th Floor at the School of Physiology.

Procedure

All questionnaires and pain sensitivity tests will take place in a private office, with only you and the investigator present. The questionnaires start off with biographical, general heath questions and socio-economic (the Household Economic and Social Status Index) questionnaires, and then move on to questionnaires that assess pain

beliefs and general psychological outlook, namely the Appropriate Pain Behaviour Questionnaire, the Pain Catastrophizing Scale (PCS),the Depression, Anxiety and Positive Outlook Scale, the Hopkins Symptoms Checklist 25. It will take about 20 minutes to complete these questionnaires. You will then complete a cold pain pressor test. Here you will be required to place your hand in a bath of cold water (about 5°C) until you can no longer bear the pain, or 5 minutes have elapsed, at which point the test will stop immediately. You will be asked to rate the intensity of the pain you experienced. After a 10 minute break you will complete a pressure pain test which involves the placing of a pressure algometer (a device with that measures how much pressure is being applied to a body part) on the nailbed of your index finger. The pressure being applied to your nailbed will gradually increase until you can no longer bear the sensation and then the test will stop immediately. Again, you will be asked to rate the pain intensity. Once both the tests have been completed, you will be asked to repeat the PCS questionnaire.

Time period

The study will take a maximum of 30 minutes. 20 minutes for the questionnaires and 10 minutes for both the pain tests. Pain or discomfort may be felt during the cold pressor test and pressure pain test, however the test will finish as soon as you indicate that the discomfort is too much.

Confidentiality

Participation in this study is completely voluntary and you are free to choose not to participate or to withdraw from the study at any stage without disadvantage to yourself. All the information we collect will be kept confidential and will be available only to the researchers and yourself. Each participant will be allocated reference number that would be used as the participants' ID number. The first page of the biographical questionnaire, which contains all your contact details, will be removed and kept separately from all other information, and all records of your results will be identified only by the reference number assigned to you so that no data will be linked to you. You will not directly benefit in any way by participating in the study or be

compensated. The outcomes of this project as a whole, but not your individual information, will be made available to the scientific and medical community. This project has been approved by the Wits University Human Ethics Research Committee.

Thank you for your time and interest, please ensure that you have read and fully understood the information leaflet before signing the informed consent. If you have any queries please contact me on 082 742 7234 or visit me at the second year teaching labs 6th Floor, School of Physiology, Wits Medical School.

Yours sincerely
Leeana Persad

APPENDIX 7

CONTACT DETAIL

(Your contact details are confidential and will not be shared. Your contact information will be kept separate from all other data, and will be used only if we need to contact you regarding the study to which you have consented to participate in.)

LAST NAME	
FIRST NAME	
DATE OF BIRTH (dd/mm/yyyy)	
PHYSICAL ADDRESS	
TELEPHONE NUMBER	
EMAIL ADDRESS	

DEMOGRAPHICS

HEIGHT (m)			
MASS (kg)		BMI (kg/m^2)	
SEX	Male ☐ Female ☐		
ETHNICITY	Black African White Indian Coloured Other		
RELIGION			
HOME LANGUAGE			
DEGREE REGISTERED FOR			
YEAR OF STUDY			

HEALTH STATUS
(Check YES or NO and all that apply)

In general, would you say your health is: *(please tick one)*
Good
Fair
Poor

Do you currently have any pain?	YES ☐ NO ☐
If yes:	
Where is the pain?	
How long have you had this pain?	
Rate the average intensity of the pain:	MILD ☐ MODERATE ☐ SEVERE ☐
Are you taking any medication for this pain?	YES ☐ NO ☐
If yes:	
What medications are you taking?	
When last did you take the medication(s)?	

Please list any other medications you are currently taking, including the dosage. (Including traditional, homeopathic and naturopathic medications)	
Medication	**Dosage**

WOMEN ONLY	**YES**	**NO**
Have you had your first menstruation (menarche)?		
If yes, when did you last menstruate (days from start of menstruation)?		
Are you currently taking oral contraceptives?		
If yes, which contraceptive pill?		
Do you have dysmenorrhoea?		
If yes, how do you treat your symptoms?		

Do you have any of the following **chronic** health conditions:	**YES**	**NO**
HIV		
Diabetes		
Cardiovascular disease		
If yes, please specify:		
Asthma		
Respiratory disease (other than asthma)		
If yes, please specify:		
Neurologic disorder		
If yes, please specify:		
Inflammatory bowel disease		
If yes, please specify:		
Irritable bowel syndrome		
Arthritis or other rheumatologic disease (including fibromyalgia)		
If yes, please specify:		
Cancer		
If yes, please specify:		
Thyroid disease		

If yes, please specify:		
Other		
If yes, please specify:		
	YES	**NO**
Do you drink caffeinated beverages (e.g., coffee, tea, cola)?		
If yes, when last did you drink a caffeinated beverage?		
Do you drink alcoholic beverages?		
If yes, when last did you drink an alcoholic beverage?		
Do you use tobacco products (e.g., cigarettes, snuff)?		
If yes, when last did you use a tobacco product?		

