Third molar surgery outcomes: a comparison between submucosal and intravenous dexamethasone

By
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Abstract

Objective
To compare the efficacy of submucosal (SM) dexamethasone and intravenous (IV) dexamethasone in reducing postoperative facial swelling, pain and trismus after third molar surgery, and its impact on quality of life.

Methods
The study was designed as a randomised, controlled, observer-, surgeon- and participant-blinded single-centre equivalence trial with two parallel groups. There were 61 participants in the IV group and 64 participants in the SM group. The IV group received 2ml intravenous saline and 8mg/2ml submucosal dexamethasone. The SM group received 8mg/2ml intravenous dexamethasone and 2 ml saline submucosal injection. Facial swelling was measured using a contactless stereophotogrammetry 3-dimensional facial camera (3dMD Inc, Atlanta, GA). These images were superimposed and analysed to calculate the volumetric difference in facial swelling. Pain was measured using a 100mm visual analogue scale (VAS). Maximum incisal distances were measured using a linear calliper. All measurements were taken immediately before the surgery and on postoperative days 2 and 7. Data were collected from participants by means of self-reported questionnaires. This study used the oral health impact profile (OHIP)-14 and a third-molar-specific oral-health-related quality of life (OHRQoL) instrument to assess changes to quality of life. Demographic and clinical characteristics of the participants were cross-tabulated and analysed by analysis of variance (ANOVA) or Pearson Chi-Square, as appropriate. P values of <0.05 were considered statistically significant.

Results
On day 2, the IV and SM group had a mean facial swelling of 7.3 cm³ and 7.8 cm³, respectively. On day 7, the swelling had reduced to 2.9 cm³ in the IV group, and 2.6 cm³ in the SM group. Mean pain scores did not differ between treatment groups on either postoperative days. Trismus was most severe on postoperative day 2 in both groups. The amount of trismus observed at both postoperative follow-up time points was similar between the groups. There were no statistically significant differences between the two
groups. Both groups experienced poorer quality of life following third molar surgery. The degree of impact on quality of life was comparable between the treatment groups.

Conclusions
There are no differences in postoperative adverse outcomes between submucosal and intravenous administration of dexamethasone in third molar surgery. Submucosal dexamethasone is a straightforward, accessible and viable route of delivery of steroid administration in patients who choose to have third molar surgery under local anaesthesia only.
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<tbody>
<tr>
<td>3D</td>
<td>Three-dimensional</td>
</tr>
<tr>
<td>BPI</td>
<td>Brief pain inventory</td>
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<tr>
<td>GA</td>
<td>General anaesthesia</td>
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<tr>
<td>IDAF</td>
<td>Index of dental anxiety and fear</td>
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<tr>
<td>IL</td>
<td>Interleukins</td>
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<tr>
<td>IM</td>
<td>Intramuscular</td>
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<td>INF</td>
<td>Interferon</td>
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<tr>
<td>IV</td>
<td>Intravenous</td>
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<tr>
<td>LA</td>
<td>Local anaesthesia</td>
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<tr>
<td>LLLT</td>
<td>Lower-level laser therapy</td>
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<td>MAPS</td>
<td>Multidimensional affect and pain survey</td>
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<tr>
<td>MPQ</td>
<td>McGill pain questionnaire</td>
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<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<tr>
<td>mRNA</td>
<td>Messenger ribonucleic acid</td>
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<tr>
<td>NRS</td>
<td>Numerical rating scale</td>
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<tr>
<td>NSAIDs</td>
<td>Non-steroidal anti-inflammatory drugs</td>
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<tr>
<td>ODSS</td>
<td>Oral diagnostic and surgical sciences</td>
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<tr>
<td>OHIP</td>
<td>Oral health impact profile</td>
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<tr>
<td>OHRQoL</td>
<td>Oral health-related quality of life</td>
</tr>
<tr>
<td>PANAS</td>
<td>Positive and negative affect schedule</td>
</tr>
<tr>
<td>PO</td>
<td>Orally</td>
</tr>
<tr>
<td>QID</td>
<td>Four times daily</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised control trial</td>
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<tr>
<td>SD</td>
<td>Standard deviation</td>
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<td>Abbreviation</td>
<td>Description</td>
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<td>----------------------------------</td>
</tr>
<tr>
<td>SES</td>
<td>Socio-economic status</td>
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<td>SM</td>
<td>Submucosal</td>
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<td>TGF</td>
<td>Transforming growth factor</td>
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<td>VAS</td>
<td>Visual analogue scale</td>
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<td>VRS</td>
<td>Verbal rating scale</td>
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1 Introduction

The mandibular third molar is the most commonly impacted tooth, with the reported prevalence of impaction in the general population to be from 18 to 60% (Kruger et al. 2001; Quek et al. 2003; Kramer and Williams 2005). An impacted third molar may remain asymptomatic and disease-free for the lifetime of a person; however, it may partially erupt into the mouth between 17 to 25 years of age and cause a range of symptoms that eventually motivate patients to seek advice or intervention from a dental professional. Common symptoms from a partially erupted, impacted third molar include pericoronitis, dental caries, periodontal loss of attachment, facial pain, food trapping and/or the presence of pathological lesions. The removal of third molars is one of the most commonly performed surgical intervention in dentistry (Moraschini et al. 2016; Chen et al. 2017). Third molars may also be removed for orthodontic purposes including orthognathic surgery, in preparation for military service or prior to travel to remote areas (NICE 2000; Marciani 2007; Steed 2014; Hyam 2018).

The surgical removal of mandibular third molars can involve reflection of a full thickness mucoperiosteal flap, removal of bone and sectioning of the tooth. This results in some degree of surgical trauma to the surrounding soft and hard tissues. Consequently, the common sequelae of third molar surgery include swelling, pain, trismus, bleeding, bruising and/or infection, culminating in 11 million patient-days of postoperative outcomes annually in the United States of America (Friedman 2007). Patients universally report pain in the mouth, difficulty eating their normal diet and an interruption of their usual daily routine after third molar surgery. This has a direct negative impact on their quality of life in the days immediately following surgery (Savin and Ogden 1997; McGrath et al. 2003; Deepti et al. 2009; Sato et al. 2009). For the patient who is undergoing ambulatory, elective third molar surgery, the recovery process and how it affects quality of life is said to be just as important to them as wound healing is to the surgeon (White et al. 2003; Shugars et al. 2006). Accordingly, there has been a concerted effort by clinicians and researchers alike to reduce the postsurgical sequelae after third molar surgery.
The use of dexamethasone has been shown to reduce adverse postoperative outcomes of swelling, pain and trismus (Alexander and Thordson 2000; Markiewicz et al. 2008; Dan et al. 2010). In the clinical setting where intravenous (IV) sedation or general anaesthesia is used, the conventional route for dexamethasone delivery is through the intravenous line. However, insertion of an intravenous line requires additional clinical skills. The administration of IV dexamethasone may not be pleasant for the awake patient because it has been linked to the sudden onset of perineal irritation (itch, burn or squeezing sensation) that lasts between 30 seconds to 4 minutes (Neff et al. 2002). Accordingly, IV dexamethasone may not be a popular choice for either the clinician or patient. As an alternative, submucosal injection is claimed to be an effective, convenient and straightforward way of administering dexamethasone (Grossi et al. 2007; Nair et al. 2013; Rana et al. 2013; Moraschini et al. 2016; Mojsa et al. 2017). Since the surgical site would already be anaesthetized for surgery, submucosal dexamethasone could be administered in a painless and expedient manner. There is however, a lack of robust and well-designed randomised clinical trials comparing submucosal and intravenous dexamethasone in the reduction of adverse postoperative outcomes after third molar surgery.

Accordingly, the question arises as to how submucosal and intravenous dexamethasone compare in their efficacy in reducing swelling, pain and trismus following third molar surgery. Such a comparison would have important clinical implications and might lead to procedural changes in third molar surgery.
2 Literature Review

The following sections will review the current understanding of postoperative swelling, pain and trismus by outlining its definition, physiology, prevention and management. Next, the impact of third molar surgery on patient’s quality of life will be explored. Finally, an overview of glucocorticosteroids and their use in oral surgery will be presented prior to undertaking a critical appraisal of the literature.

2.1 Third molar surgery outcomes

Pain, swelling and trismus are common and expected postoperative outcomes of mandibular third molar surgery. They are typically transient and benign in nature (Lopes et al. 1995; Kim et al. 2006; Markiewicz et al. 2008). They are to be distinguished from the more serious surgical complications, which include infection spread, severe haemorrhage, mandibular fracture, damage to the inferior alveolar nerve, or displacement of teeth into adjacent anatomical spaces (Bui et al. 2003; Bouloux et al. 2007). This thesis will focus on the common sequelae of swelling, pain and trismus and so, other complications will not be discussed in further detail.

2.1.1 Swelling

2.1.1.1 Definition of swelling

Swelling can be defined as ‘an abnormal palpable enlargement produced by expansion of the interstitial fluid volume’ (Sterns 2018). Both swelling and pain are familiar cardinal signs of inflammation (which also includes redness, heat and loss of function), and inflammation of appropriate intensity and duration is part of a normal physiological response to injury (for example, raising a soft tissue flap and removing bone).

Patients with deeply impacted teeth were shown to have more facial swelling after third molar surgery than patients with a more superficial impaction. Patients who underwent a longer operation ($\geq$ 10 minutes) were also shown to have more swelling than patients who had a shorter operation time (Kim et al. 2006). Age is also an important variable: patients over 30 years of age had greater swelling than younger ones (Yuasa and Sugiura 2004; Kim et al. 2006; Aznar-Arasa et al. 2014).
2.1.1.2 Prevention and management of swelling

The onset of oedema is gradual and usually peaks 48-72 hours after surgery (Alexander and Thondson 2000; Darawade et al. 2014). The eicosanoid synthesis process (outlined below in section 2.2.1) suggests the use of anti-inflammatory therapy to target specific pathways to reduce oedema and pain. A commonly used therapy includes non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, which inhibit cyclo-oxygenase and thus inhibit prostaglandin synthesis. Another potent anti-inflammatory agent is the group of drugs known as glucocorticoids. These act by down-regulating the production of specific proinflammatory genes and up-regulating that of anti-inflammatory proteins. The action of glucocorticoids and their role in reducing postoperative oedema is the main subject of interest in this study, and so it will be discussed in greater detail in Chapter 2.2.

Non-pharmacological interventions aimed at reducing postoperative swelling and pain include manual lymph drainage, soft laser, and cryotherapy (Szolnoky et al. 2007; Sortino and Cicciù 2011; Zandi et al. 2016). Cryotherapy includes various cooling procedures such as ice packs, ice massage, frozen gel packs, ice chips in a plastic bag, and application of cold compresses, including a water-circulating cooling technique called hilotherapy (Rana et al. 2011). Several authors of clinical trials have concluded that the use of ice is efficient in reducing postoperative facial swelling and pain (Filho et al. 2005; Forouzanfar et al. 2008; Rana et al. 2011; Ibikunle and Adeyemo 2016). By contrast, a very recent systematic review by Nascimento-Júnior et al. (2019) suggested that while there was small to moderate decrease in pain intensity after third molar surgery, there was no evidence that cryotherapy was effective in reducing facial swelling and trismus. This may in part be the result of a concurrent use of NSAIDs in the included clinical trials, the lack of blinding and the lack of standardization of the mode, frequency and duration of application. Overall, the state of science on cryotherapy is not settled and further high-quality randomised clinical trials need to be conducted to establish an evidence-based treatment protocol for cryotherapy after third molar surgery.

The use of low-level laser therapy (LLLT) to reduce swelling is a novel technique that has been explored in recent years. It is postulated that LLLT promotes an increase in
lymphatic drainage and a decrease in the permeability of blood vessels, and this results in a reduction in swelling. Emerging small clinical trials suggest that LLLT is effective at reducing postoperative pain, swelling and trismus although it is not yet established whether this reduction is clinically significant (Amarillas-Escobar et al. 2010; Sierra et al. 2015; Landucci et al. 2016).

Another technique shown to reduce postoperative swelling is to place a small surgical tube drain with primary closure at the buccal fold between the first and second mandibular molars (Rakprasitkul and Pairuchvej 1997; Saglam 2003; Handa et al. 2016). In these three studies, the participants in the control group had primary closure with no drain after the surgical removal of impacted third molars. The surgical tube was removed from patients in the intervention group 72 hours after surgery. It is accepted that there is a greater degree of swelling and haematoma formation at the primary closure sites (Dubois et al. 1982). Hence, caution should be exercised when interpreting the findings from the above studies because the apparent reduction of swelling in the intervention groups (drain in situ) may be exaggerated from the presence of greater swelling in the control group. Patient acceptance and comfort were also not reported from these studies.

2.1.1.3 Measuring swelling

Anthropometry is the biological science of measuring the size, weight and proportions of the human body (Lübbers et al. 2010). Craniofacial anthropometry is performed by measuring distances between landmarks defined on surfaces of the head, face and ears. Methods used for measurement of facial swelling include cast techniques, laser-scanning, callipers, tape measurement, face-bow, impression trays, ultrasonography, photogrammetry, modified face bow or cephalostat (Esen et al. 1999; John et al. 2011).

In the context of measuring facial swelling after third molar surgery, the method employed by known published clinical studies have so far been based solely on various soft tissue landmarks measured directly on the patient’s face (Chen et al. 2017). It must be recognized that facial swelling has historically been difficult to quantify accurately because it requires measurement of an irregular, convex and compressible surface in three dimensions. These “direct” methods are repeatable, convenient and inexpensive,
but there are several limitations and drawbacks (Schultze-Mosgau et al. 1995; Aldridge et al. 2005; Wong et al. 2008). Each measurement must be taken individually, requiring physical contact with the participant over a period of several minutes; the participant must remain still over the duration of measurement; there is no opportunity to achieve volumetric measurements in three dimensional space; and the soft tissue can be readily displaced or deformed when in direct contact with the participant, resulting in a source of error in direct measurement.

To address the limitations of the two-dimensional imaging systems, several types of three-dimensional camera systems and analysis software have emerged to capture the soft tissue surface of the face with correct geometry and texture information. Such cameras have already been used extensively in research, focusing on the assessment of soft tissue changes and postoperative swelling following orthognathic surgery (Kau et al. 2006; Kau et al. 2007). Facial cameras have evolved to offer the considerable advantages of obtaining fast, accurate and contactless scans in three dimensions. A system known as the 3dMD.trio system (3dMD Inc, Atlanta, GA) has been established and widely used in the medical setting. The 3dMD system is based on a combination of stereophotogrammetry and structured light patterns projected on the face. Different cameras from multiple angles capture depth information of the points in a participant. A computer program then gives the location of these points on the x, y and z axes. These axes form an object referred to as the “point cloud”. When the point clouds are combined, a wire cage-like view called a “wireframe” is obtained. The surface texture is obtained by combining a colour photograph with the aforementioned wireframe to provide a digital 3D reconstructed image of the face (Alan et al. 2016).

There are numerous advantages of using an indirect anthropometry method. First, it provides a near-instantaneous capture of data. Once the participant is seated and positioned appropriately, the photograph is taken within 0.2 seconds. This greatly reduces the potential for large motion errors. Second, acquiring the 3dMD images is completely non-invasive. Third, the images may be viewed immediately to determine their accuracy and whether further imaging is required. Fourth, the image data are easily stored and archived securely. Finally, the researcher may return to the digital images at any time to check for errors, or to collect supplementary data such as additional landmarks, surface areas, volumes, curves or any other quantitative measures (Aldridge
et al. 2005). Software tools are available that allow the user to rotate or magnify the image to facilitate the identification of landmarks, a process which can be cumbersome in direct anthropometry. Moreover, linear distances and angles can be measured directly on the images, and these measurements can be repeated without inconveniencing the patient. The disadvantages of the 3dMD system are its higher cost and its limited availability (although a unit exists within the Faculty of Dentistry at the University of Otago). Other disadvantages include difficulties in imaging shiny or shadowed surfaces, the inability to measure bony or intra-oral landmarks, and the lack of an established database of normal values for such images in third molar surgery.

A clear limitation common to both 3dMD stereophotography and traditional direct measurement is that the true volume of swelling cannot be assessed because swelling occurs both inwards and outwards in the mouth. Measurements of the external surface (like that in direct and indirect methods) is limited to swelling that presents outwards in the mouth, hence using these methods will inevitably lead to some degree of underestimation of the true volume of swelling. If true changes in volume are to be assessed, a transmissive technology such as magnetic resonance imaging (MRI) should be used. However, many factors including availability and research costs precluded the use of MRI in this study.

Despite the limitation highlighted above, the precision and accuracy of the 3dMD system are more than sufficient for clinical needs and are comparable to (or greater than) those of direct anthropometry and two-dimensional photography (Weinberg et al. 2006; Wong et al. 2008; Lübbers et al. 2010). Lübbers et al. (2010) looked specifically at the precision (repeatability and reproducibility) and accuracy of the 3dMD system. They found that data acquisition and data analysis were very reliable, with a mean global error of 0.2 mm (range 0.1-0.5 mm) for mannequin head measurements. These values align with those from another proof-of-concept study by Brüllman et al. (2014). In this study, twenty participants positioned a defined volume of water (10-30ml, carried in a water balloon) at the buccal corridor, in order to produce an artificial simulated facial swelling. A structured light scanner then photographed participants. The mean difference between applied and measured volume was 0.67 mL. Hence the average error associated with the placement of landmarks is at the sub-millimetre level. The error due to digitalization and that due to the imaging system are very low. The
system is a valid and reliable tool in the measurement of 3D craniofacial anthropometric characteristics (Aldridge et al. 2005).

2.1.2 Pain

2.1.2.1 Definition of pain

Pain (nociception) may be defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (ISAP, 2018). As a symptom, it must be measured by asking the patient.

2.1.2.2 Prevention and management of pain

Preventive analgesia is a treatment that is commenced before the surgery in order to reduce the physiological consequences of nociceptive transmission induced by the procedure (Kissin 2000). It is hypothesized that this would allow patients to prevent the pain, rather than to treat the pain after pain pathways are already established. This theory was popularized in the management of pain after thoracic, abdominal and orthopaedic surgery (Karaman et al. 2008; Coughlin et al. 2010; Nesioonpour et al. 2013). There is still debate in the literature as to whether preventive analgesia is an effective means of pain management after third molar surgery. Reviews by Dahl & Kehlet (2011) and Dahl & Møiniche (2004) suggest that there may be some benefit of this attractive working hypothesis; however, the evidence for it is inconclusive. On the other hand, various clinical trials and literature reviews conducted over the years have found no benefit of preventive analgesia in managing pain after third molar surgery (Zacharias et al. 1996; Yong and Coulthard 2010; Al-Sukhun et al. 2012; Jacob Liporaci Junior 2012; Yamaguchi and Sano 2013). There is a need for further well-designed, well-conducted clinical trials to establish the role of preventive analgesia in the management of pain.

Pharmacological interventions are the mainstay of acute pain management after third molar surgery. The medications used include the likes of acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs, such as ibuprofen, diclofenac, aspirin, cox-2 inhibitors, naproxen), opioids (such as codeine, dihydrocodeine, tramadol), and corticosteroids used as single agents or in various combinations. A 2004 Cochrane
review of studies involving over 2200 participants found high quality evidence for 200-512 mg of ibuprofen being superior to 600-1000 mg of paracetamol. It also found that paracetamol and ibuprofen have a synergistic effect in providing superior pain relief to a single drug regime (Bailey et al. 2013). This finding was consistent with findings from a meta-analysis of acute pain trials by Moore et al. (2011) and another comprehensive review by Derry et al. (2011). Opioids alone have poor analgesic effects in managing acute inflammatory pain (Moore et al. 2000; Derry et al. 2010), yet the addition of opiates (such as codeine) to paracetamol and a NSAID is common practice. However, a recent double-blind, randomized control trial found that the addition of codeine to paracetamol and ibuprofen did not result in better postoperative pain control (Best et al. 2017). Derry et al. (2011) reviewed 38 different analgesic drugs and drug combinations and found that no single drug is effective in all patients. This finding could be explained by the multi-dimensional and subjective nature of pain. The choice of analgesic in contemporary practice appears to be largely based on the treating clinician and patient preferences.

2.1.2.3 Measuring pain

Pain is a multifaceted and highly subjective experience that makes it challenging to measure. Presently, there is no valid or reliable way to objectively quantify an individual’s experience of pain. Nonetheless, there are a number of validated and sensitive tools for collecting useable pain estimate. In general, there are two broad categories of pain measurement tools; that is, there are unidimensional and multidimensional approaches. Unidimensional tools include the visual analogue scale (VAS), verbal rating scale (VRS) and numerical rating scale (NRS). Multidimensional tools include the likes of the McGill Pain Questionnaire (MPQ), brief pain inventory (BPI), and the multidimensional affect and pain survey (MAPS), to name a few (Younger et al. 2009). In the acute outpatient setting such as that in the present study, multidimensional forms are generally too time-consuming for repeated use, and a unidimensional scale (such as the VAS) is sufficient to give adequate information about patients’ pain (Correll 2007).

In measuring acute pain, the VAS is considered the gold standard approach (Bendinger and Plunkett 2016). It consists of a 100 mm unmarked line with standardized wording
‘no pain’ on the left end of the line and ‘worst pain imaginable’ on the right. The patient then places a mark on the line corresponding to their level of pain. The advantage of using the VAS is that it is a high-sensitivity, single-item measure that is simple, quick to administer and easily understood by patients. The main disadvantage is that it assigns a single value to what is a multi-dimensional, complex experience. Patients may find it difficult to choose a single digit to represent their pain sensation. Another criticism of the VAS approach is that it is limited to providing a pain rating at that particular point in time without the patient reflecting the possible fluctuations in pain levels throughout the day. There is also a ceiling effect in that, if the highest value was previously chosen, and the pain worsens, the patient is unable to communicate this worsening (Correll 2007; Younger et al. 2009; Bendinger and Plunkett 2016).

Alternatives to the VAS are the verbal rating scale (VRS) and the numerical rating scale (NRS). The VRS consists of the four ordinal descriptors no pain, mild pain, moderate pain and severe pain. It is useful when patients are unable to translate their pain experience into a numerical value but instead prefer to use verbal descriptors. The NRS is similar to the VAS in that it is bounded at the left-most end with “no pain” and at the right-most end with “worst pain imaginable”. The difference with the NRS is that, instead of a line without marks, numbers from 0 to 10 are evenly spaced across the line and patients are asked to circle the number that represents the amount of pain experienced at the time of evaluation. While the VRS and NRS are both validated, they have the same limitations as the VAS, as well as being less precise and sensitive than the VAS (Jensen et al. 1986; Bendinger and Plunkett 2016).

2.1.3 Trismus

2.1.3.1 Definition

Trismus can be defined as “a motor disturbance of the trigeminal nerve, especially spasm of the masticatory muscles, with difficulty in opening the mouth.” (Dorland’s Illustrated Medical Dictionary).
2.1.3.2 Prevention and management of trismus

Trismus after third molar surgery is usually caused by inflammation and spasm of the masticator muscles secondary to a full thickness mucoperiosteal flap having been raised. There has been a keen interest in comparing different flap designs and their effect on postoperative trismus. Baqain et al. (2012) compared envelope and triangular flap designs and found that triangular flaps were associated with greater trismus. This was likely the result of more periosteum being stripped for the anterior release of the triangular flap design. This is in contrast to the findings of three separate studies where there was no significant difference in postoperative trismus between the envelope flap and modified triangular flap design (Kirk et al. 2007; Erdogan et al. 2011; Koyuncu and Çetingül 2013).

A 2-year prospective study by Grossi et al. (2007) identified many risk factors for severe trismus following third molar surgery. Female gender, smoking, greater depth of impaction and older age were predictors of severe trismus. The two operative variables that predicted severe trismus were greater amount of bone removal and operator inexperience.

2.1.3.3 Measuring trismus

Measuring maximal inter-incisal opening (MIO) is the ubiquitous tool used in clinical trials assessing trismus (Van Gool et al. 1977; Garcia et al. 1997; Zandi et al. 2016; Balakrishnan et al. 2017). It involves measuring the differences in mouth opening (inter-incisal distance with the incisal edges of teeth as anatomical landmarks) using a rigid ruler or calliper. It is a simple and reproducible chairside method.

2.1.4 Impact of Third Molar Surgery on Quality of Life

It is well-established that lower third molar surgery affects patients’ quality of life, particularly during the first three to five days after surgery (Savin and Ogden 1997; McGrath et al. 2003; White et al. 2003; Colorado-Bonnin et al. 2006; Deepti et al. 2009). It would be prudent for the surgeon to inform patients of the risks and benefits of third molar surgery, expected outcomes and how their quality of life may be impacted during the recovery process.
Patients may experience social isolation, eating difficulties, diet variations, speaking difficulties, sleep impairment and change in physical appearance. In the early postoperative period in a study from Sato et al. (2009), patients’ main complaints were related to swelling, whereas their late postoperative period complaints were related to bad taste/breath, which was experienced by almost half of patients, even on the 7th postoperative day.

Facial swelling is one of the more common postoperative outcomes, occurring in almost half of patients, with 29% of patients “being self-conscious” and 22% of patients feeling “embarrassed” (McGrath et al. 2003; White et al. 2003; Shugars et al. 2006; Sato et al. 2009). Patients with facial swelling experienced a greater reduction in oral health related quality of life than to those without signs of swelling (McGrath et al. 2003). Patients who were self-conscious about the swelling found themselves limiting social interaction, taking days off work and experiencing an overall decreased quality of life. Patients who had more postoperative swelling also generally reported a higher degree of pain and trismus (Conrad et al. 1999; Shugars et al. 2006; Majid and Mahmood 2013).

Patients universally reported their worst pain on postoperative days 1 and 2 (Savin and Ogden 1997; Conrad et al. 1999; White et al. 2003; Colorado-Bonnin et al. 2006; Kim et al. 2006; Sato et al. 2009). Risk factors for pain exacerbation were older age and the female gender. It was suggested that older patients have greater bone density and hence may require longer surgical time (Farish and Bouloux 2007; Akadiri and Obiechina 2009). Women appear to experience more intense postoperative pain and required a longer recovery period (Conrad et al. 1999; Colorado-Bonnin et al. 2006; Sato et al. 2009). The nature of the association between surgical difficulty, surgical duration and pain experience remains controversial. A Brazilian cohort study of 128 patients showed that there was no association between surgical difficulty or surgical duration and average daily pain or peak of pain (Sato et al., 2009). This finding differs from those of several other reports of a positive association between surgical duration and postoperative pain (de Boer et al. 1995; Yuasa and Sugiura 2004; Kim et al. 2006). Thus, the nature of that association remains unclear.
Mouth opening and chewing were the activities affected the most (66%-85%) after third molar surgery (Shugars et al. 1996; Savin and Ogden 1997; Colorado-Bonnin et al. 2006; Sato et al. 2009). Restricted mouth opening may cause difficulties with many aspects of daily living, including speech, eating, and maintaining proper oral hygiene, thereby affecting the patient’s quality of life. The average number of days of eating difficulties reported ranges from 4 to 6 days (Conrad et al. 1999; Colorado-Bonnin et al. 2006). Contrary to this, aspects of life and activities that were less affected were social life, work/study and sleeping (Sato et al., 2009). Most patients took an average of 3 days off work following third molar surgery (Van Gool et al. 1977; Lopes et al. 1995; Berge 1997). Conrad et al. evaluated 249 patients for a total of 14 days in a prospective study and found that bruising was minimally evident to patients in the recovery period (Conrad et al. 1999).

2.1.4.1 Measuring oral health related quality of life (OHRQOL)

The Oral Health Impact Profile (OHIP)-14 is a short-form instrument that measures how different oral health conditions affect quality of life (Slade 1997). It is based on Locker’s conceptual model of oral health which includes seven specific mains of quality of life: functional limitation, pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap (Locker 1988). The OHIP-14 has good reliability and validity, and it has been used extensively in population research and intervention-type clinical trials (Locker et al. 2001; Locker and Allen 2002; Robinson et al. 2003).

Shugars et al. (1996) designed and validated a more targeted, condition-specific instrument that is directed at measuring oral health-related quality of life (OHRQoL) after third molar surgery. It requires patients to fill in a daily questionnaire for 7 days, designed and validated on the assumption that the recovery period after third molar surgery is considered to be short for most patients (Shugars et al. 2006). The instrument assesses the 5 key areas of pain, lifestyle, oral function, and early and late onset symptoms. Pain was measured in a 7-point Likert-type scale, with anchors of “No pain” on the far left and “Worst pain imaginable” on the far right. Oral function dealt specifically with mouth opening, chewing and talking. Questions relating to lifestyle targeted the ability to participate in routine daily activities, recreation, sleeping and
social interaction. Other measured symptoms specific to third molar surgery included bleeding, bruising, swelling, food collection in surgical sites, the presence of bad taste or breath and nausea (Shugars et al. 2006).

While overlaps exist for some outcomes, the OHIP-14 and the third-molar-surgery-specific OHRQoL instrument are complementary tools to measure quality of life outcomes (Shugars et al. 2006). The OHIP-14 and third-molar-surgery-specific OHRQoL instrument assess distinctly different outcomes, adding information that cannot be obtained by one instrument alone (White et al. 2003; Shugars et al. 2006). The third-molar-surgery-specific OHRQoL instrument does not address 3 dimensions that are covered by OHIP-14 – psychological discomfort, psychological disability and social disability. The OHIP-14 can add to understanding of recovery after third molar surgery beyond that provided by the OHRQoL instrument.

Adults who are highly dentally anxious, have negative affectivity and/or have depressive symptoms generally report poorer OHRQoL (Kressin et al. 2001). Personality characteristics appear to influence self-reports of oral health (Thomson et al. 2011). Hence, a measure of a patient’s dental anxiety and positive and negative affectivity is useful when it comes to interpreting self-reports of oral health. There is an emerging body of literature specifically exploring patients’ dental anxiety, psychosocial and personality characteristics and their influence on postoperative swelling, pain, recovery and quality of life after surgery. Muglali and Komerik (2008) showed that anxious patients had higher expected levels of pain and perceived more severe and longer duration of pain during the postoperative period. Postoperative swelling, pain and difficulty in eating were specific conditions and situations that added to patient’s anxiety. Kim et al. (2010) and Aznar-Arasa et al. (2014) found that third molar surgery was substantially more difficult in anxious patients, and concluded that anxiety levels negatively affected postoperative pain and satisfaction.

2.2 The Use of Glucocorticosteroids in Oral Surgery

There is a wealth of published literature on the effect of corticosteroids on the postoperative sequelae of third molar surgical removal. Alexander & Thondson (2000) reviewed articles published in the last 30 years on the topic of corticosteroid use
specifically for reducing postoperative swelling. Patients who receive corticosteroids experience less postoperative swelling than patients who are not given them (Skjelbred and Løkken 1982; Schaberg et al. 1984; Pedersen 1985a; Milles and Desjardins 1993; Schmelzeisen and Frolich 1993; Herrera-Briones et al. 2013). This is consistent with the findings of a systematic review and meta-analysis on corticosteroid administration in oral surgery which concluded that all trials barring one (of a total of 12 RCTs) showed significantly less swelling (Dan et al. 2010).

Corticosteroids have some inhibitory effects on prostaglandins, but steroids alone do not appear to have a clinically significant analgesic effect (Milles and Desjardins 1993; Alexander and Thronson 2000; Elangovan 2014). A systematic review and meta-analysis of 12 trials revealed no significant difference in average pain levels between patients with or without corticosteroid exposure (Markiewicz et al. 2008). Patients may also experience a mild euphoric or mood altering effect from steroids (Czock et al. 2005; Becker 2013). Given that pain is a multi-dimensional and subjective experience, steroids may also therefore help patients cope better with their postoperative sequelae.

In a study by Markiewicz et al. (2008), mouth opening differences were impressive: patients in the corticosteroid group were able to open their jaws a mean of 4.1 mm more than the control group during the early postoperative period (days 1 to 3), and 2.7 mm more than the controls during the late postoperative period (days 4 to 7). These findings are echoed by a literature review by Herrera-Briones et al. (2013) which included 28 studies (1 meta-analysis and 27 RCTs). It must be acknowledged, though, that there was a lot of variation in the type of corticosteroid used, dosage, timing and route of administration in the clinical trials that were evaluated.

The next section will give an overview of the body’s inflammatory response to injury and how corticosteroids can help to reduce swelling, pain and trismus.

2.2.1 Inflammation as a response to injury and the action of glucocorticoids

Swelling and pain are two of the commonly observed cardinal signs of inflammation (which also include redness, heat and loss of function) and inflammation of appropriate intensity and duration is part of a normal physiological response to injury (Becker
The effects of surgery on tissues can be considered to be controlled trauma inflicted with therapeutic intent.

Prostaglandins are important mediators of inflammation. In response to cellular damage, the cell membrane phospholipids release a fatty acid known as arachidonic acid. This response is catalysed by cellular phospholipases, commonly phospholipase A2 (Becker 2010). Arachidonic acid is then broken down into its metabolites (also known as “eicosanoids”) by two major classes of enzymes: cyclo-oxygenases (which produce prostaglandins and thromboxanes) and lipoxygenases (which produce leukotrienes and lipoxins), demonstrated in Figure 1. Dexamethasone blocks phospholipase A2, the enzyme that is involved in the conversion of phospholipids to arachidonic acid. Dexamethasone also acts as a vasoconstrictor and suppresses the synthesis, migration and adhesion of inflammatory cytokines, chemokines (such as IL1, IL2, IL6, IL12, INF-γ) and leucocytes while simultaneously inducing anti-inflammatory cytokines (such as IL-10, TGF-β) and their receptors (Czock et al. 2005). As a combined result of the vasoconstriction, decreased leucocyte migration and a dampened inflammatory process, there will be less fluid in the interstitial space. Clinically, this should present as a smaller area of palpable or observable oedema.

In addition to prostaglandins, the damaged tissues release other important inflammatory chemical mediators (such as cytokines, bradykinin, serotonin and histamine) to stimulate peripheral pain receptors (nociceptors), thereby initiating an action potential in free nerve endings located in the oral mucosa.
Glucocorticoid mechanisms occur via two pathways: genomic and non-genomic mechanisms. Genomic effects of glucocorticoids are characterised by a slow onset (6-8 hours) and slow dissipation due to the time-consuming process of mRNA transcription and translation. At that cellular level, glucocorticoids work by binding to specific receptors within the cytoplasm of targeted cells. The receptor-steroid complex then migrates into the nucleus and alters the genetic synthesis of proteins such as inflammatory cytokines and chemokines (Czock et al. 2005; Becker 2013). Non-genomic mechanisms exert their effect by physically dissolving into the lipid membrane and modifying its physicochemical properties. This may account for the rapid onset of effect (less than 15 minutes), since no time is spent on gene transcription and translation (Czock et al. 2005). This rapid onset is useful when corticosteroid administration is required in emergency situations such as severe anaphylaxis or Addisonian crisis.
2.2.2 Dexamethasone

Dexamethasone is a synthetic adrenocorticosteroid that belongs to the glucocorticoid group of drugs. Glucocorticoids have pleotropic effect and are used widely for purposes such as reducing postoperative swelling, postoperative nausea and vomiting, antirejection therapy in organ transplant patients and dampening down of an over-active immune system in patients with autoimmune disease, to name a few. Dexamethasone also has adverse effects, such as immunosuppression and hyperglycaemic effects.

Dexamethasone is of particular interest to surgeons because of its potent anti-inflammatory properties and its long biological half-life of 36-54 hours (Montgomery et al. 1990; Dan et al. 2010; Becker 2013). It is favoured over other types of steroids (such as prednisolone or hydrocortisone) because it has a favourable profile of virtually no mineralocorticoid (water and salt retention) side-effects, which typically include hypertension, hypokalaemia and metabolic alkalosis (Neupert et al. 1992; Alexander and Throntson 2000).

There are several water-soluble injectable formulations of dexamethasone, such as dexamethasone sodium phosphate and dexamethasone sodium metasulfobenzoate. Dexamethasone sodium phosphate is the only formulation that is available in New Zealand. Hence, all further discussion of dexamethasone will pertain to dexamethasone sodium phosphate only.

2.2.2.1 Dexamethasone and infection risk

Because dexamethasone is a potent glucocorticosteroid, it theoretically also has immunosuppressive and hyperglycaemic effects. It is possible that these actions may increase the risk of postoperative infections, particularly in patients who have diabetes mellitus or who are immunosuppressed. Currently there is a multi-centre, prospective, double blind study investigating the impact of perioperative dexamethasone exposure on surgical site infection. The findings will be stratified according to diabetes status (“Perioperative Administration of Dexamethasone and Infection Trial,” https://www.paddi.org.au/). At the time of writing, the results are not yet available.
In a recent meta-analysis of corticosteroid administration in oral surgery by Dan, Thygesen and Pinholt (2010) and a systemic review of perioperative corticosteroid use in dentoalveolar surgery by Alexander & Throndson (2000), they concluded that administration of corticosteroids in oral surgery carries no higher risk of infection and there is a minimum risk of other side-effects. This finding is in line with another systematic review and meta-analysis done by Waldron et al. (2013), which included 45 studies involving a total of 5796 patients who received a single intravenous dose of dexamethasone ranging between 1.25 and 20 mg for surgery. There was no higher rate of infection or delayed wound healing with dexamethasone, although blood glucose levels were elevated at the 24-hour mark (Waldron et al. 2013). The principal finding of a study by Tiwana et al. (2005) was that a single IV dose of a glucocorticoid administered just before third molar surgery (with no antibiotics given concurrently) had no detrimental impact on wound healing in patients predicted to be at a higher risk for delayed clinical recovery. The low incidence rate of infection in that study concurs with the consensus in the literature that a single dose of perioperative dexamethasone does not increase the risk of infection after third molar surgery (Alexander and Throndson 2000; Dan et al. 2010; Waldron et al. 2013). The following section will review the pharmacokinetics and pharmacodynamics of dexamethasone.

2.2.2.2 Pharmacology of dexamethasone sodium phosphate

Dexamethasone has a plasma half-life (the time taken for the plasma level to reach 50% of its initial concentration) of 100-300 minutes, and a biologic half-life (the time taken for a measured metabolic activity to decrease to half its initial level) of 36-54 hours (Czock et al. 2005). A small amount of dexamethasone is bound to albumin, but most of it is unbound and is available to act on the site of inflammation. By contrast, more than 90% of hydrocortisone is bound to plasma globulin or albumin, leaving a free fraction of just 10% (Dan et al. 2010). This free fraction determines the biologic activity and explains why dexamethasone has an anti-inflammatory potency 30 times that of hydrocortisone (Table 1). Metabolism of dexamethasone occurs primarily in the liver, and its metabolites are excreted in urine.
Table 1. Anti-inflammatory properties and half-lives of different types of glucocorticoids

<table>
<thead>
<tr>
<th>Type</th>
<th>Anti-inflammatory potency</th>
<th>Plasma half-life (mins)</th>
<th>Biological half-life (hours)</th>
<th>Equivalent dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocortisone</td>
<td>1</td>
<td>90</td>
<td>2-12</td>
<td>20.00</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>5</td>
<td>60-200</td>
<td>18-36</td>
<td>5.00</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>5</td>
<td>180-200</td>
<td>18-36</td>
<td>4.00</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>5</td>
<td>300</td>
<td>18-36</td>
<td>4.00</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>25</td>
<td>100-300</td>
<td>36-54</td>
<td>0.60</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>30</td>
<td>100-300</td>
<td>36-54</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Table adapted from Dan et al. (2010)

Dexamethasone sodium phosphate is a pro-drug that requires conversion to the active metabolite, dexamethasone. Rohdewald et al. (1987) established that there is a conversion factor of 1.3 (e.g. 20 mg of dexamethasone sodium phosphate is equivalent to 15 mg dexamethasone). When dexamethasone phosphate is administered in the intravenous form, peak plasma concentrations are reached within 5 to 10 minutes (Rohdewald et al. 1987). However, the peak plasma concentrations and local concentration of dexamethasone after an oral submucosal injection of dexamethasone remains unclear at present.

A number of studies in other disciplines have attempted to shed light on the pharmacokinetics of locally injected dexamethasone in tissues other than the oral mucosa). A study by Weijtens et al. (1997) investigated dexamethasone levels in human vitreous humour after local injection of 5 mg of dexamethasone sodium phosphate into the peribulbar region of the eye. They found that the average concentration of dexamethasone in serum peaked after 30 minutes at 60 ng/ml, while the concentration of dexamethasone in vitreous humour peaked after 7 hours at 13 ng/ml. Dexamethasone injection provided an anti-inflammatory potency 75 times that of the naturally occurring cortisol (5.1 ng/ml) found in vitreous humour, given that there is 2.5 times more dexamethasone than cortisol in weight per millilitre, and that dexamethasone is 30 times more potent than cortisol. A study by Gao et al. (2015) compared local and intravenous administration of dexamethasone for postoperative pain and recovery after tonsillectomy and found that local infiltration of dexamethasone was more effective than systemic administration in decreasing postoperative oedema and pain. The original
study design had included plans to detect the plasma concentrations of dexamethasone, in order to better evaluate the differences associated with local and systemic pathways. This would have provided valuable information to fill a critical gap in knowledge but there were barriers to achieve this objective because the parents of the paediatric patients were unwilling to authorize collection of peripheral blood for the purposes of the study.

The findings from these two studies provide a reasonable basis for the hypothesis that local administration allows the tissues to be exposed to a high, concentrated dose of dexamethasone without loss due to distribution or the onset of elimination. Dexamethasone may then affect the surgically-injured tissue more directly by decreasing pro-inflammatory mediators and cytokine production. There may also be delayed distribution of dexamethasone into the blood stream, which may then extend the effective time of analgesia in the local tissue. By contrast, a single intravenous injection of dexamethasone may have a wide distribution and its effect at the site of trauma may be less than optimal (Grossi et al. 2007; Herrera-Briones et al. 2013; Vivek et al. 2017).

2.3 Intravenous and submucosal routes of administration

Dexamethasone may be administered intravenously, submucosally, orally, intramuscularly or through an endo-alveolar1 approach. Each route has its advantages and disadvantages. An immeasurable number of clinical trials with different permutations of type of steroid, dosage, timing and route of administration have been performed to compare the efficacy of one regime over the other. Currently, there is no consensus on a universally accepted clinical protocol for the optimal use of glucocorticoids to reduce swelling, pain and trismus (Alexander and Thronson 2000; Markiewicz et al. 2008; Dan et al. 2010; Herrera-Briones et al. 2013). In other words, there has been no conclusive study that shows one route of administration to be superior to another. The choice is largely based on the preferences of the patient and the treating clinician. There are only few studies specifically comparing submucosal dexamethasone with intravenous dexamethasone for third molar removal. This group of studies are of

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1 Placement into the extraction socket
special relevance to the present study and will be examined in depth and critiqued in the following section.