Assessment of Socioeconomic Status (ASS)

We are interested in assessing your socioeconomic status. Please circle the option most appropriate.

I. Social status

Parents' education level

0. None
1. Primary school
2. High school
3. Tertiary level

Parents' employment status

0. No
1. Pension
2. Yes

II. Housing accommodation

Type of housing

1. None
2. Shack
3. Hostel
4. Room /garage
5. Flat cottage
6. Home shared with other families
7. Home not shared with other families

Toilet facilities

1. None
2. Pit of bucket
3. Outside toilet flush
4. Inside flush

Number of bedrooms

1. 0
2. 1
3. 2
4. 3
5. 4 or more

Refrigerator

1. No
2. Yes

Television

1. No
2. Yes

Telephone

1. No
2. Yes

Car

1. No
2. Yes

Washing machine

1. No
2. Yes

Microwave

1. No
2. Yes

. Hopkins Symptoms Checklist 25 (HSCL-25)

_____DATE _____SERIAL NUMBER

Listed below are some symptoms or problems that people sometimes have. Please read each one carefully and decide how much the symptoms bothered or distressed you in the last week, including today. Place a check in the appropriate column.

Extremely	**Quite a bit**	**A little**	**Not at all**	**Part 1** **Anxiety symptoms**	
				suddenly scared for no reason	1
				feeling fearful	2
				faintness, dizziness or weakness	3
				nervousness or shakiness inside	4
				heart pounding or racing	5
				trembling	6
				feeling tense or keyed up	7
				headaches	8
				spells of terror or panic	9
				feeling restless, can't sit still	10
				Part 2 **Depression symptoms**	
				feeling low in energy, slowed down	11
				blaming yourself for things	12
				crying easily	13
				loss of sexual interest or pleasure	14
				poor appetite	15
				difficulty falling asleep, staying asleep	16
				feeling hopeless about the future	17
				feeling blue	18
				feeling lonely	19
				thoughts of ending your life	20
				feeling of being trapped or caught	21
				worrying too much about things	22
				feeling no interest in things	23
				feeling everything is an effort	24
				feelings of worthlessness	25

Source: (Derogatis *et al.* 1974)

APBQ-MALES

Please answer the following questions by picking the number, which best describes what you believe are appropriate/inappropriate ways for **MALES** to express/respond to pain.

(Please Note - Try and focus your responses on what you think is appropriate/acceptable behaviour for **MALES** experiencing pain **IN THE PRESENCE OF OTHERS** - not what you would normally do when you are in pain.)

1 3 5 7
Strongly disagree Strongly agree

1 It is acceptable for men to cry when in pain _____

2It is okay for men to communicate their pain to others _____

3. It is all right for men to frown when in pain _____

4. I feel sympathy towards men who are displaying pain _____

5. It is unacceptable for men to tell others about their pain* _____

6. I believe men should keep pain private* _____

7. It is all right for men to groan when in pain _____

8. It is appropriate for men to ignore their pain* _____

9. I regard it a sign of weakness for men to show pain* _____

10. It is okay for men to complain when in pain _____

11. It is acceptable for men to complain when in pain _____

12. It is appropriate for men to lie down when in pain _____

13. It is unacceptable for men to bend over/clutch at the area in pain* _____

14. Men should be able to tolerate pain in most circumstances* _____

APBQ-FEMALES

Please answer the following questions by picking the number, which best describes what you believe are appropriate/inappropriate ways for **FEMALES** to express/respond to pain.

(Please Note - Try and focus your responses on what you think is appropriate/acceptable behaviour for **FEMALES** experiencing pain **IN THE PRESENCE OF OTHERS** - not what you would normally do when you are in pain.)

1	3	5	7
Strongly disagree			Strongly agree

1. It is acceptable for women to cry when in pain _____
2. It is okay for women to communicate their pain to others _____
3. It is all right for women to frown when in pain _____
4. I feel sympathy towards women who are displaying pain _____
5. It is unacceptable for women to tell others about their pain* _____
6. I believe women should keep pain private* _____
7. It is all right for women to groan when in pain _____
8. It is appropriate for women to ignore their pain* _____
9. I regard it a sign of weakness for women to show pain* _____
10. It is okay for women to complain when in pain _____
11. It is acceptable for women to complain when in pain _____
12. It is appropriate for women to lie down when in pain _____
13. It is unacceptable for women to bend over/clutch at the area in pain* _____
14. Women should be able to tolerate pain in most circumstances* _____

Pain Catastrophizing Scale (PCS)

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.
We are interested in the types of thoughts and feeling that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

Source: (Sullivan *et al.* 1995)

APPENDIX 13

Cold pressor test

Tolerance (s): _____

VAS

No pain _____ The worst pain imaginable

Pressure-pain test

Tolerance (s): _____

VAS

No pain _____ The worst pain imaginable