A literature search was undertaken in five article databases: Medline; Cochrane Library; PubMed; EMBASE and Google Scholar. The following keywords and Boolean operators were used:

“wisdom teeth” OR “wisdom tooth” OR “third molar” OR “third molars”

AND

“dexamethasone”

AND

“submucosal”

AND

“intravenous”

The search yielded five intervention studies involving dexamethasone administered using the submucosal or intravenous routes for the amelioration of post-operative adverse outcomes in third molar surgery (Majid and Mahmood 2013; Bhargava et al. 2014; Gopinath et al. 2017; Kumar 2017; Vivek et al. 2017). For clarity, the main characteristics of each of the five studies were tabulated prior to appraisal. It is then explained how the present study differed from them and why it was important to conduct it. All of the studies were conducted in different institutions across India, except for the study by Majid & Mahmood (2013), which was conducted in Iraq.
Table 2. Design characteristics of the five relevant studies

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Randomized</th>
<th>Double Blind</th>
<th>Centre(s)</th>
<th>Operator(s)</th>
<th>Review days</th>
<th>Number of teeth and jaw arch</th>
<th>Age (years)</th>
<th>Measurement of QoL^a</th>
<th>Level of evidence ^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Majid &amp; Mahmood (2013)</td>
<td>Yes</td>
<td>No</td>
<td>Single</td>
<td>Single</td>
<td>Day 1, 3 and 7</td>
<td>Unilateral mandibular impacted third molar</td>
<td>18 and above</td>
<td>Yes</td>
<td>3</td>
</tr>
<tr>
<td>Bhargava et al. (2014)</td>
<td>Yes</td>
<td>Yes</td>
<td>Single</td>
<td>Single</td>
<td>Day 1, 3 and 7</td>
<td>Unilateral mandibular impacted third molar</td>
<td>19 to 30</td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>Gopinath et al. (2017)</td>
<td>Yes</td>
<td>No</td>
<td>Single</td>
<td>Single</td>
<td>Day 2 and 7</td>
<td>Unilateral mandibular impacted third molar</td>
<td>18 and above</td>
<td>No</td>
<td>3</td>
</tr>
<tr>
<td>Kumar (2017)</td>
<td>Yes</td>
<td>Yes</td>
<td>Single</td>
<td>Single</td>
<td>Day 2 and 7</td>
<td>Not specified</td>
<td>18 and above</td>
<td>No</td>
<td>2</td>
</tr>
<tr>
<td>Vivek et al. (2017)</td>
<td>Yes</td>
<td>No</td>
<td>Single</td>
<td>Single</td>
<td>Day 1, 3 and 7</td>
<td>Not specified</td>
<td>18 to 45</td>
<td>No</td>
<td>3</td>
</tr>
</tbody>
</table>

^a Quality of life
^b The Oxford 2011 Levels of Evidence
Table 3. Design characteristics of the five relevant studies

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Impaction type (Gregory and Pell, unless specified)</th>
<th>Flap design</th>
<th>Parallel groups</th>
<th>Total participants</th>
<th>Dexamethasone dosage and routes of administration</th>
<th>Time of delivery</th>
<th>Application of ice</th>
</tr>
</thead>
</table>
| Majid & Mahmood (2013) | Class II and III Positions A, B and C | Ward’s incision | 6 | 72 | Group 1: IV 4 mg  
Group 2: SM 4 mg  
Group 3: IM 4 mg (deltoid muscle)  
Group 4: 4 doses of 1 mg oral tablets every 6 h on first postoperative day  
Group 5: Endoalveolar powder  
Group 6: No steroid | Postoperative | Not specified |
| Bhargava et al. (2014) | Class II Position B | Modified ward’s incision | 6 | 60 | Group 1: 4 mg dexamethasone + 1.8 ml 2% lignocaine 1:200 000 adrenaline  
Group 2: SM 4 mg  
Group 3: IM 4 mg (deltoid muscle)  
Group 4: IV 4 mg  
Group 5: PO 4 mg  
Group 6: No steroid | Preoperative | Not specified |
| Gopinath et al. (2017) | Pederson’s difficulty score of 5 to 10 | Not specified | 3 | 120 | Group 1: SM 4 mg  
Group 2: IV 4 mg  
Group 3: No steroid | Preoperative | Not specified |
| Kumar (2017) | Class II and III Positions A, B and C | Ward’s incision | 2 | 38 | Group 1: IV 4 mg  
Group 2: SM 4 mg | Perioperative | Not specified |
| Vivek et al. (2017) | Class II Position B | Ward’s incision | 3 | 45 | Group 1: IV 8 mg  
Group 2: SM 8 mg  
Group 3: IM 8 mg (masseter muscle) | Postoperative | Yes, for the first 6 hours after surgery |
Table 4. Assessment methods and findings of the five relevant studies, specific to swelling

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Day of oedema measurement</th>
<th>Method of oedema measurement</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Majid &amp; Mahmood (2013)</td>
<td>Day 1, 3 and 7</td>
<td>Flexible tape measure&lt;br&gt;Schultze-Mosgau technique&lt;br&gt;Sum of two values – tragus to pogonion; tragus to corner of mouth</td>
<td>SM group had more swelling than IV group on all postoperative days. Data were presented only in a graph; however, the legend depicting SM and IV was erroneously the same.</td>
</tr>
<tr>
<td>Bhargava et al. (2014)</td>
<td>Day 1, 3 and 7</td>
<td>Flexible tape measure&lt;br&gt;Single measure – tragus to menton</td>
<td>There was no difference between the two groups on both postoperative day 2 and 7.</td>
</tr>
<tr>
<td>Gopinath et al. (2017)</td>
<td>Day 2 and 7</td>
<td>Flexible tape measure&lt;br&gt;Schultze-Mosgau technique&lt;br&gt;Sum of two values – tragus to pogonion; tragus to corner of mouth</td>
<td>SM group had more swelling than IV group on both postoperative day 2 and 7.</td>
</tr>
<tr>
<td>Kumar (2017)</td>
<td>Day 2 and 7</td>
<td>Flexible tape measure&lt;br&gt;Sum of two values – tragus to midline; gonion to lateral canthus of eye</td>
<td>SM group had more swelling than IV group on both postoperative day 2 (4.7mm and 2.5mm respectively) and day 7 (2.0 mm and 1.1 mm respectively).</td>
</tr>
<tr>
<td>Vivek et al. (2017)</td>
<td>Day 1, 3 and 7</td>
<td>Flexible tape measure&lt;br&gt;Schultze-Mosgau technique&lt;br&gt;Sum of two values – tragus to pogonion; tragus to corner of mouth</td>
<td>There was no difference between the two groups on both postoperative day 2 and 7.</td>
</tr>
</tbody>
</table>
Table 5. Assessment methods and findings of the five relevant studies, specific to pain

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Day of pain measurement</th>
<th>Method of pain measurement</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Majid &amp; Mahmood (2013)</td>
<td>Day 1, 3 and 7</td>
<td>100-mm visual analogue scale and number of rescue analgesic</td>
<td>SM group had higher pain scores than IV group on both postoperative day 2 and 7. Data was presented in a graph form only.</td>
</tr>
<tr>
<td>Bhargava et al. (2014)</td>
<td>Day 1, 3 and 7</td>
<td>100-mm visual analogue scale</td>
<td>There was no difference between the SM and IV groups on both postoperative day 2 and 7.</td>
</tr>
<tr>
<td>Gopinath et al. (2017)</td>
<td>Day 2 and 7</td>
<td>100-mm visual analogue scale</td>
<td>SM group had lower pain scores than IV group on postoperative day 2 (6.2 and 6.7 respectively) and day 7 (0.7 and 0.9 respectively).</td>
</tr>
<tr>
<td>Kumar (2017)</td>
<td>Day 2 and 7</td>
<td>100-mm visual analogue scale</td>
<td>SM group had more severe pain (n=12) scores than IV group (n=5) on postoperative day 2. There was no difference between the SM and IV groups on postoperative day 7.</td>
</tr>
<tr>
<td>Vivek et al. (2017)</td>
<td>Day 1, 3 and 7</td>
<td>100-mm visual analogue scale</td>
<td>SM had a slightly higher pain scores than IV group on both postoperative day 3 (5.9 and 4.7 respectively) and day 7 (2.8 and 2.4 respectively).</td>
</tr>
</tbody>
</table>
Table 6. Assessment methods and findings of the five relevant studies, specific to trismus

<table>
<thead>
<tr>
<th>Authors (year)</th>
<th>Time of mouth opening measurement</th>
<th>Method of mouth opening measurement</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Majid &amp; Mahmood (2013)</td>
<td>Day 1, 3 and 7</td>
<td>Maximum distance between maxillary and mandibular incisors</td>
<td>There was no difference between the two groups on both postoperative day 2 and 7.</td>
</tr>
<tr>
<td>Bhargava et al. (2014)</td>
<td>Day 1, 3 and 7</td>
<td>Maximum distance between maxillary and mandibular incisors</td>
<td>There was no difference between the two groups on both postoperative day 2 and 7.</td>
</tr>
<tr>
<td>Gopinath et al. (2017)</td>
<td>Day 2 and 7</td>
<td>Maximum distance between maxillary and mandibular incisors</td>
<td>SM group had less trismus (reduction of 4.6mm) than the IV group (reduction of 7.5mm) on postoperative day 2.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>There was no difference between the two groups on postoperative 7.</td>
</tr>
<tr>
<td>Kumar (2017)</td>
<td>Day 2 and 7</td>
<td>Maximum distance between maxillary and mandibular incisors</td>
<td>SM group had more trismus (reduction of 16.4 mm) than to IV group (reduction of 13.2 mm) on postoperative day 2.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>There was no difference between the two groups on postoperative day 7.</td>
</tr>
<tr>
<td>Vivek et al. (2017)</td>
<td>Day 1, 3 and 7</td>
<td>Maximum distance between maxillary and mandibular incisors</td>
<td>There was no difference between the two groups on both postoperative day 2 and 7.</td>
</tr>
</tbody>
</table>
In the clinical trial by Kumar (2017), it was found that patients who received IV dexamethasone had markedly lower swelling and less pain than patients who received SM dexamethasone, on both early and late review periods (day 2 and day 7). There was no difference in maximum incisor distance. This was a promising study with good intentions. However, there are issues with the research design that may compromise the validity of the findings: simple typographical errors which state ‘intramuscular route’ instead of ‘intravenous route’; a lack of blinding; vague description of patient numbers (“approximately 38 patients with 19 patients in each group.”) and no indication of the upper age limit. The authors acknowledged potential confounders such as age, gender, type of impaction and operating time. However, there was no indication as to whether any of these cofounders were accounted for during the analysis of the data. Important confounders such as the postoperative application of ice and rescue analgesics were not taken into consideration. Another potential flaw was the discrepancy between how pain was measured and how it was reported: pain was measured using a visual analogue scale with 0 meaning no pain and 100 meaning worst possible pain. This numerical continuous scale was then converted to a categorical scale of “no pain, mild pain, moderate pain and severe pain” in an undisclosed manner. While there were some strengths in this study, the conclusions need to be considered with caution in light of its various limitations.

Vivek et al. (2017) compared the efficacy of dexamethasone 8 mg delivered via three routes: intramuscular, intravenous and submucosal. They observed the IV group to experience better pain control than the SM group. Reported mean VAS pain scores for the intravenous group on days 1, 3 and 7 were 4.7, 2.4 and 0.0 respectively while mean pain scores for the SM group on days 1, 3 and 7 were 5.9, 2.8 and 0.0 respectively. This is in line with the findings by Kumar (2017), but it differs in that Vivek et al. (2017) found that the IV and SM routes showed comparable swelling and mouth opening findings. The dosage of dexamethasone was 8 mg, twice that used in the Kumar study. The study by Vivek et al. (2017) was a well thought-out and well-executed study. It considered operating time and number of rescue analgesics as potential confounding factors. Furthermore, the duration of postoperative ice application were standardized in the postoperative instructions to intermittently for the first 6 hours. Patients were randomly allocated, but there was no mention of any blinding, and this may make the study vulnerable to bias.
Bhargava et al. (2013) compared five routes of administration (submucosal, intravenous, intramuscular, pterygomandibular space and oral dexamethasone) with the control group receiving no steroids. This study is relatively unique being the only randomized double-blind clinical trial available. The main emphasis of the discussion in this trial focused on the comparison between the twin-mix injection of lignocaine and 4 mg dexamethasone into the pterygomandibular space with the control group. The findings showed that the intravenous and submucosal routes had comparable VAS pain scores, mouth opening and swelling profiles on all days. The authors concluded that the steroid groups appeared to have better clinical outcomes, with better quality of life post-operatively than the non-steroid study group. However, it may be difficult to draw conclusions on the impact on quality of life when the outcomes measured were limited to the clinically observed parameters of swelling, pain and mouth opening measurements. Other important metrics to consider in quality of life include social, work and physical limitations and to see how different personality types could influence a patient’s recovery perception. Hence, there is merit in collecting data on aspects of personality and oral health-related quality of life before and after third molar surgery.

The Majid and Mahmood (2013) study compared five routes of dexamethasone administration (intramuscular, submucosal, intravenous, oral and endoalveolar). It found that, when swelling on the first three postoperative days was concerned, the IV route gave the best improvement, followed by the IM, SM, oral and endoalveolar routes. The difference in swelling between the IV and SM routes was significant here: on day 1, the SM group had 1.5 cm of swelling while the IV group only had 0.9 cm of swelling; on day 3, the SM group had 1.2 cm of swelling while the IV group only had 0.2 cm of swelling. For trismus, the SM route performed better than other routes on day 1. When pain was assessed, the IV was the best at all intervals. The note-worthy advantage of the Majid and Mahmood study is their inclusion of a modified questionnaire to evaluate patients’ quality of life after third molar extraction. Their questionnaire involved different items addressing social isolation, working isolation, eating ability and diet variations, speaking ability, sleep impairment and physical appearance. For quality of life, IV and SM had equal impact on the number of days affected in terms of social, eating, speech and sleep, except in appearance, as explained by the greater swelling experienced by SM patients, giving IV a
better score than SM for the duration of the effect on quality of life. They concluded that the comparable outcomes obtained among treatment groups indicate the advantage of local dexamethasone as an effective alternative to systemic administration. This was an excellent study barring three minor flaws: no blinding; a small sample size; and the use of a direct linear measurement of facial swelling. In their protocol, dexamethasone was administered immediately post-surgery on the rationale that corticosteroid therapy is indicated only in technically challenging third molar surgery. This is contrary to the recommendations from a review by Alexander and Throndson (2000), which argued for all steroids to be administered before the infliction of tissue damage and not during or after surgery. Further research is required to clarify this notion.

Gopinath et al. (2017) equally divided 120 patients into 3 groups, whereby group I were given 4 mg dexamethasone submucosally, group II received 4 mg dexamethasone intravenously, and group III (control) did not receive any dexamethasone. The authors concluded that the intravenous route was superior to the submucosal route in respect of its lower swelling, pain and trismus. However, the bulk of the Results section concentrated on differences between the dexamethasone groups and the control group. There was little direct comment on the differences in outcomes between the SM group and the IV group. On further careful examination of the graphs presented, I found that, contrary to the conclusion of the study, the SM group had less severe trismus (mouth opening was reduced by 4.6 mm on day 2) than to the IV group (mouth opening was reduced by of 7.5 mm). I also noted that there were omission of crucial details such as the type of flap used, mean surgical duration, postoperative analgesic regime and the lack of any statistical methods and analyses.

There are several limitations common to the five clinical trials discussed above. The first is their small sample size: Vivek’s study had 15 participants in each group; Bhargava had 10 participants in each group; Kumar had 19 participants in each group; and Mahjid and Mahmood had 12 participants in each group. The small sample size makes these prone to Type II error, which is the probability of not detecting a significant difference when there really is one. This may explain why the swelling, pain and mouth opening profile of intravenous and submucosal dexamethasone were comparable in both the Vivek and Bhargava studies, with the sample size being too small to allow a true difference to be
observed. Second, all five studies failed to report the method of treatment allocation. Third, four clinical trials included postoperative oral amoxicillin use for five days (except for the Kumar study where the duration of antibiotic is undisclosed). The inclusion of postoperative antibiotics as part of the study protocol may mask any infection secondary to potential immunosuppression arising from dexamethasone exposure. Majid and Mahmood acknowledged that the routine use of antibiotics might be the cause behind the absence of infection in their study; they suggested that this is a point that may require further research. Moreover, there is a lack of evidence for the routine use of prophylactic antibiotics along with the use of corticosteroids for preventing infection (Alexander and Throndson 2000). It was acknowledged by Majid & Mahmood (2013) to be a cultural expectation that had to be met for antibiotics to be dispensed after surgery. Fourth, there was little standardization of the soft tissue landmarks used to measure facial swelling. The measurements made by Kumar (2017) were from the tragus to the midline, and the gonion to the lateral canthus of the eye. Majid & Mahmood (2013) used similar measurements that included the tragus-midline, tragus-commissure of the mouth, and gonion-lateral canthus of the eye. When the distances measured from the tragus, lateral canthus, gonion and midline are considered, large areas of the face that do not swell following third molar removal (chin, cheekbone) are included in the calculation. By including areas that do not swell, the actual changes in areas where swelling occurs may be underestimated because there is difficult to detect small changes in large linear measurements (Neupert et al. 1992). Thus, this approach may lack the sensitivity required to detect important differences in swelling. Vivek et al. (2017) limited their landmarks to the three reference points of the tragus, pogonion and corner of the mouth. Bhargava et al had just two reference points, the tragus and menton. Limiting measurements to the specific area of interest will allow higher sensitivity to any volumetric changes. The final limitation in all five studies was that the linear measurements were performed directly on each participant’s skin using traditional instruments (such as tape measurements and callipers) to measure distances between these soft tissue landmarks.

The study by Vivek et al. (2017) was the only trial that used 8 mg of dexamethasone in their study. All other trials administered a total of 4 mg of dexamethasone to each participant. The rationale for limiting the total dosage of dexamethasone to 4 mg was largely based on a study by Grossi et al. (2007), who showed that dose regimes of 4mg or 8mg dexamethasone led to no differences in clinical outcome. In contrast to this
observation, it was reported that 8 mg dexamethasone produced a better control of swelling than to treatment of 4 mg dexamethasone (Filho et al. 2008). In a systematic review and meta-analysis by Dan et al. (2010), administered doses of corticosteroid in the included studies were recalculated to equivalent anti-inflammatory doses of methylprednisolone in order to allow a fair and standardized unit of comparison. Calculations are based on the equivalent dose with regard to anti-inflammatory effect, as listed in Table 7.

Table 7. Equivalent dose with respect to anti-inflammatory effect

<table>
<thead>
<tr>
<th>Type</th>
<th>Anti-inflammatory potency</th>
<th>Half-life (hours)</th>
<th>Equivalent dose with respect to anti-inflammatory effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylprednisolone</td>
<td>3-5</td>
<td>12-36</td>
<td>4.00 mg</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>20-30</td>
<td>36-54</td>
<td>0.75 mg</td>
</tr>
</tbody>
</table>

Table adapted from Dan et al. (2010)

In general, corticosteroids must be administered in doses exceeding the normal physiologic amounts released by the body (Alexander and Throndson 2000). In oral surgery, the threshold dose value of dexamethasone is expected to be above 25 mg methylprednisolone for there to be a significant decrease in oedema. Using the conversion table above, 8 mg of dexamethasone = 8mg/0.75mg x 4 = 42 mg methylprednisolone, whereas 4 mg of dexamethasone = 4 mg / 0.75 mg x 4 = 21.3 mg methylprednisolone. Dosages of methylprednisolone of <40 mg will reportedly not produce any adverse systemic effect (Alexander and Throndson 2000). Thus, a total of 4 mg dexamethasone appears to be at subtherapeutic levels (and so the protocol for the current study was a total of 8 mg dexamethasone per participant).

2.4 Overview

Critical appraisal of the published literature revealed that both intravenous and submucosal dexamethasone can reduce postoperative swelling, pain and trismus after third molar surgery. However, there has not been a high-quality randomized, double-blind study to directly compare the efficacy of these two routes of administration by objectively quantifying the volume of postoperative swelling. The aforementioned published studies show high variability in aspects such as the timing of administration, the dosage of
dexamethasone, and the landmarks used in facial swelling measurement. It is also apparent that clinical trials of this nature may benefit from larger sample sizes so that Type II error can be avoided. Accordingly, it remains to be scientifically determined how IV administration compares to the SM administration of dexamethasone in improving postoperative outcomes after third molar surgery. As a matter of convenience, many surgeons use intravenous dexamethasone in conjunction with IV sedation. SM dexamethasone is equally convenient and may be used in patients who do not have an intravenous line in place. It remains unknown whether better anti-inflammatory effects are achieved with intravenous or with submucosal dexamethasone. This leads to the following two important clinical questions: how does submucosal dexamethasone compare to intravenous dexamethasone in reducing adverse post-operative outcomes (swelling, pain, trismus) after third molar surgery; and do the different routes of administration differ in their ways of affecting a patient’s postoperative quality of life?
3 Objectives

3.1 Aim

The primary aim of this study was to compare the efficacy of submucosal dexamethasone and intravenous dexamethasone in reducing adverse post-operative outcomes in third molar surgery. A secondary aim was to compare the two routes of administrations and its impact on patient’s quality of life after third molar removal.

3.2 Study hypothesis

There is no difference between submucosal and intravenous administration of dexamethasone in reducing adverse postoperative outcomes from third molar surgery.

3.3 Research significance

The proposed study aimed to compare two different routes of administration for using dexamethasone in third molar surgery. Gaining intravenous access in a patient requires additional skills and armamentarium. Many general dental practitioners performing third molar surgery under local anaesthesia may not be adequately skilled in IV cannulation. The study findings may potentially provide an argument for the routine administration of submucosal dexamethasone at the surgical site (in preference to IV administration) in order to reduce postoperative swelling, pain and trismus. This may translate to an improvement in patient satisfaction and quality of life after third molar surgery. Given that a submucosal injection of dexamethasone is cost-effective, simple and easy to administer, more patients may benefit from a submucosal injection regardless of whether they have it done in the dental office, or in a hospital setting with intravenous access support.
4 Methods

4.1 Ethics approval and Māori consultation

This study received full approval from the Health and Disability Ethics Committee (Appendix 1) and was registered with the Australian New Zealand Clinical Trials Registry (Appendix 2). The requirement for Māori consultation through the University of Otago was met with the Ngāi Tahu Research Consultation Committee noting the study’s importance for Māori (Appendix 3).

4.2 Study design

The study was a prospective, randomised, controlled and double-blinded single-centre clinical trial with two parallel arms.

4.2.1 Randomization

Randomization helps to achieve similarity of baseline characteristics (such as demographic characteristics or degree and type of third molar impaction) between treatment groups in order to minimize confounding. Confounding is defined as “the situation in which the intervention effect is biased because of some difference between the treatment groups, apart from the planned intervention” (CONSORT Group 2010). If confounding was to exist, any differences in outcomes between the treatment groups may not result from differences in treatment received, but from differences in the baseline characteristics (Sedgwick 2014). This in turn reduces the internal validity of a trial in that it may not permit the inference of causality to be ascribed to differences in treatments received. Randomization in a trial involves the two important processes of sequence generation and allocation concealment (Schulz et al. 1995).

4.2.1.1 Sequence generation

A biostatistician used simple randomization to allocate participants into two treatment groups in blocks of 10. That is, once a group of 10 participants were recruited, they were randomised into 2 treatments. For that, 13 sets of Bernoulli (0/1) random numbers with 10 numbers in each set were generated for the targeted sample size of 130 participants. The
randomization incidentally included 65 ‘0’s and 65 ‘1’s, whereby 10 numbers were generated in each set so that each number can be ‘0’ or ‘1’ with 0.5 probability, with no correlation among the 13 sets. In this way, as the participants were recruited over a 10-month period, each participant had an equal probability of being allocated to treatment group A (submucosal administration of dexamethasone) or treatment group B (IV administration of dexamethasone). This randomization allowed equal-sized groups while also allowing even distribution of baseline characteristics between the groups.

4.2.1.2 *Allocation concealment*

Allocation concealment eliminates selection bias during recruitment and randomization. The randomization sequence was delegated to the hospital pharmacist based at Dunedin Hospital. Accordingly, as and when participants were recruited, the pharmacist assigned them to their group by following the randomization sequence.

4.2.1.3 *Blinding*

The hospital pharmacist was the only non-blinded person involved in the study. The participants, primary researcher, research supervisors, and all auxiliaries (including dental assistant, registered nurses, receptionists, referring dentists) were blinded to the randomization and group allocation. The blinding process remained in place for all parties throughout the clinical trial, including during data entry and statistical analysis.

4.3 Participants

4.3.1 Patient sample

Participants were recruited from a pool of patients who had been referred by a dental practitioner or a medical practitioner to the Oral Surgery Unit at the School of Dentistry (University of Otago) for an assessment for the surgical removal of at least two impacted mandibular third molar teeth. Patients were interviewed in person at an out-patient consultation clinic by a clinician (Oral Surgery Registrar or an Oral and Maxillofacial Consultant) for surgical assessment. This included assessing the degree of wisdom tooth impaction, the anticipated level of surgical difficulty, and the patient’s preference for
perioperative pain control method. For the latter, the options included local anaesthesia, local anaesthesia with intravenous sedation and general anaesthesia. Patients who chose to have intravenous sedation (and met the inclusion/exclusion criteria) were then invited to participate in the study. A verbal explanation accompanied by a written information sheet was provided to all patients before they were requested to sign a written consent to participate in the study. Participation was entirely voluntary, and participants were assured that their rights for receiving treatment would not be affected in any manner based on their decision to participate or not, and also if they decide later on to withdraw from the trial (see section 4.3.6 for more details).

4.3.2 Location and setting of study

All recruitment, surgery and follow-up appointments took place at the Department of Oral Diagnostics and Surgical Sciences (ODSS) at the School of Dentistry.

4.3.3 Sample size determination

The sample size was determined through consultation with a biostatistician. In order to obtain a study power of 80%, a significance level of 0.05 and to detect an anticipated effect size of 5, the minimum total required number of participants was estimated to be 104, divided equally between two groups (“intravenous group” and the “submucosal group”) with 52 participants each (Cohen 1988). The targeted total sample size was set at 130 to account for any participants who may fail to complete the clinical trial for any reason.

4.3.4 Eligibility criteria

All patients deemed suitable for participation in the study were further assessed using inclusion and exclusion criteria to determine their eligibility before they were invited to participate in the study. The decision to invite participation was based on the following.

Inclusion criteria:

1. Patient participation had to be entirely voluntary.
2. The patient had to be between 16-40 years of age.
3. The patient had to be screened by an Oral Surgery Registrar or Consultant at the University of Otago, and be deemed appropriate for participation in the present study by that clinician.

4. The patient required the removal of bilateral mandibular bony impacted third molars.

5. Bone removal was expected for removal of the mandibular third molars.

6. The patient had to be medically fit for third molar surgery.

7. The patient had to be medically fit to undergo intravenous sedation.

8. The patient had to be consented for surgical removal of third molars under local anaesthesia and intravenous sedation.

*Exclusion criteria*

Patients with any of the following features were not eligible for participation in the study.

1. Anyone under 16 years of age, or above 40 years of age.

2. Anyone who must drive a motor vehicle or operate machinery within 24 hours following wisdom teeth surgery.

3. Anyone with one or more of the following:
   a. Immunosuppressive medications.
   b. Non-steroidal anti-inflammatory (NSAID) drug-induced asthma.
   c. Regular or long term pain management (such as paracetamol, NSAIDS, opioids).
   d. Systemic or inhaled corticosteroids.
   e. Disease-modifying drugs for chronic autoimmune conditions.
   f. Long-term anti-depressants or anti-convulsants.
   g. A history of organ transplantation or on chronic anti-rejection drugs.
   h. Blood thinners (anticoagulants).
   i. Gastric or intestinal bleeding or ulceration.
   j. Bleeding disorder.
   k. Kidney impairment.
   l. Liver impairment.
   m. Respiratory depression.
   n. Chronic obstructive pulmonary disease.
   o. Alcoholism.
p. Opioid addiction.
q. Central nervous system depressants.
r. Hypersensitivity to morphine.
s. An absolute contraindication to receiving corticosteroids (such as: active or incompletely treated tuberculosis; active viral or fungal infections, especially ocular herpes; active acne vulgaris; primary glaucoma; or a history of psychoses or psychotic tendencies).

4. Inability to have midazolam, paracetamol or ibuprofen.
5. Inability to or are unwilling to have IV sedation.
6. Inability to give informed consent.
7. Refuse the removal of facial hair (beard and/or moustaches) for the purposes for obtaining an accurate 3D photograph of the face.
8. Refuse involvement in the study and/or are unable to attend follow-up appointments.

4.3.5 Obtaining patient consent for participation

All patients who met the eligibility criteria were invited to participate in the study. They received a verbal explanation of the purpose of the study, their level of involvement and responsibilities during their participation and the possible benefits and risks involved. All patients invited to participant were also given a written “Information Sheet for Participants” and were encouraged to read and discuss it with family and friends before reaching a final decision on participation in this study. Those who chose to participate then completed a written consent form to formally enrol.

4.3.6 Assurances to participants

As part of the process of obtaining written consent for formal enrolment into this study, all participants received the following assurances.

1. Both routes of dexamethasone administration are established methods and there is no higher risk of participation in the study. However, if adverse events were to occur as a result of the trial, it would be promptly reviewed and reported to an independent data safety monitoring committee.
2. The study had full ethical approval from the Health and Disability Ethics Committee, and has been registered with the Australia New Zealand Clinical Trials Registry.

3. Participation and all data collected remained strictly confidential and would be used only for the purposes of the study.

4. Participants would not be identifiable in any publication of the study result, unless written consent is separately and formally sought for the use of photographs solely for the purpose of research conferences, academic presentations and/or journal publications.

5. The names of participants would not appear in the thesis or in any future scientific publications that may arise from the research.

6. Participants could withdraw from the study on their own volition at any time with no adversity to their rights to receive treatment.

7. Participants would be informed of potential side-effects of the medications used and/or prescribed during treatment. The medications were: Paracetamol, Ibuprofen, Codeine, Saline, Parecoxib, Dexamethasone, Midazolam and Chlorhexidine.

8. Participants may request a copy of the final finding of the research if they so desired.

9. Participants had the right to access their personal data (As per protocol set up by the School of Dentistry) if they so desire.

10. Participants had access to the primary researcher during and after the research period should postoperative complications occur. During business hours, contact can be made via the oral surgery unit. If after-hours contact is required, contact numbers for the emergency on-call oral and maxillofacial team was provided.

4.3.7 Participation incentives

There were no added incentives for the participants to be involved in this study.

4.3.8 Participant responsibility

Patients who consented to participate in the research study agreed to:

1. Complete a preoperative questionnaire;

2. Have preoperative and postoperative 3-dimensional photographs of their face taken;
3. Have measurements of the maximum mouth opening during the study period;
4. Attend the surgical appointment for the removal of their third molar(s) under intravenous sedation;
5. Complete a 7-day diary, starting the day after surgery;
6. Attend postoperative review appointments on day 2 and day 7;
7. Complete postoperative questionnaires; and to
8. Bear the financial cost of the consultation appointment and surgical removal of third molar(s) under intravenous sedation, according to the Dental School 2017-18 fee schedule.

4.4 Treatment groups

Participants allocated to Group A received 8 mg/2ml submucosal dexamethasone and 2ml of intravenous saline (placebo). Participants allocated to Group B received 8mg/2ml intravenous dexamethasone and 2ml of submucosal saline (placebo).

The hospital pharmacist prepared all research medication on the morning of the surgery. Each participant had an individually prepared and labelled single-use brown paper bag containing two syringes. The two syringes were identical in size and volume, and both contained an odourless, colourless liquid. For safety reasons, both syringes were also labelled with the participant’s name, date of birth, address and national health index number (NHI). One syringe was labelled “For intravenous administration”, while the other syringe was labelled “For submucosal administration.”

4.5 Study procedure

All recruited participants were placed on a surgery waitlist. A preoperative oral health-related quality of life questionnaire was provided to all participants, and a preoperative measurement of facial soft tissue contour (using the facial camera) and maximum mouth opening (incisal distance) was taken at the start of the surgical appointment. Participants were reviewed on postoperative day 2 and day 7 for a facial scan, pain assessment and measurement of maximum incisal distance. A self-reported OHRQoL diary was completed by participants throughout the first 7 days of recovery to provide information on the degree of social isolation, days off work, and a measure of their quality of life as a result of
swelling, pain and/or limitation in mouth opening. The summarized study protocol is presented in Figure 2.
Figure 2. Flow chart of study procedure

Patient referred to Oral Surgery Department for surgical removal of third molar teeth

Appointment 1: Consultation
- Inclusion and exclusion criteria met
- Information sheet provided

Appointment 2: Surgical appointment under IV sedation
- Consent obtained
- Preoperative questionnaire (SES, OHIP-14, IDAF4C, PANAS) completed
- Pre-operative measures taken (Facial photograph, maximum mouth opening, pain score)

Patients are pre-allocated to either group:
Group A (SM group)
- 40mg IV parexocib
- Titrated dose of IV midazolam
- 2ml IV saline
- 8mg/2ml submucosal dexamethasone

or
Group B (Intravenous group)
- 40mg IV parecoxib
- Titrated dose of IV midazolam
- 2ml submucosal saline
- 8mg/2ml IV dexamethasone

All participants are given a 7-day diary (OHRQoL) to complete.

Appointment 3: Day 2 post-operation
- Complete additional OHIP-14 questionnaire
- Early postoperative measurements taken (Facial photograph, maximum mouth opening, pain score)

Appointment 4: Day 7 post-operation
- Complete “After-surgery” questionnaire
- Late postoperative measurements taken (Facial photograph, maximum mouth opening, pain score)
- Return completed 7-day diary
- End of participant commitment
All participants received intravenous access via a 22-gauge cannula placed by the operator. Medication was administered in the following order:

1. 40 mg IV parecoxib.
2. IV injection of either 8mg/2ml dexamethasone, or 2 ml saline; depending on allocated group.
3. Titrated dose of IV midazolam.
4. Local anaesthetic (Lignocaine 2% 1:80 000 adrenaline) administered as an inferior dental block, long buccal nerve infiltration and buccal subperiosteal infiltration adjacent to third molar site.
5. SM injection of either 8mg/2ml dexamethasone, or 2 ml saline; depending on allocated group.

A lag-time of 5 minutes was allowed before placing an incision in the mucosal tissues. At the time of surgery, no participants had any signs or symptoms of acute pericoronitis. All participants had their third molars surgically removed by the author (primary surgeon for this study), using aseptic surgical technique. All mandibular third molars were surgically approached by raising a standardised two-sided buccal envelope flap with lingual alveolar exposure and removal of overlying bone, before being disimpacted and removed. Soft tissue re-approximation was achieved via secondary intention using resorbable polyglactin (Vicryl Rapide, Ethicon, United States) sutures with a tapered needle.

The author administered all intravenous and submucosal medications. A registered nurse who is appropriately trained and qualified in IV sedation was present and continuously monitored all participants during surgery and in the immediate post-sedation recovery phase. As part of the clinical record keeping, the operator kept a record of the time required (in minutes) for the surgical removal of each mandibular third molar, and the depth and type of impaction classified and graded according to the Pell and Gregory classification of impacted third molars (Pell and Gregory 1933). All participants were discharged with a standard prescription for analgesics (6-hourly paracetamol 1000 mg tablets, 6-hourly ibuprofen 400 mg tablets, 6-hourly codeine phosphate 30-60 mg tablets) and chlorhexidine gluconate 0.2% mouthwash. Participants who were unable to tolerate codeine phosphate (or have had poor analgesic control with codeine phosphate) were
prescribed an alternative opioid of tramadol (50-100 mg capsules to be taken at 6-hourly intervals).

4.6 Data collection

Outcomes were recorded in two forms:

1. Direct observation by the primary investigator; and
2. Self-reported questionnaires completed by participants.

4.6.1 Measurement of swelling

The primary outcome measured was postoperative swelling. The 3dMD.trio system (3dMD Inc, Atlanta, GA) camera system was used to take a three-dimensional digital photograph of each participant’s face (from ear to ear) just prior to surgery, and then again on postoperative days 2 and 7. As per the manufacturer’s protocol, system calibration was undertaken prior to each imaging session. The three-dimensional data acquisition was performed with the participant in maximum intercuspation, maintaining natural head posture with Frankfurt horizontal line parallel to the floor and in a neutral facial expression. Participants were asked to swallow, relax their lips and keep their eyes open. Hair was secured off the participant’s face and high-quality images were acquired with a capture time of less than 0.2 milliseconds.

The captured digital images were pre-processed by removing the hair and neck regions to exclude obvious error regions during the superimposition process (Maal et al. 2010). The images then went through a surface-based registration process using the 3dMD.vultus software (3dMD Inc, Atlanta, GA). The preoperative image represents baseline data upon which postoperative day 2 and 7 images were separately superimposed on to. Superimposition was a two-step process. First, the images were manually aligned by the observer with the use of 5 stable soft tissue points (lateral profile: glabella, nasion and tip of the nose; frontal profile: medial and lateral canthus of both the right and left eyes) using a mouse-driven cursor. Next, an in-built software algorithm was used to fine-tune the image superimposition using the abovementioned soft tissue points in order to achieve precision and accuracy with an deviation of less than 0.5 mm.
Facial swelling was quantified by volumetric differences between the preoperative (baseline) image and postoperative images. That is, the preoperative image and postoperative day 2 image were superimposed and measurements were made to calculate the amount of swelling that was present on postoperative day 2. Next, the preoperative image and postoperative day 7 image were superimposed to calculate how much facial swelling remained 7 days after surgery (Figure 3). Separate measurements were also taken for the right and left side of the face of each participant (Figure 4 and Figure 5). A 4-point soft tissue landmark (Figure 6) was used to outline the area of interest: the tragus of the ear, soft tissue gonion, cheilion and the parasympyseal region (by dropping a vertical line down from the cheilion). The lasso tool was used to place nodes at these soft tissue landmarks, hence determining the area of interest for comparison. Volumetric measurement of facial swelling was measured in cubic millimetres. All measurements were repeated three times and the average of these three was taken as the final measurement. All data capture, image registration and measurements were done by the author under conditions of allocation concealment and blinding in order to minimize bias.
Figure 3. Facial swelling on day 2 (top image) and day 7 (bottom image). The region of facial swelling is marked by the arrows.
The swelling in both right and left cheeks can be well appreciated from a down oblique angle, as seen in Figure 3 above. The top image in Figure 3 is composed of the preoperative photograph superimposed with the postoperative day 2 photograph (set at 50% translucency). The area of swelling is indicated by the yellow arrows. The bottom image in Figure 3 is composed of a superimposition of the preoperative photograph and postoperative day 7 photograph (set at 50% translucency). Note that while facial swelling had fully subsided on the right cheek by day 7, there remained a small degree of facial swelling on the left cheek by day 7, as pointed out by the green arrow.

The images in Figure 4 are composed of a superimposition of the preoperative photograph and postoperative photographs (set at 50% translucency) showing the difference in surface volume in the right lower cheek, in an oblique profile view. The top image in Figure 4 highlights the noticeable difference in surface volume between preoperative and day 2, marked by the yellow arrow. The bottom image in Figure 4 illustrates near-full resolution of facial swelling on day 7. Similarly, the images in Figure 5 show the amount of facial swelling on day 2 (top image) and day 7 (bottom image), but of the left cheek instead. In this patient, the swelling of the left cheek was more pronounced than the right cheek by day 7.
Figure 4. Facial swelling on the right cheek on day 2 (top image) and day 7 (bottom image), in an oblique profile view.
Figure 5. Facial swelling on the left cheek on day 2 (top image) and day 7 (bottom image), in an oblique profile view.
Figure 6. A 4-point soft tissue landmark determined the area of interest for volumetric measurement: tragus of the ear, cheilion, the parasympyseal region (determined by a vertical line from the cheilion) and the soft tissue gonion, in the oblique lateral view.
4.6.2 Measurement of pain

Postoperative pain was quantified mainly using a 100 mm visual analogue scale (VAS), labelled “no pain” at the left pole and “worst pain imaginable” on the right pole. Participants were asked to complete a VAS immediately before the surgery, and at review appointments on postoperative days 2 and 7. Postoperative pain was also assessed by means of a 7-point Likert-type scale with anchors of “No pain” (1) and the “Worst pain imaginable” (7). Participants were asked to limit their pain scores to the mandibular third molars. They were also asked to record the type and amount of analgesia taken to manage their pain levels.

4.6.3 Measurement of maximum mouth opening

Maximum mouth opening was measured as the inter-incisal distance between the maxillary right central incisor and mandibular right central incisor (tooth 11 and 41), using a metal ruler. Measurements were made preoperatively and on postoperative days 2 and 7.

4.6.4 Other information

Data were collected from participants by means of self-reported questionnaires. The types of data collected include demographic characteristics (age, sex, ethnicity, occupation, education level), current smoking use, reasons for seeking third molar removal, current temporomandibular joint symptoms, dental anxiety score and the positive and negative affect schedule (PANAS). The study used reliable, valid and useful instruments known as the IDAF-4C and the PANAS to control for aspects of patients’ anxiety levels and personality (Watson et al. 1988; Armfield 2010). The IDAF-4C module is an 8-item scale that assesses emotional, behavioural, physiological and cognitive aspects of the fear and anxiety response (Armfield 2010). The Positive and Negative Affect Schedule (PANAS) was used in this study to evaluate the influence of positive affect (PA) and negative affect (NA) on surgical outcomes (Watson et al. 1988). The PANAS scale comprises 10 statements in each PA and NA categories.

This study used two separate instruments to assess quality of life. Both the OHIP-14 and OHRQoL were used because of how they work in synergy to improve assessment of patients’ perspective and help clinicians understand the multiple aspects of the recovery
period following third molar surgery (Shugars et al. 2006; Kanatas and Rogers 2010). The percentage of people reporting 1 or more OHIP-14 items as either ‘fairly often’ or ‘very often’ was computed as a measure of prevalence. An item reported ‘fairly often’ or ‘very often’ was considered important clinically as being detrimental to quality of life.

4.7 Statistical Methods

Following the computation of descriptive statistics, the two groups were compared using (a) cross-tabulations and chi-square tests for categorical variables, and (b) analysis of variance for continuous variables. Linear regression modelling was used to control for confounding, where appropriate. Statistical analysis was performed using SPSS software (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IMB Corp).

4.8 Funding and Payment for Treatment

All participants were fee-paying patients whose treatment cost was outlined by the 2017-2018 fee schedule determined by the School of Dentistry. This study received a research grant of NZD$9700.00 from the New Zealand Dental Association Research Fund to meet the costs involved in drug preparation for each individual participant by a dedicated research trial hospital pharmacist (Appendix 4).
5 Results

The purpose of this chapter is to present the findings of the study. To begin with, there will be a description of the flow of participants through the study, followed by a description of the number of participants and their baseline characteristics. Next, the main findings of this study will be presented and described, before concluding with a report on the ancillary data collected.

5.1 Participant flow

A total of 150 patients presenting for surgical removal of impacted third molar teeth to the School of Dentistry were assessed for eligibility to participate in the study. Among them, 17 (11%) did not meet the inclusion criteria and one (0.7%) declined to participate since he was unwilling to remove his facial hair. Complete shaving of the male beard was essential to capture accurate measurements from clinical photographs to measure the extent of facial swelling. Hence, a total of 132 participants were enrolled in the study and were subsequently allocated to one of the two treatment groups by the process of block randomisation described in section 4.2.1. The random allocation yielded 66 participants each in the treatment groups, all of whom received their allocated treatment on the day of surgery. All participants underwent surgical removal of impacted third molar teeth and attended follow-up reviews on postoperative days 2 and 7. However, a technical fault developed in the camera at one point and took a week to resolve. Consequently, a total of 6 participants (4 from the IV group, 2 from the SM group) were unable to have their facial photographs taken in a timely manner according to the study procedure (refer to Figure 2 above) and were excluded from the facial swelling analysis. One participant from the IV group had a severe haematoma from the surgical removal of a deeply impacted left maxillary third molar requiring overnight hospitalization for intravenous antibiotics and observation. He was excluded from the trial as it became difficult for him to continue with the follow-up protocols. The exclusion of these 7 participants brought the total number of participants in the study to 125, which still exceeded the minimum required participant number (104 participants with complete data) for statistical analysis. The participant flow described above is summarised in Figure 7.
5.2 Protocol deviations

There were no protocol deviations from the research methods described in Chapter 4.

5.3 Recruitment and follow-up

Recruitment, surgery and follow-up took place at the School of Dentistry. The recruitment period starts in November 2017 and ended in July 2018. Surgical procedures were performed between December 2017 and August 2018, with each patient having a follow-up period of 7 days from the date of surgery.
Figure 7. Flow of participants through each stage

Enrolment

Assessed for eligibility (n= 150)

Excluded (n= 18)
- Not meeting inclusion criteria (n= 17)
- Declined to participate (n= 1)

Study participants (n= 132)

Allocation

Submucosal Group (n= 66)
Received Submucosal Dexamethasone (n= 66)

Follow-up
Lost to follow-up (n= 0)
Discontinued Intervention (n= 0)

Excluded (n =2)
- No facial photographs (n= 2)

Analysed (n= 64)

Intravenous Group (n= 66)
Received IV Dexamethasone (n= 66)

Follow-up
Lost to follow-up (n= 0)
Discontinued Intervention (n= 0)

Excluded (n =5)
- No facial photographs (n = 4)
- Severe facial swelling due to a haematoma from removal of maxillary 3rd molar (n = 1)

Analysed (n= 61)
5.3.1 Baseline data

The participants’ demographic characteristics, oral care and smoking habits are presented by group in Table 8.

Table 8. Sociodemographic characteristics, self-care and self-reported oral health by group (brackets contain row percentages unless otherwise indicated)

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>Both combineda</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV</td>
<td>SM</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28 (42.4)</td>
<td>29 (43.9)</td>
<td>57 (43.2)</td>
</tr>
<tr>
<td>Female</td>
<td>38 (57.6)</td>
<td>37 (56.1)</td>
<td>75 (56.8)</td>
</tr>
<tr>
<td>Age group (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16-20</td>
<td>17 (25.8)</td>
<td>26 (39.4)</td>
<td>43 (32.6)</td>
</tr>
<tr>
<td>21-24</td>
<td>33 (50.0)</td>
<td>24 (36.4)</td>
<td>57 (43.2)</td>
</tr>
<tr>
<td>25-37</td>
<td>16 (24.2)</td>
<td>16 (24.2)</td>
<td>32 (24.2)</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>22.6 (3.9)</td>
<td>22.5 (4.3)</td>
<td>22.6 (4.1)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pākeha</td>
<td>36 (54.5)</td>
<td>45 (68.2)</td>
<td>81 (61.3)</td>
</tr>
<tr>
<td>Māori</td>
<td>8 (12.1)</td>
<td>7 (10.6)</td>
<td>15 (11.4)</td>
</tr>
<tr>
<td>Pasifika</td>
<td>1 (1.5)</td>
<td>1 (1.5)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Asian</td>
<td>21 (31.8)</td>
<td>13 (19.7)</td>
<td>34 (25.8)</td>
</tr>
<tr>
<td>Tertiary educationb</td>
<td></td>
<td></td>
<td>0.58</td>
</tr>
<tr>
<td>No</td>
<td>33 (50.0)</td>
<td>28 (45.2)</td>
<td>61 (47.7)</td>
</tr>
<tr>
<td>Yes</td>
<td>33 (50.0)</td>
<td>34 (54.8)</td>
<td>67 (52.3)</td>
</tr>
<tr>
<td>Brush more than once/dayc</td>
<td></td>
<td></td>
<td>0.67</td>
</tr>
<tr>
<td>No</td>
<td>19 (28.8)</td>
<td>16 (25.4)</td>
<td>35 (27.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>47 (71.2)</td>
<td>47 (74.6)</td>
<td>94 (72.9)</td>
</tr>
<tr>
<td>Current smokerc</td>
<td></td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>No</td>
<td>57 (86.4)</td>
<td>56 (88.9)</td>
<td>113 (87.6)</td>
</tr>
<tr>
<td>Yes</td>
<td>9 (13.6)</td>
<td>7 (11.1)</td>
<td>16 (12.4)</td>
</tr>
<tr>
<td>All combined</td>
<td>66 (50.0)</td>
<td>66 (50.0)</td>
<td>132 (100.0)</td>
</tr>
</tbody>
</table>

aColumn percentages

b4 missing responses

c3 missing responses

Both groups had a mean age of early to mid-twenties, a higher proportion of females than males, a higher proportion of New Zealand Europeans, a low number of current smokers and the majority of participants also brushed more than once daily. In both groups, approximately half the participants had tertiary level education. There were no statistically significant socio-demographic differences between the two groups (P>0.05). The majority
of participants in each group had a history of third molar pain, with most reporting moderate pain intensity at some time in the 4 weeks prior to surgery.

Preoperative third molar pain was also assessed for each group (Table 9). The preoperative pain scores on a 100-mm visual analogue scale between the groups were similar.

Table 9. Preoperative third molar pain, by group (brackets contain row percentages unless otherwise indicated)

<table>
<thead>
<tr>
<th></th>
<th>IV</th>
<th>SM</th>
<th>Both combinedb</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History of third molar pain</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>56 (84.8)</td>
<td>56 (88.9)</td>
<td>112 (86.8)</td>
</tr>
<tr>
<td>No</td>
<td>10 (15.2)</td>
<td>7 (11.1)</td>
<td>17 (13.2)</td>
</tr>
<tr>
<td><strong>Third molar pain in last 4 weeks</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always</td>
<td>4 (6.1)</td>
<td>4 (6.3)</td>
<td>8 (6.2)</td>
</tr>
<tr>
<td>Often</td>
<td>8 (12.1)</td>
<td>9 (14.3)</td>
<td>17 (13.2)</td>
</tr>
<tr>
<td>Sometimes</td>
<td>24 (36.4)</td>
<td>17 (27.0)</td>
<td>41 (31.8)</td>
</tr>
<tr>
<td>Occasionally</td>
<td>13 (19.7)</td>
<td>15 (23.6)</td>
<td>28 (21.7)</td>
</tr>
<tr>
<td>Never</td>
<td>17 (25.8)</td>
<td>18 (28.6)</td>
<td>35 (27.1)</td>
</tr>
<tr>
<td><strong>Intensity of pain/discomfort</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>4 (12.5)</td>
<td>10 (23.3)</td>
<td>14 (18.7)</td>
</tr>
<tr>
<td>Moderate</td>
<td>26 (81.3)</td>
<td>33 (76.7)</td>
<td>59 (78.7)</td>
</tr>
<tr>
<td>Mild</td>
<td>2 (6.3)</td>
<td>0 (0.0)</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td><strong>Mean VASa (SD)</strong></td>
<td>1.6 (2.1)</td>
<td>1.3 (1.9)</td>
<td>1.5 (2.0)</td>
</tr>
</tbody>
</table>

aVisual analogue scale
bColumn percentage
IDAF-4C scores for dental anxiety and fear were collected before surgery. The data, along with mean PANAS scores and OHIP-14 scores, are presented in Table 10.

Table 10. Positive and negative affect scores, dental anxiety and fear scores and oral health index profile scores by group, at preoperative (brackets contain standard deviations unless otherwise indicated)

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>Both combined</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean positive affect score</td>
<td>24.4 (7.2)</td>
<td>26.4 (9.1)</td>
<td>25.3 (8.2)</td>
</tr>
<tr>
<td>Mean negative affect score</td>
<td>16.9 (4.3)</td>
<td>17.3 (5.7)</td>
<td>17.1 (5.0)</td>
</tr>
<tr>
<td>Mean IDAF4C+ scorea</td>
<td>14.4 (5.8)</td>
<td>13.9 (6.3)</td>
<td>14.2 (6.0)</td>
</tr>
<tr>
<td>Prevalence of 1+ impactsb</td>
<td>19 (28.8)</td>
<td>26 (39.4)</td>
<td>45 (34.1)</td>
</tr>
<tr>
<td>Mean OHIP-14a</td>
<td>9.5 (8.4)</td>
<td>10.7 (9.5)</td>
<td>10.1 (8.9)</td>
</tr>
</tbody>
</table>

*aIDAF4C = Index of Dental Anxiety and Fear, basic module only
bFairly often or very often, brackets contain row percentages

Positive and negative dispositions of research participants were equally distributed between the two groups as reflected by close mean positive and mean negative affect scores in IDAF-4C scores for dental anxiety and fear were collected before surgery. The data, along with mean PANAS scores and OHIP-14 scores, are presented in Table 10. Furthermore, participants in both groups were dentally anxious and fearful to a similar extent, and had similar mean OHIP-14 scores and impact prevalence. Participants’ personality and dental anxiety data were collected in case there was the need to control for participants’ personality if the two groups showed a significant difference in personality types. However, there was no difference, and so no such adjustment was required.
Table 11 provides a summary of the types and depths of impaction of the mandibular third molar teeth present in this study by group.

Table 11. Number and type of mandibular impactions (Pell and Gregory classification) and angulation type (Winter’s classification), by group (brackets contain column percentages unless otherwise indicated)

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th></th>
<th>Both combined</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV</td>
<td>SM</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tooth 38</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.52</td>
</tr>
<tr>
<td>1a</td>
<td>10 (15.2)</td>
<td>12 (18.2)</td>
<td>22 (16.7)</td>
<td></td>
</tr>
<tr>
<td>1b</td>
<td>7 (10.6)</td>
<td>6 (9.1)</td>
<td>13 (9.8)</td>
<td></td>
</tr>
<tr>
<td>1c</td>
<td>3 (4.5)</td>
<td>1 (1.5)</td>
<td>4 (3.0)</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>23 (34.8)</td>
<td>32 (48.5)</td>
<td>55 (41.7)</td>
<td></td>
</tr>
<tr>
<td>2b</td>
<td>11 (16.7)</td>
<td>8 (12.1)</td>
<td>19 (14.4)</td>
<td></td>
</tr>
<tr>
<td>2c</td>
<td>2 (3.0)</td>
<td>2 (3.0)</td>
<td>4 (3.0)</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>7 (10.6)</td>
<td>3 (4.5)</td>
<td>10 (7.6)</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>1 (1.5)</td>
<td>2 (3.0)</td>
<td>3 (2.3)</td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>2 (3.0)</td>
<td>0 (0.0)</td>
<td>2 (1.5)</td>
<td></td>
</tr>
<tr>
<td><strong>Angulation type</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.60</td>
</tr>
<tr>
<td>Vertical</td>
<td>21 (31.8)</td>
<td>25 (37.9)</td>
<td>46 (34.8)</td>
<td></td>
</tr>
<tr>
<td>Mesial</td>
<td>17 (25.7)</td>
<td>19 (28.8)</td>
<td>36 (27.3)</td>
<td></td>
</tr>
<tr>
<td>Horizontal</td>
<td>13 (19.7)</td>
<td>13 (19.7)</td>
<td>26 (19.7)</td>
<td></td>
</tr>
<tr>
<td>Distal</td>
<td>11 (16.7)</td>
<td>8 (12.1)</td>
<td>19 (14.4)</td>
<td></td>
</tr>
<tr>
<td>Transverse</td>
<td>4 (6.1)</td>
<td>1 (1.5)</td>
<td>5 (3.8)</td>
<td></td>
</tr>
<tr>
<td><strong>Tooth 48</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.63</td>
</tr>
<tr>
<td>1a</td>
<td>10 (15.2)</td>
<td>14 (21.2)</td>
<td>24 (18.2)</td>
<td></td>
</tr>
<tr>
<td>1b</td>
<td>6 (9.1)</td>
<td>3 (4.5)</td>
<td>9 (6.8)</td>
<td></td>
</tr>
<tr>
<td>1c</td>
<td>2 (3.0)</td>
<td>2 (3.0)</td>
<td>4 (3.0)</td>
<td></td>
</tr>
<tr>
<td>2a</td>
<td>27 (40.9)</td>
<td>25 (37.9)</td>
<td>52 (39.4)</td>
<td></td>
</tr>
<tr>
<td>2b</td>
<td>7 (10.6)</td>
<td>13 (19.7)</td>
<td>20 (15.2)</td>
<td></td>
</tr>
<tr>
<td>2c</td>
<td>4 (6.1)</td>
<td>2 (3.0)</td>
<td>6 (4.5)</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>4 (6.1)</td>
<td>4 (6.1)</td>
<td>8 (6.1)</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>6 (9.1)</td>
<td>3 (4.5)</td>
<td>9 (6.8)</td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td><strong>Angulation type</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.62</td>
</tr>
<tr>
<td>Vertical</td>
<td>19 (28.8)</td>
<td>22 (33.3)</td>
<td>41 (31.1)</td>
<td></td>
</tr>
<tr>
<td>Mesial</td>
<td>21 (31.8)</td>
<td>20 (30.3)</td>
<td>41 (31.1)</td>
<td></td>
</tr>
<tr>
<td>Horizontal</td>
<td>12 (18.2)</td>
<td>16 (24.2)</td>
<td>28 (21.2)</td>
<td></td>
</tr>
<tr>
<td>Distal</td>
<td>13 (19.7)</td>
<td>7 (10.6)</td>
<td>20 (15.2)</td>
<td></td>
</tr>
<tr>
<td>Transverse</td>
<td>1 (1.5)</td>
<td>1 (1.5)</td>
<td>2 (1.5)</td>
<td></td>
</tr>
</tbody>
</table>

The most common type of impaction was type 2a, followed by 1a and then 2b, categorised according to the Pell and Gregory classification (Pell and Gregory 1933). The most common impaction angulation was vertical, followed by mesial and then horizontal.
impaction (Winter 1926). There were no statistically significant differences between the two groups.

Overall, the two groups were very similar in demographic characteristics, surgical difficulty, history of frequency and intensity of third molar pain and its impact on quality of life.

5.4 Outcomes

5.4.1 Swelling, pain and mouth opening

Overall, participants in both groups had more facial swelling, pain and trismus on day 2 than on day 7. This observation was consistent across both groups (Table 12).

Table 12. Facial swelling, mouth opening distances and pain outcomes by group (brackets contain standard deviation unless otherwise indicated)

<table>
<thead>
<tr>
<th></th>
<th>IV</th>
<th>SM</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean facial swelling (cm³)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days 0-2</td>
<td>7.3 (4.2)</td>
<td>7.8 (4.4)</td>
<td>0.51</td>
</tr>
<tr>
<td>Days 0-7</td>
<td>2.9 (1.6)</td>
<td>2.6 (1.6)</td>
<td>0.24</td>
</tr>
<tr>
<td>Mean pain (VAS in mm)a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>16 (21)</td>
<td>13 (19)</td>
<td>0.40</td>
</tr>
<tr>
<td>Day 2</td>
<td>31 (23)</td>
<td>33 (22)</td>
<td>0.65</td>
</tr>
<tr>
<td>Day 7</td>
<td>18 (21)</td>
<td>21 (24)</td>
<td>0.54</td>
</tr>
<tr>
<td>Mean mouth opening (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>50.5 (6.5)</td>
<td>50.1 (7.3)</td>
<td>0.74</td>
</tr>
<tr>
<td>Day 2</td>
<td>33.7 (10.6)</td>
<td>34.5 (10.5)</td>
<td>0.66</td>
</tr>
<tr>
<td>Day 7</td>
<td>43.6 (11.8)</td>
<td>43.3 (12.1)</td>
<td>0.88</td>
</tr>
</tbody>
</table>

*aVisual analogue scale

The volume of facial swelling in the two treatment groups did not differ on either postoperative day. Participants in the IV group were 2.5 times less swollen on day 7 than on day 2. Participants in the SM group were 3.0 times less swollen on day 7 than on day 2. The difference between the groups was not statistically significant.

Mean pain scores did not differ between treatment groups on either postoperative days. In both groups, pain scores peaked on postoperative day 2 and had declined by day 7. In both groups, mean pain scores on postoperative day 7 were higher than the preoperative pain
scores. There was no complete resolution of pain by the 7th postoperative day. No statistically significant differences were observed between the two groups.

Limitation of mouth opening was most severe on postoperative day 2 in both groups. The amount of limitation observed at both postoperative follow-up time points was similar between the groups. From postoperative day 2 to day 7, there was a similar improvement to the restriction in the restriction of mouth opening in both groups. Complete recovery from restricted mouth opening was not achieved in either group by day 7.

No multivariate analysis of these outcomes was undertaken because the two groups were very similar.
5.4.2 Oral-health-related quality of life

OHIP-14 data were collected again on postoperative days 2 and 7, and the differences between preoperative and postoperative data are shown in Table 13.

Table 13. Impact of third molar surgery on quality of life over time by group (brackets contain standard deviation unless otherwise indicated)

<table>
<thead>
<tr>
<th>Group</th>
<th>Both combined</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>SM</td>
<td></td>
</tr>
<tr>
<td>Mean OHIP-14(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>9.5 (8.4)</td>
<td>10.7 (9.5)</td>
</tr>
<tr>
<td>Day 2</td>
<td>21.3 (9.6)</td>
<td>20.7 (9.7)</td>
</tr>
<tr>
<td>Day 7</td>
<td>21.0 (9.8)</td>
<td>22.2 (10.6)</td>
</tr>
<tr>
<td>Prevalence of 1+ impacts(^b)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>57 (86.4)</td>
<td>59 (89.4)</td>
</tr>
<tr>
<td>Day 7</td>
<td>53 (80.3)</td>
<td>58 (87.9)</td>
</tr>
</tbody>
</table>

\(^a\)OHIP-14 = Oral health impact profile – short version

\(^b\)Fairly often or very often; brackets containing row percentages

Both groups experienced poorer oral-health-related quality of life following third molar surgery, reflected in a marked increase in mean OHIP-14 scores on postoperative days 2 and 7. Preoperative OHIP scores were notably similar between the two groups but doubled from preoperative to day 2.

On day 2, more than 85% of participants in both groups had a detrimental impact to their quality of life. The impairment in quality of life continued at postoperative day 7.

On day 7, OHIP score remained as high as day 2 OHIP score in the IV group, while the SM group had a slight but further increase in OHIP score. The prevalence of 1+ impacts in both groups remained the same on day 7 as it was on day 2. On day 7, OHIP scores in both groups had neither returned to preoperative score nor fallen below preoperative scores. The potential reasons for the aforementioned observation will be discussed in Chapter 6.
Further analysis was undertaken to better understand the specific aspects of OHRQoL which were adversely affected by the surgical removal of mandibular third molars. This was done by analysing OHIP-14 subscale scores (Table 14).

Table 14. Mean OHIP-14 subscale scores before surgery, day 2 and day 7 by group (brackets contain standard deviations unless otherwise indicated)

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>IV group</th>
<th></th>
<th>Preoperative</th>
<th>SM group</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day 2</td>
<td>Day 7</td>
<td></td>
<td>Day 2</td>
<td>Day 7</td>
</tr>
<tr>
<td>Functional limitation</td>
<td>0.6 (1.0)</td>
<td>2.2 (1.5)</td>
<td>2.1 (1.7)</td>
<td>0.8 (1.2)</td>
<td>1.8 (1.5)</td>
<td>2.2 (1.9)</td>
</tr>
<tr>
<td>Physical pain</td>
<td>3.1 (2.3)</td>
<td>5.3 (1.6)</td>
<td>5.7 (1.7)</td>
<td>3.3 (2.2)</td>
<td>5.6 (1.7)</td>
<td>6.2 (1.6)</td>
</tr>
<tr>
<td>Psychological discomfort</td>
<td>1.6 (1.7)</td>
<td>2.6 (1.8)</td>
<td>2.0 (1.6)</td>
<td>1.8 (2.0)</td>
<td>2.5 (2.2)</td>
<td>2.1 (1.9)</td>
</tr>
<tr>
<td>Physical disability</td>
<td>1.1 (1.7)</td>
<td>4.8 (2.1)</td>
<td>4.7 (2.3)</td>
<td>1.5 (1.7)</td>
<td>4.6 (2.0)</td>
<td>5.2 (2.2)</td>
</tr>
<tr>
<td>Psychological disability</td>
<td>1.2 (1.3)</td>
<td>2.4 (1.8)</td>
<td>2.0 (1.6)</td>
<td>1.3 (1.5)</td>
<td>2.2 (1.8)</td>
<td>2.1 (1.8)</td>
</tr>
<tr>
<td>Social disability</td>
<td>1.2 (1.6)</td>
<td>2.6 (1.8)</td>
<td>2.7 (1.8)</td>
<td>1.2 (1.8)</td>
<td>2.6 (1.9)</td>
<td>2.9 (2.1)</td>
</tr>
<tr>
<td>Handicap</td>
<td>0.8 (1.3)</td>
<td>1.8 (1.9)</td>
<td>1.7 (1.8)</td>
<td>0.9 (1.4)</td>
<td>1.5 (1.7)</td>
<td>1.6 (1.9)</td>
</tr>
</tbody>
</table>

Mean OHIP-14 subscale scores increased in all subscales from preoperative to day 2 in both groups, with physical pain being the highest scoring subscale in both groups. The subscale with the biggest increase from preoperative to day 2 and day 7 was the physical disability subscale. This indicates that participants experienced a substantial interruption to their ability to eat their usual diet. Subscale scores remained the same from day 2 to day 7 in both groups, with the exception of physical pain, which increased in both groups. A complete recovery or improvement of quality of life was not achieved in either group by 7 days.
Patient self-reported data on time off work and the number of days where eating was affected are reported in Table 15.

Table 15. Recovery after surgery by group (brackets contain column percentages)

<table>
<thead>
<tr>
<th></th>
<th>Group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV</td>
<td>SM</td>
</tr>
<tr>
<td>Extraction affected work</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>45 (69.2)</td>
<td>48 (73.8)</td>
</tr>
<tr>
<td>No</td>
<td>20 (30.8)</td>
<td>17 (26.2)</td>
</tr>
<tr>
<td>Days taken off work</td>
<td>0.63</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>5 (7.7)</td>
<td>8 (12.5)</td>
</tr>
<tr>
<td>1-2</td>
<td>23 (35.4)</td>
<td>16 (25.0)</td>
</tr>
<tr>
<td>3-5</td>
<td>23 (35.4)</td>
<td>27 (42.2)</td>
</tr>
<tr>
<td>6 or more</td>
<td>14 (22.5)</td>
<td>13 (20.3)</td>
</tr>
<tr>
<td>Days eating affected</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>1-2</td>
<td>5 (7.6)</td>
<td>5 (7.6)</td>
</tr>
<tr>
<td>3-5</td>
<td>23 (34.8)</td>
<td>13 (20.0)</td>
</tr>
<tr>
<td>6 or more</td>
<td>38 (57.6)</td>
<td>47 (72.4)</td>
</tr>
</tbody>
</table>

In both groups, more than two-third of participants reported that the surgical procedure affected their work. Approximately a third of participants in both groups required 3-5 days off work after surgery. About a-fifth of participants in both groups had to take more than 6 days off work, or were still taking time off by day 7. A large proportion of participants found their eating pattern to be affected for more than 6 days. There were no differences in recovery after surgery between the two groups.
Specific post-surgical symptoms reported by participants are summarised by group in Table 16.

Table 16. Prevalence of post-surgery symptoms on day 2 and day 7 by group (brackets contain column percentages unless otherwise indicated)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Day 2</th>
<th>Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV&lt;sup&gt;a&lt;/sup&gt;</td>
<td>SM&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Swelling of cheeks</td>
<td>29 (43.9)</td>
<td>26 (37.4)</td>
</tr>
<tr>
<td>Bruising</td>
<td>9 (13.6)</td>
<td>6 (9.1)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>4 (6.1)</td>
<td>5 (7.6)</td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (15.8)</td>
<td>3 (4.5)</td>
</tr>
<tr>
<td>Bad taste/bad breath</td>
<td>18 (27.3)</td>
<td>9 (13.6)</td>
</tr>
<tr>
<td>Food collection in socket</td>
<td>7 (10.6)</td>
<td>6 (9.1)</td>
</tr>
</tbody>
</table>

<sup>a</sup>3 missing  
<sup>b</sup>2 missing  
<sup>c</sup>3 missing  
<sup>d</sup>3 missing

On day 2, the most prevalent post-surgery symptom was the facial swelling, with approximately 40% of participants in each group reporting swollen cheeks. By day 7, the prevalence of swelling was markedly reduced to 4 participants in total. These 4 participants had swelling measurements between 7.04 cm<sup>3</sup> and 15.03 cm<sup>3</sup> on day 7. Between day 2 and day 7, the symptom that showed the greatest improvement was postoperative swelling. On day 7, the symptom with the highest prevalence was food collection in socket, followed closely by bad taste/breath. This was equally prevalent in the two groups. Postoperative bleeding, bruising or nausea was not common in either group on either day.
5.5 Ancillary analyses

Analysis was carried out to determine whether participants who had maxillary third molars removed under the same IV sedation procedure experienced more postoperative swelling than participants who only had 2 mandibular third molars removed.

Table 17. Mean facial swelling in participants who had at least one maxillary third molar extracted (in addition to bilateral mandibular third molars) on day 2 and 7, both groups combined.

<table>
<thead>
<tr>
<th></th>
<th>Surgical removal of 38 and 48 only</th>
<th>Surgical removal of 38, 48 and at least one maxillary third molar</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 45)</td>
<td>(n = 80)</td>
<td></td>
</tr>
<tr>
<td>Mean facial swelling (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 2</td>
<td>8.6 (5.1)</td>
<td>7.0 (3.7)</td>
<td>0.06</td>
</tr>
<tr>
<td>Day 7</td>
<td>3.0 (2.0)</td>
<td>2.6 (1.3)</td>
<td>0.12</td>
</tr>
</tbody>
</table>

Participants who also had maxillary third molars removed had less swelling (on average), on both postoperative days, than those who had had only two mandibular third molars removed. The difference was not statistically significant.

Surgical time was measured from the time of mucosal incision to the placement of the final suture (for the two mandibular third molars only). The surgical time required was similar between the groups. Participants in each group also applied ice on the face for a similar duration of time, although there was considerable variation in the duration of postoperative application of ice within each group.

Table 18. Mean surgical time and duration of postoperative ice application by group (brackets contain standard deviation unless otherwise indicated)

<table>
<thead>
<tr>
<th></th>
<th>IV</th>
<th>SM</th>
<th>Combined average</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean surgical time (mins)(^a)</td>
<td>27.2 (12.7)</td>
<td>26.9 (12.5)</td>
<td>26.6 (12.4)</td>
<td>0.78</td>
</tr>
<tr>
<td>Mean duration of ice application (mins)</td>
<td>43.2 (99.0)</td>
<td>43.8 (101.9)</td>
<td>44.4 (105.2)</td>
<td>0.95</td>
</tr>
</tbody>
</table>

\(^a\)For mandibular third molars only
A linear regression model examined the amount of facial swelling present on day 7, controlling for relevant factors that may affect facial swelling (Table 19).

Table 19. Regression model for mean day 7 facial swelling

<table>
<thead>
<tr>
<th></th>
<th>Regression coefficient</th>
<th>95% Confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower bound</td>
<td>Upper bound</td>
</tr>
<tr>
<td>Day 2 swelling</td>
<td>0.17</td>
<td>0.11</td>
<td>0.23</td>
</tr>
<tr>
<td>Group</td>
<td>0.38</td>
<td>-0.12</td>
<td>0.89</td>
</tr>
<tr>
<td>Female</td>
<td>0.17</td>
<td>-0.35</td>
<td>0.68</td>
</tr>
<tr>
<td>Age</td>
<td>-0.01</td>
<td>-0.07</td>
<td>0.06</td>
</tr>
<tr>
<td>Surgical time taken</td>
<td>0.01</td>
<td>-0.01</td>
<td>0.03</td>
</tr>
<tr>
<td>Total time spent</td>
<td>0.00</td>
<td>0.00</td>
<td>0.01</td>
</tr>
</tbody>
</table>

The amount of swelling on day 2 had a weak positive linear association with the amount of facial swelling present on day 7; that is, the more swelling experienced by day 2, the greater the residual swelling observed by day 7 (Table 19). Facial swelling by day 7 was greater (on average) among those with more facial swelling after 2 days. Those who had spent more time applying ice to the face also had greater day 7 swelling. There were no differences by group.
Further analysis was done on surgical time required and recovery after surgery, as shown in Figure 8. The longer the surgical time, the greater the duration for which eating was affected.

Figure 8. Mean surgical time and days eating affected, both groups combined
5.6 Adverse Events

One participant from the IV group developed a large haematoma from the surgical removal of a deeply impacted left maxillary third molar requiring overnight hospitalization for intravenous antibiotics and observation. This was more likely the result of a greater degree of trauma from a technically difficult surgical extraction and was assumed to be unrelated to the dexamethasone exposure.

Eight participants experienced a known postoperative outcome that was unlikely to be attributed to the treatment allocation. In the IV group, 3 participants had alveolar osteitis and 1 participant had postoperative infection requiring socket irrigation and postoperative oral antibiotics. In the SM group, 2 participants had alveolar osteitis, 1 participant had postoperative infection and 1 participant reported prolonged socket bleeding not requiring professional intervention.

By day 7, a total of 11 participants (4 from the IV group and 7 from the SM group) reported insufficient pain control on the standardized prescription of Paracetamol 1000 mg oral tablets QID, ibuprofen 400 mg oral tablets QID, codeine 60 mg oral tablets QID. These participants were then advised to cease ibuprofen, and were prescribed a 5-day course of a selective cox-2 inhibitor, Etoricoxib, 120 mg tablet once daily.

There were no unexpected adverse events that required reporting or discontinuation of the trial.
6 Discussion

This chapter first presents a critical appraisal of the strengths and limitations of the methods employed in this study. The following sections will then consider the two key research questions that this study sought to answer. They were: (i) how do submucosal dexamethasone and intravenous dexamethasone compare in the reduction of postoperative swelling, pain and trismus in third molar surgery; and (ii) what is the subsequent impact on patients’ quality of life? The chapter will then conclude with a discussion of the clinical implications of the study findings, followed by consideration of the directions for further research.

6.1 Appraisal of methods

6.1.1 Study design

To my knowledge at the time of writing, the present study is the first randomised control trial to compare the efficacy of submucosal and intravenous dexamethasone in the reduction of swelling, pain and trismus following third molar surgery and using a contactless 3D imaging technology to objectively quantify facial swelling. This trial involved a total of 125 participants, a sample size greater than the minimum required (104) for an anticipated effect size of 0.5, a significance level of 0.05 and a power of 80%.

It is important to eliminate or reduce bias resulting from participants’ or the investigator’s perceived expectation of how the route of dexamethasone administration might affect postoperative outcomes of swelling, pain and trismus. A major strength of the study was that the only non-blinded person involved in the study was the hospital pharmacist. The blinding remained in place for all other parties until the statistical analysis was completed. This minimised (if not eliminated) bias in measurement and reporting of the outcomes. Another strength of the study was the random allocation of participants into the two treatment groups. Baseline characteristics were similar for both groups (see 5.3.1 Baseline data), indicating that the random allocation of participants obtained two comparable groups for the study. It reduced the likelihood that the study outcomes were the result of uncontrolled or unknown confounders. Moreover, the study standardized treatment by ensuring: that a single operator performed all surgical procedures using a standardized soft
tissue flap design and bone removal for the extraction of both mandibular third molars; that all participants were administered 40 mg IV parecoxib and a titrated dose of IV midazolam and local anaesthesia; that all participants received a standardized prescription of drug for analgesics; that image acquisition of each participant was done in maximum intercuspation, natural head posture and a neutral facial expression; and that a single observer conducted the superimposition and data acquisition of facial swelling for all participants using the 3dMD.vultus software.

The surgical difficulty of a third molar extraction can influence the degree of adverse postoperative outcomes. The more difficult or time-consuming the extraction, the more surgical trauma there would be to the hard and soft tissues, resulting in pain afterwards (Pedersen 1985b). The Pell and Gregory classification has been extensively adopted and applied in clinical practice as an indicator of the difficulty of a mandibular third molar extraction (Pell and Gregory 1933). It is based on the tooth’s spatial relationship (as revealed by radiograph) with the ascending ramus of the mandible and with the occlusal plane. It does not take into account other important radiographic and clinical factors that contribute to the difficulty of extraction. Akadiri & Obiechina (2009) demonstrated that depth, angulation and root morphology were consistent determinants of surgical difficulty. Carvalho & Vasconcellos (2011) concluded that root number, tooth position, periodontal space and second molar relation were important predictors of surgical difficulty. The Pell and Gregory classification does not take into account the type of impaction (mesial, horizontal, vertical, distal or oblique impaction), which also is a contributory factor in determining the surgical difficulty of an extraction. Hence, that classification can lack specificity and sensitivity (Aznar-Arasa et al. 2014). Despite the shortfalls of the Pell and Gregory classification, many clinical trials continue to use it (Graziani et al. 2005; Ram and Siar 2005; Antunes et al. 2011; Majid and Mahmood 2011; Alcântara et al. 2014; Koçer et al. 2014; Chaudhary et al. 2015). To maintain uniformity and consistency with the existing literature, the Pell and Gregory classification appeared most appropriate for the present study.

The present study used a take-home diary to collect pain and quality of life data. There are a number of challenges in collecting real-world measures, such as a lack of control over measure completion, which can result in missing data. There is also poor control over the
environment and circumstances in which the assessment is done. Younger et al. (2009) have pointed out that collection via paper diaries is prone to “backfilling” (which is, to fill in by retrospectively guessing). To minimize that, participants were reminded at each postoperative visit to fill in their diaries, and were encouraged to fill in the take-home diary every day at a consistent time of day. There were a total of 5 participants (2 from the IV dexamethasone group, 3 from the SM dexamethasone group) who did not return their diary, and so they had to be excluded from the quality of life analyses. The exclusion of these participants did not negatively affect the statistical power of the trial, since there were a greater number of participants (125) than the minimum required (104).

Clinical trials that have specifically investigated how dexamethasone affected postoperative swelling, pain and trismus after third molar surgery typically measured these outcomes on days 2 or 3, and day 7. Observation periods have not extended beyond postoperative day 7 (Bhargava et al. 2013; Majid and Mahmood 2013; Saravanan et al. 2016; Gopinath et al. 2017; Kumar 2017; Mojsa et al. 2017; Vivek et al. 2017). Accordingly, the observation period for this study was up to day 7. It was interesting to note that, in this study, a complete recovery or improvement of quality of life was not achieved in either group by 7 days. It may be of value to extend the duration of such studies to well beyond 7 days, until participants report full recovery. This may add value to our current understanding of patients’ recovery processes. However, a potential disadvantage of a longer period of study is a higher number of patient drop-outs and poorer adherence to data collection procedures (Merry et al. 2010).

It is postulated that local infiltration around the surgical site may provide a repository effect that would slow absorption and result in a prolonged duration of action than with intravenous injection (Antunes et al. 2011). Accordingly, systemic dexamethasone may be less effective at the site of surgical trauma than a local infiltration. A key point of interest that remains unclear is whether submucosal dexamethasone acts strictly on the local tissues alone without systemic absorption. Submucosal dexamethasone was administered after the administration of local anaesthesia containing adrenaline. The use of adrenaline results in vasoconstriction, thereby reducing the amount of dexamethasone being carried away from the area of interest by the blood supply. While the adrenaline temporarily keeps the dexamethasone acting locally, the current study was not designed to make any
observations on its systemic absorption. In order to determine this, blood and urine samples would need to be collected from participants at multiple time points (e.g. ¼, ½, 1, 2, 4, 6, 8 hour blood samples and overnight urine), for analysis via radioimmunoassay (English et al. 1975; Zirker et al. 1976). This was not feasible in the present study.

6.1.2 Study sample

The study sample consisted mainly of healthy young adults, with a mean age of 22.6 years old. This is consistent with the expected eruption timeline of third molars, with the greatest need for third molar surgery being between the late teenage years and the early twenties. It may be argued that this sample is not representative of the general population. On the other hand, this sample was appropriate given that it is precisely this age group that is more likely to undergo third molar surgery. Moreover, RCTs are conducted primarily to examine the efficacy of particular interventions, with generalizability of findings not usually a primary goal.

6.2 Research Questions

This section will consider the implications of the findings of this study, and how the findings relate to the research questions that this study sought to answer.

6.2.1 How did submucosal dexamethasone and intravenous dexamethasone compare in the reduction of postoperative swelling, pain and trismus after third molar surgery?

In the present study, there were no differences in swelling, pain and trismus between the groups at any time. This finding is consistent with the only other randomized, double-blind clinical trial by (Bhargava et al. 2014). While their method of measuring facial swelling was different from the one used in the present study, the outcomes measured showed very similar findings, in that there were no differences in swelling, pain and trismus on both days 1, 3 and 7. The common strengths in both studies includes both being double-blinded, and both involving participants who were randomly allocated into the treatment groups, thereby minimizing bias.
The present study findings show that participants in both groups had more swelling, pain and trismus on day 2 than on day 7. This observation was consistent across both groups (Table 12) and could be regarded as a normal trend in postoperative recovery following minor oral surgery. Participants in both groups experienced a marked reduction in facial swelling from day 2 to day 7. For the majority of participants in both groups, facial swelling had subsided to the point where they no longer considered themselves to be swollen by day 7. This finding is consistent with that of the 5 relevant clinical trials included in the literature review (Section 2.3). This also suggests that the mean residual swelling (2.9 cm³ in the IV group, 2.6 cm³ in the SM group) by day 7 is not clinically significant.

Interestingly, despite an improvement in the VAS pain scores and mouth opening measurements between day 2 and day 7, day 7 pain scores and mouth opening measurement in both groups had not returned to preoperative values (Table 12). In other words, participants continued to experience a small degree of pain and trismus at the end-point of the study. This observation is consistent with the findings reported by Majid and Mahmood (2013), Gopinath et al. (2017) and Kumar (2017).

A possible reason for participants continuing to experience trismus is ongoing pain. There was empirical evidence in this study for this observation: participants frequently remarked during mouth opening measurement that they “can open wider, but it will start to hurt”. This implies two findings: first, the presence or size of swelling was not directly related to pain or trismus; and second, limiting mouth opening was a voluntary act in order to avoid pain. These findings are consistent with findings from a clinical trial reported by Pedersen (1985b), who concluded that swelling does not correspond with either trismus or pain. Instead, there was a strong inter-relation between pain and trismus, indicating that pain was an important reason for reduced mouth opening after third molar surgery. Accordingly, the logical suggestion that follows is that, in the absence of pain, there should not be any reported trismus. This was shown to be the case in two separate clinical trials by Bhargava et al. (2014) and Vivek et al. (2017). In both trials, patients with full resolution of pain by day 7 also reported full resolution of trismus.
Food impaction in the extraction socket is a possible reason for ongoing pain or discomfort. In the present study, food impaction in the socket was the most prevalent symptom reported by patients on day 7 (Table 16). This may be the result of their attempting a regular diet, having been on a softer, non-chew diet in the days immediately after surgery. At the same time, mucosal healing by day 7 would have resulted in a smaller and less conspicuous soft tissue opening that is less amenable to good oral hygiene (Dubois et al. 1982). This finding is consistent with observations reported from other clinical trials. In a Brazilian study of 128 patients, 21.9% of patients reported collection of food particles in the extraction site on the 7th day. Some 47% of patients still presented with bad taste/breath on the 7th day (Sato et al., 2009). An American survey of 201 patients after third molar surgery reported that food collection in the surgical sites posed the biggest problem for patients on day 9. This had only gradually resolved by the end of a 2-week period (Conrad et al. 1999). Food impaction in the socket could also be a contributory factor to the persistent elevated pain scores observed in the current study on day 7. A recent clinical trial by Cho et al. (2018) compared the differences in food impaction after using chlorhexidine mouthwash and chlorhexidine syringe irrigation. They found that the irrigation group had lower levels of food impaction and subsequently experienced less postoperative pain and had a lower incidence of alveolar osteitis. It was interesting to note, however, that all wounds were closed by primary intention, which by itself, would not have left an open socket for food to accumulate. There is a need for further clinical trials to compare socket irrigation to mouth-rinsing and its effectiveness in preventing food accumulation in sockets that are closed by secondary intention.

### 6.2.2 What was the subsequent impact on patients’ quality of life?

Both groups experienced poorer oral-health-related quality of life following third molar surgery, reflected in a markedly higher mean OHIP-14 scores on postoperative days 2 and 7 (Table 13). There was no detected difference in OHIP-14 scores between the two groups on either day.

Interestingly, there was little or no improvement in OHIP-14 scores from day 2 to day 7 in either group. One possible reason for this is that, during the early days, participants benefitted from the mild euphoria that has been reported and observed in patients for up to 72 hours after administration of dexamethasone (Schaberg et al. 1984; Neupert et al. 1992;
Becker 2013), resulting in an artificially lowered OHIP-14 score on day 2. Another possible reason that that participants were psychologically prepared for (and accepting of) swelling, pain and trismus during the immediate days following surgery but were less prepared for these adverse outcomes to persist for a week after the surgery.

It was interesting to note that OHIP-14 subscale scores remained the same from day 2 to day 7 in both groups, with the exception of physical pain, which increased in both groups (Table 14). This is in contrast to the mean VAS scores (Table 12) which decreased from 2 to day 7 in both groups. A possible explanation for this contradictory observation may be directly related to the limitations of the 100mm VAS: participants may find it difficult to choose a single digit to represent what is a multi-dimensional and complex experience; and the VAS is limited to providing a pain rating at the particular point in time without reflecting possible fluctuations in pain levels throughout the day. Additionally, it must be noted that the OHIP-14 instrument is not solely a pain measure, whereas the VAS is used exclusively as a pain measurement tool. It is also important to consider that the usual reference period of the OHIP-14 is four weeks, in that each item elicits information about how frequently patients experience a specific impact in the last month. In the present study, the reference period was modified for a shorter time timeframe of seven days.

By the end of the study period, many participants still experienced poorer oral health related quality of life than their preoperative status. This was likely due to ongoing pain and trismus by day 7, as discussed above. This observation is consistent with that of Ruvo et al. (2005) in their study of delayed clinical healing after third molar surgery and its impact on quality-of-life recovery. Ruvo et al. (2005) reported that delayed clinical healing (in specific, delayed resolution of pain, food collection or bad taste/breath, delayed recovery of mouth opening, regular diet and/or chewing) substantially impacted quality-of-life recovery after third molar surgery.

The findings of the present study also suggest that the adverse outcomes of third molar surgery frequently persist beyond one week. This finding was similar to the findings of a prospective cohort study by McGrath et al. (2003) in Hong Kong. Similarly, Savin and Ogden (1997) found that almost half of their patients were still experiencing pain one
week later, with no significant improvement in pain experienced over that week. Conrad et al. (1999) observed that patients reported only minimal pain by 9 days after surgery.

6.3 Clinical implications of the study findings

With comparable impact on postoperative outcomes to IV administration, submucosal administration of dexamethasone is an efficacious method of delivery for the reduction of adverse postoperative swelling, pain and trismus after third molar surgery. Patients undergoing third molar surgery under local anaesthesia only (that is, without an IV line in place) can reap the benefits of a submucosal injection of dexamethasone. Submucosal dexamethasone is cost-effective, simple and easy to administer for specialists and general dental practitioners alike. In the case of IV sedation, where the patient maintains consciousness, the operator may choose to administer dexamethasone via the submucosal route to avoid the unpleasant, known side-effect of a perineal itch or burn that is occasionally experienced during intravenous administration of dexamethasone (Neff et al. 2002; Dylla et al. 2018).

6.4 Generalizability of findings to other surgical fields

Many autogenous block bone grafts in the field of implantology are harvested from the oral cavity, including from the external oblique ridge, mandibular ramus and the chin region. Surgical access to these donor sites requires a substantial amount of stripping of the periosteum and muscle attachment (for example, the mentalis muscle at the menton, and the masseter at the ramus of the mandible), resulting in significant postoperative swelling. To date, there are no randomised clinical trials investigating the role of dexamethasone in reducing adverse postoperative outcomes at the donor site following harvesting of a block bone graft. Given that some patients may opt to have a bone graft procedure performed under local anaesthesia only, an injection of submucosal dexamethasone at the donor site may provide anti-inflammatory benefits in improving postoperative recovery.

The administration of submucosal dexamethasone after apicectomy surgery has recently been explored. Kan et al. (2016) concluded that 4 mg submucosal dexamethasone had minimal impact on swelling, pain, bruising and wound healing at any time over a 7-day interval. Contrary to this, Shah et al. (2011) found that 4 mg submucosal dexamethasone
resulted in significant reduction in swelling and pain after apicectomy. More high quality randomised control trials are needed to evaluate the efficacy of submucosal dexamethasone in postoperative recovery from apicectomy procedures.

Gao et al. (2015) conducted a clinical trial to compare local infiltration of dexamethasone to intravenous injection for postoperative pain and recovery after tonsillectomy. They found that submucosal injection of dexamethasone shortened the time to first postoperative oral water and solid food intake than intravenous dexamethasone. However, it was pointed out that intravenous dexamethasone provided a better anti-emetic effect in patients undergoing general anaesthesia (GA). This highlights an important limitation of submucosal dexamethasone, which may limit its popularity as a route of administration when procedures are performed under GA.

6.5 Future directions

The use of 3D stereophotography to measure and analyse facial swelling after third molar surgery is a relatively new application of the technology. Further research of a similar nature is required to standardise and validate a soft tissue surface landmark to clearly define the area of swelling after third molar surgery. This will facilitate consistency in reporting in future trials for better comparison of results. The superimposition and analysis process was a tedious and time-consuming process that required more than 150 man-hours in this study. More powerful software algorithms and automation may improve efficiency and accuracy for the superimposition of images that were taken on different days.

There is a need to improve our current understanding of the pharmacodynamics and pharmacokinetics of dexamethasone in the oral submucosal tissue in order to evaluate the differences associated with local (eg. submucosal) and systemic (eg. intravenous) routes of administration. Future studies are needed to assess serum levels of locally administered dexamethasone in order to shed light on this important determinant.

Oral intake of dexamethasone is another possible route of administration. In terms of its ease of use, it is comparable with submucosal dexamethasone. It would be useful for a RCT to compare the efficacy of oral and submucosal dexamethasone in the reduction of adverse postoperative outcomes after third molar surgery.
7 Conclusions

Based on the findings of this study, the following conclusions are presented.

There are no differences in postoperative adverse outcomes between submucosal and intravenous administration of dexamethasone in third molar surgery.

Submucosal dexamethasone is a cost-effective, simple and effective route of dexamethasone administration for patients undergoing third molar surgery with local anaesthesia only.

Third molar surgery results in a poorer oral-health-related quality of life following third molar surgery, and it can affect patients for more than 7 days after surgery.
8 References


Majid OW, Mahmood WK. 2013. Use of dexamethasone to minimise post-operative


Rohdewald P, Möllmann H, Barth J, Rehder J, Derendorf H. 1987. Pharmacokinetics of


Appendices

Appendix 1. Health and Disability Ethics Committees Approval

Health and Disability Ethics Committees
Ministry of Health
133 Molesworth Street
PO Box 5019
Wellington
0411

(0604) 4 ETHICS
hdvee@mohe.govt.nz

14 August 2017

Ms Arlewyn Lau
310 Great King Street
Dunedin 9016

Dear Ms Lau

Re: Ethics ref: 17/NTB/127

Study title: A comparative study of the efficacy of intravenous (iV) dexamethasone versus submucosal (SM) dexamethasone in the reduction of post-operative outcomes after surgical removal of third molars: A double-blind randomized controlled trial.

I am pleased to advise that this application has been approved by the Northern B Health and Disability Ethics Committee. This decision was made through the HDEC-Full Review pathway.

Conditions of HDEC approval

HDEC approval for this study is subject to the following conditions being met prior to the commencement of the study in New Zealand. It is your responsibility, and that of the study’s sponsor, to ensure that these conditions are met. No further review by the Northern B Health and Disability Ethics Committee is required.

Standard conditions:

1. Before the study commences at any locality in New Zealand, all relevant regulatory approvals must be obtained.

2. Before the study commences at any locality in New Zealand, it must be registered in a clinical trials registry. This should be a WHO-approved such as the Australia New Zealand Clinical Trials Registry, www.anzctr.org.au. However, https://clinicaltrials.gov/ is acceptable provided registration occurs prior to the study commencing at any locality in New Zealand.

3. Before the study commences at a given locality in New Zealand, it must be authorised by that locality in Online Forms. Locality authorisation confirms that the locality is suitable for the safe and effective conduct of the study, and that local research governance issues have been addressed.

Non-standard conditions:

— The committee note the lower age threshold for inclusion has been amended to 15 years old and the upper age threshold to 40 years. Please ensure this is amended in all relevant study documents such as the protocol.

Non-standard conditions must be completed before commencing your study. Non-standard conditions do not need to be submitted to or reviewed by HDEC before commencing your study.
If you would like an acknowledgement of completion of your non-standard conditions letter you may submit a post approval form amendment. Please clearly identify in the amendment that the changes relate to non-standard conditions and ensure that supporting documents (if requested) are tracked/highlighted with changes.

For information on non-standard conditions please see section 128 and 129 of the Standard Operating Procedures at http://ethics.health.govt.nz/home.

After HDEC review

Please refer to the Standard Operating Procedures for Health and Disability Ethics Committees (available on www.ethics.health.govt.nz) for HDEC requirements relating to amendments and other post-approval processes.

Your next progress report is due by 13 August 2018.

Participant access to ACC

The Northern B Health and Disability Ethics Committee is satisfied that your study is not a clinical trial that is to be conducted principally for the benefit of the manufacturer or distributor of the medicine or item being trialled. Participants injured as a result of treatment received as part of your study may therefore be eligible for publicly-funded compensation through the Accident Compensation Corporation (ACC).

Please don’t hesitate to contact the HDEC secretariat for further information. We wish you all the best for your study.

Yours sincerely,

Kate O’Connor
Chairperson
Northern B Health and Disability Ethics Committee

End: appendix A: documents submitted
      appendix B: statement of compliance and list of members
## Appendix A

### Documents submitted

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Appendix B
Statement of compliance and list of members

Statement of compliance

The Northern B Health and Disability Ethics Committee:

- is constituted in accordance with its Terms of Reference
- operates in accordance with the Standard Operating Procedures for Health and Disability Ethics Committees, and with the principles of international good clinical practice (GCP)
- is approved by the Health Research Council of New Zealand’s Ethics Committee for the purposes of section 25(1)(c) of the Health Research Council Act 1990
- is registered (number 00008715) with the US Department of Health and Human Services’ Office for Human Research Protection (OHRP).

List of members

<table>
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<th>Name</th>
<th>Category</th>
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<td>Mr John Harlock</td>
<td>Lay (the law)</td>
<td>14/12/2015</td>
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<td>Dr Nora Lynch</td>
<td>Non-lay (health/disability service provision)</td>
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<td>Miss Terehisa Macfarlane</td>
<td>Lay (consumer/community perspectives)</td>
<td>30/05/2017</td>
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<td>Mrs Kate O’Connor</td>
<td>Lay (ethics/moral reasoning)</td>
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<td>14/12/2018</td>
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<td>Mrs Stephanie Poland</td>
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<td>01/07/2015</td>
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<td>Mrs Leesa Russell</td>
<td>Non-lay (intervention studies), Non-lay (observational studies)</td>
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<td>Mrs Jane Wylie</td>
<td>Non-lay (intervention studies)</td>
<td>20/05/2017</td>
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Unless members resign, vacate or are removed from their office, every member of HDEC shall continue in office until their successor comes into office (HDEC Terms of Reference)

http://www.ethics.health.govt.nz
Appendix 2. Registration with Australian New Zealand Clinical Trials Registry

Your ACTRN (registration number): ACTRN12617001203347

info@actr.org.au
toadelyn.lau

Dear Adelyn Lau,

Re: Routes of Desamethasone Administration during Wisdom Teeth Removal

Thank you for submitting the above trial for inclusion in the Australian New Zealand Clinical Trials Registry (ANZCTR).

Your trial has now been successfully registered and allocated the ACTRN: ACTRN12617001203347


Date submitted: 10/08/2017 7:23:26 PM
Date registered: 17/08/2017 10:21:58 AM
Registered by: Adelyn Lau
Principal Investigator: Adelyn Lau

If you have already obtained Ethics approval for your trial, please send a copy of at least one Ethics Committee approval letter to info@actr.org.au or by fax to (+61 2) 9665 1863, attention to ANZCTR.

Note that updates should be made to the registration record as soon as any trial information changes or new information becomes available. Updates can be made at any time and the quality and accuracy of the information provided is the responsibility of the trial’s primary sponsor or their representative (the registrant). For instructions on how to update please see http://www.anzctr.org.au/SupportHowToUpdate.aspx.

Please also note that the original data lodged at the time of trial registration and the tracked history of any changes made as updates will remain publicly available on the ANZCTR website.

The ANZCTR is recognised as an ICMJE acceptable registry (http://www.icmje.org/ifp.pdf) and a Primary Registry in the WHo registry network (http://www.who.int/clinicaltrialsregister/en/index.html).

If you have any enquiries please send a message to info@actr.org.au or telephone +61 2 9665 5333.

Kind regards,
ANZCTR Staff
T: +61 2 9665 5333
F: +61 2 9665 1863
E: info@actr.org.au
W: www.ANZCTR.org.au
Appendix 3. Maori consultation

Ngāi Tahu Research Consultation Committee
Te Komiti Rakaahu ki Kai Tahu

Tuesday, 02 May 2017.

Associate Professor Rohana De Silva,
Faculty of Dentistry - Department of Oral Diagnostic and Surgical Sciences,
DUNEDIN.

Tēnā Koe Associate Professor Rohana De Silva,

A comparative study of the efficacy of intravenous (IV) dexamethasone versus submucosal (SM) dexamethasone in the reduction of post-operative outcomes (swelling, pain, trismus) and its impact on quality of life after third molar surgery.

The Ngāi Tahu Research Consultation Committee (the committee) met on Tuesday, 02 May 2017 to discuss your research proposition.

By way of introduction, this response from The Committee is provided as part of the Memorandum of Understanding between Te Rūnanga o Ngāi Tahu and the University. In the statement of principles of the memorandum it states "Ngāi Tahu acknowledges that the consultation process outlined in this policy provides no power of veto by Ngāi Tahu to research undertaken at the University of Otago". As such, this response is not "approval" or "mandate" for the research, rather it is a mandated response from a Ngāi Tahu appointed committee. This process is part of a number of requirements for researchers to undertake and does not cover other issues relating to ethics, including methodology they are separate requirements with other committees, for example the Human Ethics Committee, etc.

Within the context of the Policy for Research Consultation with Māori, the Committee base consultation on that defined by Justice McGeorge:

"Consultation does not mean negotiation or agreement. It means: setting out a proposal not fully decided upon; adequately informing a party about relevant information upon which the proposal is based; listening to what the others have to say with an open mind (in that there is room to be persuaded against the proposal); undertaking that task in a genuine and not cosmetic manner. Reaching a decision that may or may not alter the original proposal."

The Committee notes this is Southern District Health Board research.

The Committee considers the research to be of importance to Māori health.

As this study involves human participants, the Committee strongly encourage that ethnicity data be collected as part of the research project. That is the questions on self-identified ethnicity and descent, those questions are contained in the latest census.

The Committee suggests dissemination of the findings to relevant Māori health organisations, for example the National Māori Organisation for Dental Health, Oranga Noho and to Professor John Broughton and Malcolm Dacker, who are involved in Māori Dental Health, University of Otago.

The Ngāi Tahu Research Consultation Committee has membership from:
Te Rūnanga o Ōrākei Incorporated
Kīti Haurapa Rūnanga ki Pukerewa
Te Rūnanga o Moeraki
We wish you every success in your research and the Committee also requests a copy of the research findings.

This letter of suggestion, recommendation and advice is current for an 18 month period from Tuesday, 02 May 2017 to 2 November 2018.

Nāhaku noa, nā

Mark Brunton
Kaiwhakahuere Rangahau Māori
Research Manager Māori
Research Division
Te Whare Wānanga o Otago
Pte: +64 3 479 8738
Email: mark.brunton@otago.ac.nz
Web: www.otago.ac.nz

The Ngāi Tahu Research Consultation Committee has membership from:

Te Rūnanga o Ōtākou Incorporated
Kāti Huiŋaunui Rūnaka ki Pokaiareiakura
Te Rūnanga o Moeraki
Appendix 4. New Zealand Dental Association Research Fund

ADVICE OF RESEARCH FUNDING GRANT APPLICATION AS ASSESSED BY THE BOARD
OF THE NEW ZEALAND DENTAL RESEARCH FOUNDATION
NZDA HOUSE, 19 JULY 2017

Date of Advice 3 August 2017

Name of Applicant/s Adelyn LAU, D Tong, M Thomson, R De Silva, H De Silva

Award Reference RF8.09 2017

Title of Research

Amount Awarded $9,700 Continuing Dental Education Trust (Auckland) Award Note. The request for $800 data storage costs was not supported by the NZDRA Board

Condition/s of Award Funding of this project is conditional on the applicants providing assurance that the project can be completed with this level of funding, on ethics approval being obtained, and in accordance with the reporting conditions below. A payment of $9,700 will be made on the receipt of an invoice for such. Progress Reports, a Final Report and abstract are due on the dates shown below. Please provide copies of any publications arising from the research with your reports.

Project Start Date 01/11/2017
Project End date 31/10/2019

1st Progress Report due 15/05/18 Please email your report (template here http://www.otago.ac.nz/otago409403.html) to research@otago.ac.nz

2nd Progress Report due 15/05/19 Please email your report (template here http://www.otago.ac.nz/otago409403.html) to research@otago.ac.nz

Final report and Abstract due 31/10/19 Please email your report (template here http://www.otago.ac.nz/otago409403.html) to research@otago.ac.nz

General Comments
The project ranked sufficiently for the Board to agree to award $9,700 subject to the payment conditions. Publications should acknowledge funding support from the NZ Dental Research Foundation and Continuing Dental Education Trust (Auckland), and include the award reference number.

Signed: Richard Jeffreys (Chair, New Zealand Dental Research Foundation Board)

The Principal Researcher should sign and date this advice notice in the panel below and then return a COPY to research@otago.ac.nz to acknowledge the conditions and enable payment of the Award. If the Principal Researcher is a post-graduate student, then the student's supervisor should sign and return this form. Thank you.

Name: R. K. De Silva Signed: Signed: Date: 4/11/2017

Principal Researcher OR Student Supervisor

1 Abstract should be suitable for publication in the NZDA News
Appendix 5. Information sheet for participants

INFORMATION SHEET FOR PARTICIPANTS

Study title: Routes of dexamethasone administration during wisdom teeth removal
Locality: Department of Oral Diagnostics and Surgical Sciences, Faculty of Dentistry
Lead investigator: Adelyn Lau
Lead supervisor: Mr Rohana De Silva (Consultant Oral and Maxillofacial Surgeon)
Contact number: 479 7023
Ethics committee reference: 17/NTB/127 (Health and Disability Ethics Committee)

You are invited to take part in a study on the route of dexamethasone administration during wisdom teeth removal. Whether or not you take part is your choice. If you do not want to take part, you do not have to give a reason, and it will not affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is 5 pages long, including the Consent Form. Please make sure you have read and understood all the pages.
What is the purpose of the study?
Dexamethasone is a steroid injection used routinely in the removal of wisdom teeth to reduce swelling. The steroid can be injected into the veins (intravenous) or into the gums (submucosal). At the dental school, we have been giving it intravenously. However, the best way of giving the steroid to achieve maximum anti-swelling effects is not known. The aim of this study is to address this unknown, and this is done by measuring the differences in swelling and pain in these two groups after wisdom teeth removal. Patients will be randomly allocated into a group using a computer. Neither the surgeon nor the you will be told which group you are placed into as this helps to reduce any bias or placebo results.

What will my participation in the study involve?
You have met our inclusion and exclusion criteria which can be summarized as anyone, between the ages of 16 to 40, who requires the removal of at least 2 impacted lower wisdom teeth and has a physical health status of ASA (American Society of Anaesthesiology) 1 or 2. 16 years old is the legal age for independent consent, and patients above 40 years of age tend to present with a higher level of surgical difficulty and a more complex medical background.

Should you agree to take part in this project, you will be asked to:
1. Before the surgery:
   • Fill out a short questionnaire asking about things such as your age, gender, occupation, oral hygiene practice, past or present pain associated with your wisdom teeth, and whether you experience anxiety at the dentist.
   • Take measurements of your face using a 3D facial camera.
2. Attend the surgery
3. After the surgery:
   • Attend Post-Surgical appointments with Dr Adelyn Lau on Days 2 and 7 after your procedure for repeat measurements to be taken with a measuring tape, as well as with a 3D facial scanner.
   • Fill in a 7-day daily diary.

What are the possible benefits and risks of this study?
The use of intravenous steroid is part of our routine care provided at the School of Dentistry. There are therefore no increased risks of participating in the study, since you will be given the same dosage of steroid (Dexamethasone) in both groups, only that the route of administration will vary. Both routes of administration are established methods in the context of wisdom teeth removal.

If you were injured in this study, which is unlikely, you would be eligible to apply for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will be automatically accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery. If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won’t affect your cover.
Who pays for this study?
This research is undergoing funding application with the New Zealand Dental Research Funding (NZDARF) body. The funds are going into the preparation of the steroids used in this research. You will be fee-paying for the consultation and surgical removal of your wisdom teeth according to the fee schedule provided by the Faculty of Dentistry.

What are my rights?
Your participation in this study is strictly confidential. Any personal information such as your name, age, gender, and contact details will remain anonymous. The facial images will be stored separately from the other study data to protect your identify. The “raw data” collected will be stored securely at the University of Otago for a period of 10 years, after which time the data will be destroyed. You will not be identified in any form of publication.

What happens after the study or if I change my mind?
Your participation in this research is entirely voluntary and you can withdraw at any time without affecting your dental care.

This data will be used only be the primary research and the four supervisors involved in this project. The results of this study will be written up in the form of a thesis and may later be summarized and published in an internationally recognized dental journal in order that other dentists and their patients may benefit. You are welcome to request a copy of the final results of this research project if you so desire. You have the right to access your personal data through the Dental School protocols as well.

Who do I contact for more information or if I have concerns?
If you require any additional information, please do not hesitate to contact Dr Adelyn Lau or Mr Rohana De Silva on (03) 479 7023 during business hours.

If you need to contact the oral surgery team following your wisdom teeth surgery, you may do so during business hours on (03) 479 23, or alternatively, as an after-hours emergency on 027 228 4604.

If you need to contact a Maori cultural support person, please contact Professor John Broughton, Associate Dean (Māori) of the Faculty of Dentistry on (03) 479 7639.
CONSENT FORM

Routes of Dexamethasone Administration during Wisdom Teeth Removal

Please tick to indicate you consent to the following

<table>
<thead>
<tr>
<th>Statement</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have read, or have had read to me in my first language, and I understand the Participant Information Sheet.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have been given sufficient time to consider whether or not to participate in this study.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my dental care.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I consent to the research staff collecting and processing my information, including information about my health.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I understand the compensation provisions in case of injury during the study.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
I know who to contact if I have any questions about the study in general. Yes ☐ No ☐

I understand my responsibilities as a study participant. Yes ☐ No ☐

I wish to receive a summary of the results from the study. Yes ☐ No ☐

Declaration by participant:
I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Declaration by member of research team:
I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date:

Thank you for your participation.
PRE-OPERATIVE QUESTIONNAIRE

General Information

Oral and Maxillofacial Surgery research project
Department of Oral Diagnostic and Surgical Sciences, School of Dentistry, University of Otago

Principal Researcher: Adelyn Lau (Doctor of Clinical Dentistry, Oral Surgery post-graduate student)

Principal Supervisor: Mr Rohana De Silva (Consultant Oral and Maxillofacial Surgeon)

Thank you for taking the time to fill in this questionnaire.

For information about this research project, please read the form entitled: “Information sheet for participants: Routes of Dexamethasone Administration during Wisdom Teeth Removal.”

All personal information will remain strictly confidential.

Please answer honestly. There will be no criticism or judgment of you for your answers.
Question 1
How old are you?

Question 2
What sex are you? (please circle)

Male  Female

Question 3
Which ethnic groups do you belong to? (please circle all which apply)

New Zealand European

Māori

Samoan

Cook Island Māori

Tongan

Niuean

Chinese

Indian

Others (please state):
Question 4
What is your occupation?

Question 5
What is the highest level of education you have attained? (please circle)

Primary school
Secondary school
Trade qualification
Tertiary education

Question 6
Do you currently smoke? (Please circle)

Yes  No

Question 7
a) Have you ever had any pain or discomfort with your wisdom teeth? (Please circle)

Yes  No

b) In the last 4 weeks, have you had pain or discomfort with your wisdom teeth? (Please circle)

Always  Often  Sometimes  Occasionally  Never

c) How would you describe the usual intensity of that pain or discomfort? (Please circle)

Mild  Moderate  Severe
Question 8
How would you describe the health of your teeth and mouth? (Please circle)

- Excellent
- Very good
- Good
- Fair
- Poor

Question 9
How often do you usually brush your teeth? (Please circle)

- More than once a day
- Once a day
- Not every day
- Less than once a week
- Never

Question 10

Place a vertical mark on the line below to indicate your current level of pain.

________________________________________________________________________

No pain

Worst pain imaginable
**Question 11**
For each question, please tick the box of the answer which comes closest to how you feel.

<table>
<thead>
<tr>
<th>How much do you agree with the following statements?</th>
<th>Disagree</th>
<th>Agree a little</th>
<th>Somewhat agree</th>
<th>Moderately agree</th>
<th>Strongly agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) I feel anxious shortly before going to the dentist.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>(b) I generally avoid going to the dentist because I find the experience unpleasant or distressing.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>(c) I get nervous or edgy about upcoming dental visits.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>(d) I think that something really bad would happen to me if I were to visit a dentist.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>(e) I feel afraid or fearful when visiting the dentist.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>(f) My heart beats faster when I go to the dentist.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>(g) I delay making appointments to go to the dentist.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>(h) I often think about all the things that might go wrong prior to going to the dentist.</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Do the following statements apply to you?</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) My avoidance or fear of going to the dentist significantly interferes with my life in some way (normal routine, occupational or academic functioning, social activities, or relationship).</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>(b) I am greatly distressed about my level of dental fear.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>(c) I consider my level of dental fear to be excessive or unreasonable.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>(d) I am afraid of going to the dentist because I am concerned I may have a panic attack (abrupt fear with sweating, pounding heart, fear of dying or losing control, chest pain etc.)</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>(e) I am afraid of going to the dentist because I am generally highly self-conscious or concerned about being watched or judged in social situations.</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>To what extent are you anxious about the following things when you go to the dentist?</td>
<td>Not at all</td>
<td>A little</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>(a) Painful or uncomfortable procedures</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(b) Feeling embarrassed or ashamed</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(c) Not being in control of what is happening</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(d) Feeling sick, queasy or disgusted</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(e) Numbness caused by the anaesthetic</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(f) Not knowing what the dentist is going to do</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(g) The cost of dental treatment</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(h) Needles of injections</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(i) Gagging or choking</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(j) Having an unsympathetic or unkind dentist</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
Question 12 - Indicate to what extent you have felt this way over the past week (please circle your answer).

<table>
<thead>
<tr>
<th>Term</th>
<th>Very slightly or not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Quite a bit</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interested</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distressed</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Excited</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Upset</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Strong</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Guilty</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Scared</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Hostile</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Enthusiastic</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Proud</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Irritable</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Alert</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Ashamed</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Inspired</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Nervous</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Determined</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Attentive</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Jittery</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Active</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>Afraid</td>
<td>Very slightly or not at all</td>
<td>A little</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
</tbody>
</table>
Question 13
For each of the following questions, please circle the answer which best applies to you during the last 4 weeks.

Because of trouble with your teeth, mouth or dentures, have you:

<table>
<thead>
<tr>
<th>Question</th>
<th>Never</th>
<th>Hardly ever</th>
<th>Sometimes</th>
<th>Fairly often</th>
<th>Very often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Had trouble pronouncing any words?</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Felt that your sense of taste has worsened?</td>
<td></td>
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<tr>
<td>Had painful aching in your mouth?</td>
<td></td>
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<tr>
<td>Found it uncomfortable eating any foods?</td>
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</tr>
<tr>
<td>Been self-conscious?</td>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Felt tense?</td>
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<td></td>
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</tr>
<tr>
<td>Had a change in diet?</td>
<td></td>
<td></td>
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<tr>
<td>Had to interrupt meals?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Found it difficult to relax?</td>
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<td></td>
</tr>
<tr>
<td>Been embarrassed?</td>
<td></td>
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<td></td>
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<tr>
<td>Been irritable with other people?</td>
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<tr>
<td>Had difficulty doing your usual jobs?</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Felt that life in general was less satisfying?</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Been totally unable to function?</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

End of questionnaire.

Thank you.
Appendix 7. Postoperative day 2 questionnaire

POST-OPERATIVE QUESTIONNAIRE
(to be completed at Day 2)

Oral and Maxillofacial Surgery research project
Department of Oral Diagnostic and Surgical Sciences, School of Dentistry, University of Otago

Principal Researcher: Adelyn Lau (Doctor of Clinical Dentistry, Oral Surgery post-graduate student)
Principal Supervisor: Mr Rohana De Silva (Consultant Oral and Maxillofacial Surgeon)

Thank you for taking the time to fill in this questionnaire.

For information about this research project, please read the form entitled: “Information sheet for participants: Routes of Dexamethasone Administration during Wisdom Teeth Removal.”

All personal information will remain strictly confidential.
Please answer honestly. There will be no criticism or judgment of you for your answers.
For each of the following questions, please circle the answer which best applies to you during the last 7 days.

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Hardly ever</th>
<th>Sometimes</th>
<th>Fairly often</th>
<th>Very often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Had trouble pronouncing any words?</td>
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<td>Found it uncomfortable eating any foods?</td>
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<td>Had to interrupt meals?</td>
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<td>Found it difficult to relax?</td>
<td></td>
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<tr>
<td>Been a bit embarrassed?</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Been a bit irritable with other people?</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Had difficulty doing your usual jobs?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Felt that life in general was less satisfying?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Been totally unable to function?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Place a vertical mark on the line below to indicate your current level of pain.

________________________________________

No pain                                      Worst pain imaginable

End of questionnaire.
Thank you.
Appendix 8. Postoperative day 7 questionnaire

POST-OPERATIVE QUESTIONNAIRE
(to be completed at Day 7)

Oral and Maxillofacial Surgery research project
Department of Oral Diagnostic and Surgical Sciences, School of Dentistry, University of Otago

Principal Researcher: Adelyn Lau (Doctor of Clinical Dentistry, Oral Surgery post-graduate student)
Principal Supervisor: Mr Rohana De Silva (Consultant Oral and Maxillofacial Surgeon)

Thank you for taking the time to fill in this questionnaire.

For information about this research project, please read the form entitled: “Information sheet for participants: Routes of Dexamethasone Administration during Wisdom Teeth Removal.”

All personal information will remain strictly confidential.
Please answer honestly. There will be no criticism or judgment of you for your answers.
Question 1
Did you need to see your doctor/dentist about your pain or discomfort? (please circle)

   Yes       No

Question 2
Did you need the socket to be treated by a dentist? (please circle)

   Yes       No

If yes, why did the socket need to be treated? (please circle)

Dry socket   Prolonged bleeding   Infection/abscess   Insufficient wound care

Other (please specify):

Question 3
Did having the extraction affect your work? (please circle)

   Yes       No

Question 4
How many days off work/normal daily activities did you have to take to recover? (Please circle)

0 days   1-2 days   3-5 days   6-8 days   Still taking time off

Question 5
How many days did it take for you to get back to your normal diet? (Please circle)

0 days   1-2 days   3-5 days   6-8 days   Still not eating normally

Question 6
How would you rate your overall experience with your operation?

Unacceptable   Poor   Satisfactory   Good   Excellent

Question 7
How closely did your experience match your expectations?

Below expectations   Somewhat close   Matched exactly   Exceeded expectations
Question 8
For each of the following questions, please circle the answer which best applies to you during the last 7 days.

Because of trouble with your teeth, mouth or dentures, have you:

<table>
<thead>
<tr>
<th>Had trouble pronouncing any words?</th>
<th>Never</th>
<th>Hardly ever</th>
<th>Sometimes</th>
<th>Fairly often</th>
<th>Very often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Felt that your sense of taste has worsened?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Had painful aching in your mouth?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Found it uncomfortable eating any foods?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Been self-conscious?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Felt tense?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Had a change in diet?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Had to interrupt meals?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Found it difficult to relax?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Been abit embarrassed?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Been abit irritable with other people?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Had difficulty doing your usual jobs?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Felt that life in general was less satisfying?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
<tr>
<td>Been totally unable to function?</td>
<td>Never</td>
<td>Hardly ever</td>
<td>Sometimes</td>
<td>Fairly often</td>
<td>Very often</td>
</tr>
</tbody>
</table>
Place a vertical mark on the line below to indicate your current level of pain.

______________________________________________________________

No pain

Worst pain imaginable

End of questionnaire.

Thank you.
Appendix 9. Diary

DIARY
(to be completed each day after surgery)

Oral and Maxillofacial Surgery research project
Department of Oral Diagnostic and Surgical Sciences, School of Dentistry, University of Otago

Principal Researcher: Adelyn Lau (Doctor of Clinical Dentistry, Oral Surgery post-graduate student)
Principal Supervisor: Mr Rohana De Silva (Consultant Oral and Maxillofacial Surgeon)

Thank you for taking the time to fill in this questionnaire.

For information about this research project, please read the form entitled: “Information sheet for participants: Routes of Dexamethasone Administration during Wisdom Teeth Removal.”

All personal information will remain strictly confidential.
Please answer honestly. There will be no criticism or judgment of you for your answers.
Day 1

Directions: Completely fill in the ONE circle for each statement that best applies to you.

A. PAST 24 HOURS
1. In the past 24 hours, how much have your teeth or mouth given you trouble with:
   
   a. Eating the foods you want
   
   b. Chewing foods easily
   
   c. Opening your mouth wide
   
   d. Sleeping
   
   e. Talking so that people can understand you
   
   f. Going about your everyday routine
   
   g. Taking part in your regular social life
   
   h. Taking part in your favorite sports / hobbies

2. In the past 24 hours, how much have you had:

   a. Swelling of your cheeks
   
   b. Bruising
   
   c. Bleeding
   
   d. Nausea
   
   e. Bad taste / bad breath
   
   f. Food collecting in the hole left after the teeth were pulled

3. Rate the WORST pain you have felt in your teeth, mouth or face during the past 24 hours.

4. Rate the AVERAGE pain you have felt in your teeth, mouth or face during the past 24 hours.
B. NOW

1. Rate the pain you are feeling in your teeth, mouth or face **RIGHT NOW**.

<table>
<thead>
<tr>
<th>No pain</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Worst pain imaginable</th>
</tr>
</thead>
</table>

2. Please read the entire list of words before making a selection. Completely fill in the **ONE** circle for the word from the A-Words list and the **ONE** from the S-Words list which best describes the pain in your teeth, mouth or face **RIGHT NOW AT THIS MOMENT**.

   **A-Words**
   - Neutral
   - Very Distressing
   - Annoying
   - Intolerable
   - Slightly Annoying
   - Unpleasant
   - Distressing
   - Very Unpleasant
   - Slightly Distressing
   - Very Annoying
   - Slightly Unpleasant
   - Very Intolerable
   - Slightly Intolerable

   **S-Words**
   - Nothing
   - Very Intense
   - Very Weak
   - Intense
   - Weak
   - Strong
   - Very Mild
   - Barely Strong
   - Slightly Intense
   - Mild
   - Extremely Intense
   - Moderate
   - Faint

3. Did you take any medication **today** to relieve pain or swelling?  
   - Yes  
   - No

   If yes, please write in the type of medication, the strength and the number of pills.

<table>
<thead>
<tr>
<th>Name of medication</th>
<th>Strength (such as 8 mg)</th>
<th>Number of pills taken in last 24 hours</th>
</tr>
</thead>
</table>
   a.                  |                         |                                       |
   b.                  |                         |                                       |
Day 2

Directions: Completely fill in the ONE circle for each statement that best applies to you.

A. PAST 24 HOURS
1. In the past 24 hours, how much have your teeth or mouth given you trouble with:

<table>
<thead>
<tr>
<th></th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
</table>
a. Eating the foods you want | ☐ | ☐ | ☐ | ☐ | ☐ |
b. Chewing foods easily | ☐ | ☐ | ☐ | ☐ | ☐ |
c. Opening your mouth wide | ☐ | ☐ | ☐ | ☐ | ☐ |
d. Sleeping | ☐ | ☐ | ☐ | ☐ | ☐ |
e. Talking so that people can understand you | ☐ | ☐ | ☐ | ☐ | ☐ |
f. Going about your everyday routine | ☐ | ☐ | ☐ | ☐ | ☐ |
g. Taking part in your regular social life | ☐ | ☐ | ☐ | ☐ | ☐ |
h. Taking part in your favorite sports / hobbies | ☐ | ☐ | ☐ | ☐ | ☐ |

2. In the past 24 hours, how much have you had:

<table>
<thead>
<tr>
<th></th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
</table>
a. Swelling of your cheeks | ☐ | ☐ | ☐ | ☐ | ☐ |
b. Bruising | ☐ | ☐ | ☐ | ☐ | ☐ |
c. Bleeding | ☐ | ☐ | ☐ | ☐ | ☐ |
d. Nausea | ☐ | ☐ | ☐ | ☐ | ☐ |
e. Bad taste / bad breath | ☐ | ☐ | ☐ | ☐ | ☐ |
f. Food collecting in the hole left after the teeth were pulled | ☐ | ☐ | ☐ | ☐ | ☐ |

3. Rate the WORST pain you have felt in your teeth, mouth or face during the past 24 hours.

<table>
<thead>
<tr>
<th></th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Lots of pain</th>
</tr>
</thead>
</table>

4. Rate the AVERAGE pain you have felt in your teeth, mouth or face during the past 24 hours.

<table>
<thead>
<tr>
<th></th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Lots of pain</th>
</tr>
</thead>
</table>
B. NOW

1. Rate the pain you are feeling in your teeth, mouth or face RIGHT NOW.

<table>
<thead>
<tr>
<th>No pain</th>
<th></th>
<th></th>
<th></th>
<th>Worst pain imaginable</th>
</tr>
</thead>
</table>

2. Please read the entire list of words before making a selection. Completely fill in the ONE circle for the word from the A-Words list and the ONE from the S-Words list which best describes the pain in your teeth, mouth or face RIGHT NOW AT THIS MOMENT.

**A-Words**
- Neutral
- Very Distressing
- Annoying
- Intolerable
- Slightly Annoying
- Unpleasant
- Distressing
- Very Unpleasant
- Slightly Distressing
- Very Annoying
- Slightly Unpleasant
- Very Intolerable
- Slightly Intolerable

**S-Words**
- Nothing
- Very Intense
- Very Weak
- Intense
- Weak
- Strong
- Very Mild
- Barely Strong
- Slightly Intense
- Mild
- Extremely Intense
- Moderate
- Faint

3. Did you take any medication today to relieve pain or swelling?  ○ Yes  ○ No

   If yes, please write in the type of medication, the strength and the number of pills.

<table>
<thead>
<tr>
<th>Name of medication</th>
<th>Strength (such as 8 mg)</th>
<th>Number of pills taken in last 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Day 3

Directions: Completely fill in the **ONE** circle for each statement that best applies to you.

A. PAST 24 HOURS
1. In the **past 24 hours** how much have your teeth or mouth given you trouble with:

   a. Eating the foods you want
   b. Chewing foods easily
   c. Opening your mouth wide
   d. Sleeping
   e. Talking so that people can understand you
   f. Going about your everyday routine
   g. Taking part in your regular social life
   h. Taking part in your favorite sports / hobbies

<table>
<thead>
<tr>
<th></th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Eating the foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Chewing foods</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Opening your</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Sleeping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Talking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Going about</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Taking part in</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h. Taking part in</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. In the **past 24 hours** how much have you had:

   a. Swelling of your cheeks
   b. Bruising
   c. Bleeding
   d. Nausea
   e. Bad taste / bad breath
   f. Food collecting in the hole left after the teeth were pulled

<table>
<thead>
<tr>
<th></th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Swelling of your</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Bruising</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Nausea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Bad taste / bad</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Food collecting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Rate the **WORST** pain you have felt in your teeth, mouth or face during the **past 24 hours**.

<table>
<thead>
<tr>
<th></th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Impossibly</th>
</tr>
</thead>
</table>

4. Rate the **AVERAGE** pain you have felt in your teeth, mouth or face during the **past 24 hours**.

<table>
<thead>
<tr>
<th></th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Impossibly</th>
</tr>
</thead>
</table>
B. NOW

1. Rate the pain you are feeling in your teeth, mouth or face RIGHT NOW.

<table>
<thead>
<tr>
<th>No pain</th>
<th>○</th>
<th>○</th>
<th>○</th>
<th>○</th>
<th>○</th>
<th>○</th>
<th>○</th>
<th>Worst pain imaginable</th>
</tr>
</thead>
</table>

2. Please read the entire list of words before making a selection. Completely fill in the ONE circle for the word from the A-Words list and the ONE from the S-Words list which best describes the pain in your teeth, mouth or face RIGHT NOW AT THIS MOMENT.

<table>
<thead>
<tr>
<th>A-Words</th>
<th>S-Words</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutral</td>
<td>Nothing</td>
</tr>
<tr>
<td>Very Distressing</td>
<td>Very Intense</td>
</tr>
<tr>
<td>Annoying</td>
<td>Very Weak</td>
</tr>
<tr>
<td>Intolerable</td>
<td>Intense</td>
</tr>
<tr>
<td>Slightly Annoying</td>
<td>Weak</td>
</tr>
<tr>
<td>Unpleasant</td>
<td>Strong</td>
</tr>
<tr>
<td>Distressing</td>
<td>Very Mild</td>
</tr>
<tr>
<td>Very Unpleasant</td>
<td>Barely Strong</td>
</tr>
<tr>
<td>Slightly Distressing</td>
<td>Slightly Intense</td>
</tr>
<tr>
<td>Very Annoying</td>
<td>Mild</td>
</tr>
<tr>
<td>Slightly Unpleasant</td>
<td>Extremely Intense</td>
</tr>
<tr>
<td>Very Intolerable</td>
<td>Moderate</td>
</tr>
<tr>
<td>Slightly Intolerable</td>
<td>Faint</td>
</tr>
</tbody>
</table>

3. Did you take any medication today to relieve pain or swelling?  ○ Yes  ○ No

If yes, please write in the type of medication, the strength and the number of pills.

<table>
<thead>
<tr>
<th>Name of medication</th>
<th>Strength (such as 8 mg)</th>
<th>Number of pills taken in last 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Day 4

**Directions:** Completely fill in the **ONE** circle for each statement that best applies to you.

**A. PAST 24 HOURS**
1. In the past 24 hours, how much have your teeth or mouth given you trouble with:

<table>
<thead>
<tr>
<th>Statement</th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Eating the foods you want</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Chewing foods easily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Opening your mouth wide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Sleeping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Talking so that people can understand you</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Going about your everyday routine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Taking part in your regular social life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h. Taking part in your favorite sports / hobbies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. In the past 24 hours, how much have you had:

<table>
<thead>
<tr>
<th>Condition</th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Swelling of your cheeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Bruising</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Nausea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Bad taste / bad breath</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Food collecting in the hole left after the teeth were pulled</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Rate the **WORST** pain you have felt in your teeth, mouth or face during the past 24 hours.

<table>
<thead>
<tr>
<th>Level</th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Impossibly</th>
</tr>
</thead>
</table>

4. Rate the **AVERAGE** pain you have felt in your teeth, mouth or face during the past 24 hours.

<table>
<thead>
<tr>
<th>Level</th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Impossibly</th>
</tr>
</thead>
</table>
B. NOW

1. Rate the pain you are feeling in your teeth, mouth or face RIGHT NOW.

| No pain | ○ | ○ | ○ | ○ | ○ | ○ | ○ |

2. Please read the entire list of words before making a selection. Completely fill in the ONE circle for the word from the A-Words list and the ONE from the S-Words list which best describes the pain in your teeth, mouth or face RIGHT NOW AT THIS MOMENT.

**A-Words**
- Neutral
- Very Distressing
- Annoying
- Intolerable
- Slightly Annoying
- Unpleasant
- Distressing
- Very Unpleasant
- Slightly Distressing
- Very Annoying
- Slightly Unpleasant
- Very Intolerable
- Slightly Intolerable

**S-Words**
- Nothing
- Very Intense
- Very Weak
- Intense
- Weak
- Strong
- Very Mild
- Barely Strong
- Slightly Intense
- Mild
- Extremely Intense
- Moderate
- Faint

3. Did you take any medication today to relieve pain or swelling?  ○ Yes   ○ No

If yes, please write in the type of medication, the strength and the number of pills.

<table>
<thead>
<tr>
<th>Name of medication</th>
<th>Strength (such as 8 mg)</th>
<th>Number of pills taken in last 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Day 5

Directions: Completely fill in the ONE circle for each statement that best applies to you.

A. PAST 24 HOURS
1. In the past 24 hours, how much have your teeth or mouth given you trouble with:

<table>
<thead>
<tr>
<th></th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Eating the foods you want</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Chewing foods easily</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Opening your mouth wide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Sleeping</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Talking so that people can understand you</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Going about your everyday routine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Taking part in your regular social life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>h. Taking part in your favorite sports / hobbies</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. In the past 24 hours, how much have you had:

<table>
<thead>
<tr>
<th></th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Swelling of your cheeks</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Bruising</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. Bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Nausea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Bad taste / bad breath</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Food collecting in the hole left after the teeth were pulled</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Rate the WORST pain you have felt in your teeth, mouth or face during the past 24 hours.

<table>
<thead>
<tr>
<th></th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Unimaginable</th>
</tr>
</thead>
</table>

4. Rate the AVERAGE pain you have felt in your teeth, mouth or face during the past 24 hours.

<table>
<thead>
<tr>
<th></th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Unimaginable</th>
</tr>
</thead>
</table>
B. NOW

1. Rate the pain you are feeling in your teeth, mouth or face RIGHT NOW.

<table>
<thead>
<tr>
<th>No pain</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Worst pain imaginable</th>
</tr>
</thead>
<tbody>
<tr>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td></td>
</tr>
</tbody>
</table>

2. Please read the entire list of words before making a selection. Completely fill in the ONE circle for the word from the A-Words list and the ONE from the S-Words list which best describes the pain in your teeth, mouth or face RIGHT NOW AT THIS MOMENT.

   **A-Words**
   - Neutral
   - Very Distressing
   - Annoying
   - Intolerable
   - Slightly Annoying
   - Unpleasant
   - Distressing
   - Very Unpleasant
   - Slightly Distressing
   - Very Annoying
   - Slightly Unpleasant
   - Very Intolterable
   - Slightly Intolerable

   **S-Words**
   - Nothing
   - Very Intense
   - Very Weak
   - Intense
   - Weak
   - Strong
   - Very Mild
   - Barely Strong
   - Slightly Intense
   - Mild
   - Extremely Intense
   - Moderate
   - Faint

3. Did you take any medication today to relieve pain or swelling? ○ Yes ○ No

   If yes, please write in the type of medication, the strength and the number of pills.

   Name of medication | Strength (such as 8 mg) | Number of pills taken in last 24 hours
   a. ____________________ | ______________________ | ______________________
   b. ____________________ | ______________________ | ______________________
Day 6

Directions: Completely fill in the **ONE** circle for each statement that best applies to you.

A. PAST 24 HOURS
1. In the *past 24 hours* how much have your teeth or mouth given you trouble with:
   - a. Eating the foods you want
   - b. Chewing foods easily
   - c. Opening your mouth wide
   - d. Sleeping
   - e. Talking so that people can understand you
   - f. Going about your everyday routine
   - g. Taking part in your regular social life
   - h. Taking part in your favorite sports / hobbies

2. In the *past 24 hours* how much have you had:
   - a. Swelling of your cheeks
   - b. Bruising
   - c. Bleeding
   - d. Nausea
   - e. Bad taste / bad breath
   - f. Food collecting in the hole left after the teeth were pulled

3. Rate the **WORST** pain you have felt in your teeth, mouth or face during the *past 24 hours.*

4. Rate the **AVERAGE** pain you have felt in your teeth, mouth or face during the *past 24 hours.*
B. NOW

1. Rate the pain you are feeling in your teeth, mouth or face RIGHT NOW.

   | No pain | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

2. Please read the entire list of words before making a selection. Completely fill in the ONE circle for the word from the A-Words list and the ONE from the S-Words list which best describes the pain in your teeth, mouth or face RIGHT NOW AT THIS MOMENT.

   **A-Words**
   - Neutral
   - Very Distressing
   - Annoying
   - Intolerable
   - Slightly Annoying
   - Unpleasant
   - Distressing
   - Very Unpleasant
   - Slightly Distressing
   - Very Annoying
   - Slightly Unpleasant
   - Very Intolerable
   - Slightly Intolerable

   **S-Words**
   - Nothing
   - Very Intense
   - Very Weak
   - Intense
   - Weak
   - Strong
   - Very Mild
   - Barely Strong
   - Slightly Intense
   - Mild
   - Extremely Intense
   - Moderate
   - Faint

3. Did you take any medication today to relieve pain or swelling? ☐ Yes ☐ No

   If yes, please write in the type of medication, the strength and the number of pills.

   a. ___________________________  ___________________________  ___________________________
   b. ___________________________  ___________________________  ___________________________
Day 7

Directions: Completely fill in the ONE circle for each statement that best applies to you.

A. PAST 24 HOURS
1. In the past 24 hours, how much have your teeth or mouth given you trouble with:

<table>
<thead>
<tr>
<th>Option</th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
<th>Lots of trouble</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Eating the foods you want</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Chewing foods easily</td>
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<td></td>
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<tr>
<td>c. Opening your mouth wide</td>
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<td>d. Sleeping</td>
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<td>f. Going about your everyday routine</td>
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<td></td>
<td></td>
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<td>g. Taking part in your regular social life</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>h. Taking part in your favorite sports / hobbies</td>
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<td></td>
<td></td>
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</table>

2. In the past 24 hours, how much have you had:

<table>
<thead>
<tr>
<th>Option</th>
<th>No trouble</th>
<th>A little trouble</th>
<th>Some trouble</th>
<th>Quite a bit of trouble</th>
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<td>b. Bruising</td>
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<tr>
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<td></td>
<td></td>
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<tr>
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<td></td>
<td></td>
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<td>e. Bad taste / bad breath</td>
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<td>f. Food collecting in the hole left after the teeth were pulled</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Rate the WORST pain you have felt in your teeth, mouth or face during the past 24 hours.

<table>
<thead>
<tr>
<th>Pain level</th>
<th>No pain</th>
<th>A little pain</th>
<th>Some pain</th>
<th>Quite a bit of pain</th>
<th>Most pain</th>
</tr>
</thead>
</table>

4. Rate the AVERAGE pain you have felt in your teeth, mouth or face during the past 24 hours.
B. NOW

1. Rate the pain you are feeling in your teeth, mouth or face RIGHT NOW.

2. Please read the entire list of words before making a selection. Completely fill in the ONE circle for the word from the A-Words list and the ONE from the S-Words list which best describes the pain in your teeth, mouth or face RIGHT NOW AT THIS MOMENT.

A-Words
- Neutral
- Very Distressing
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- Unpleasant
- Distressing
- Very Unpleasant
- Slightly Distressing
- Very Annoying
- Slightly Unpleasant
- Very Intolerable
- Slightly Intolerable

S-Words
- Nothing
- Very Intense
- Very Weak
- Intense
- Weak
- Strong
- Very Mild
- Barely Strong
- Slightly Intense
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- Extremely Intense
- Moderate
- Faint

3. Did you take any medication today to relieve pain or swelling? ☐ Yes ☐ No

If yes, please write in the type of medication, the strength and the number of pills.

<table>
<thead>
<tr>
<th>Name of medication</th>
<th>Strength (such as 8 mg)</th>
<th>Number of pills taken in last 24 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 10. Patient consent for use of images

Patient consent for medical photography

Clinical trial: The efficacy of submucosal and intravenous dexamethasone in the reduction of adverse postoperative outcomes after third molar surgery
ACTRN registration number: ACTRN12617001203347
HDEC ethical reference number: 17/NTB/127
Primary investigator: Adelyn Lau (DelinDent Oral Surgery candidate)
Primary supervisor: Mr Rohana De Silva (Oral and Maxillofacial surgeon)

I give consent for medical photographs (clinical images) to be taken of me.

I understand that copies of my photograph may be used for education, publication and research. For example, use in scientific presentations and posters, research thesis and research articles.

Allowing my photograph to be used will not involve any additional costs to me. I will not receive any compensation.

I understand that I have the right to withdraw consent at any time. However, once the article/research is written and published, it will not be possible to withdraw it.

I understand that my personal information (e.g. name, date of birth, contact details) will not be disclosed, or any information that identified me as an individual. When the article is published or presented, my identity will not be disclosed.

I understand that I will not directly benefit from participating in this clinical trial. The information that can be shared with other health care professionals, however, may improve the care that is received by others in the future.

Name:  _____________________________

Signature:  _____________________________

Date:   _____________________________