The Medical Management of Saliva in Tracheostomised Patients:

A case series

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A dissertation submitted in fulfilment of the requirements for the Doctorate in Speech and Language Therapy (DSLT) in the Faculty of Life Sciences, University College London

Declaration

I declare that this dissertation is my own unaided work. It is submitted for the Doctorate in Speech and Language Therapy (DSLT) at University College London (UCL). It has not been submitted before for any other degree or examination in any other University.

Chetan Vyas

04th July, 2016

Signed_____

Acknowledgements

I would like to express my sincere thanks to the following people and agencies:

Dr. Christina Smith, my supervisor, for her guidance, support, encouragement and belief that I could be a researcher as well as a clinician. Professor Jane Maxim, co-supervisor, for her support, advice and encouragement.

The patients, their primary caregivers and the nursing staff, who were involved in this study and who assisted in the data collection.

Dr. Gordon Craig, for his advice on data collection and statistical analysis.

The Speech and Language Therapy team at The Wellington Hospital who were involved in identifying suitable candidates for participation within the study and who continued to provide treatment intervention whilst the study was implemented and executed, you are all amazing therapists.

Ms. Lesley Pope and the executive management team at The Wellington Hospital and HCA International Ltd. for supporting me throughout the study.

My family, who allowed me the space and time to complete this dissertation and finally to my partner, who encouraged, supported and motivated me to continue working on this dissertation.

Abstract

Background: Saliva is a common problem in tracheostomised patients, whereby saliva is spilled through the faucial isthmus creating risk of aspiration. These individuals are dependent on tracheal suctioning to clear saliva from the airway. There is currently no evidence about the relative effectiveness of any of the pharmacological treatments to manage saliva in this patient population.

Methods and Procedures: This prospective interrupted time series study investigated the medical management of saliva in tracheostomised patients. Three inpatients at The Wellington Hospital London were enrolled, prescribed treatment using Hyoscine (Scopoderm® TTS). Unstimulated whole saliva was collected, using the swab method, at one-week prior, one-week, two-weeks, four-weeks, eight-weeks and at 12 weeks post treatment. The primary outcome measure was dental roll weights measured at these time-points. Primary carer and nursing reports in relation to the amount of oral secretions and tracheostomy self-perceptions were also recorded at these same time intervals, using a visual analogue scale and a questionnaire. The frequency and reasoning of tracheal suctioning was also recorded, by the same nurse at these time-points. Data was analysed using linear regression for oral secretions and a Chi-Square test was performed for frequency of tracheal suctioning.

Outcomes and Results: There was a significant reduction in oral secretions post treatment intervention, $F= 27.252$, $df= 1, 52$; $p<0.001$, $F=11.62$, $df=1, 52$, $p<0.001$, $F=159.314$, $df=1, 52$, $p<0.001$. There was a significant reduction in the frequency of tracheal suctioning performed post intervention, Fisher's Exact Test $p=0.094$; with the primary reason recorded as audible or visible secretions. All primary caregivers and the same one-to-one nurse reported that oral secretions had reduced.

Conclusion and Implications: The medical management of saliva in tracheostomised patients, using Hyoscine (Scopoderm® TTS) was effective in reducing saliva and tracheal suctioning. This study suggests that further research is required in order to establish clinical practice guidelines in the use of Hyoscine (Scopoderm® TTS) in this patient population.

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Introduction

Patients who have swallowing difficulties and who are unable to safely swallow their saliva, following neurological injury are often managed with the insertion of a tracheostomy tube. A tracheostomy is an opening (made by an incision) through the neck into the trachea (windpipe). A tracheostomy tube is a small tube inserted into the tracheostomy, which aids breathing and allows access to the windpipe, in order to assist in the clearance of saliva that has fallen into the airway, during tracheal suctioning. The problems that arise when managing these patients are that;

1. There are no national government supported guidelines or policies to direct the medical management of saliva

2. There are no licensed medications to manage excessive pooled saliva, secondary to swallowing difficulties (UK Medicines Information 2012)

3. All prescribed medication is issued ‘off-label’. This is when a licensed medicine is used in a manner that is not described in the medicine’s summary of product characteristics (SPC), for example, a different dose, indication, patient group or route of administration. It is therefore being prescribed outside its approved terms of use, known as being used ‘off-label’ or ‘off-licence’ (Medicines and Healthcare Products Regulatory Agency 2009)

4. Knowledge and practice amongst healthcare professionals caring for the tracheostomised patient, including tracheal suctioning is poor (Day, Farnell et al. 2002)

5. If tracheal suctioning is required long-term to clear aspirated saliva, the tracheostomy tube cannot be removed successfully, as airway access is required in order to remove the saliva and therefore the tracheostomy tube cannot be closed-off

If saliva can be successfully managed in this patient population, then the tracheostomy tube can be closed-off and ultimately result in the removal of the tube, resulting in 'normalised' breathing via the nose and mouth and removal of the artificial opening in the neck (Kent and Christopher 2005).

As well as swallowing difficulties, patients post neurological injury may also present with a disorder of consciousness or with receptive and / or expressive cognitive-communication impairments which result in an inability to participate in direct therapy programmes or benefit from more conservative management options to treat the pooling of saliva orally, such as behavioural techniques or postural changes. It has also been documented that the presence of a tracheostomy tube can occasionally adversely affect swallowing in patients who previously had no dysphagia, and may further impair the swallowing function in those who already have neurological or mechanical disorders of swallowing.

It is clearly documented in the evidence that knowledge and practice in caring for the tracheostomised patient is poor (Day, Farnell et al. 2002) and associated tracheal suctioning practice is poor amongst healthcare professionals (Day, Farnell et al. 2002). Poor practice often leads to further complications such as hypoxia microatelectasis (alveolar damage), laryngospasm and tracheal wall damage (Fiorentini 1992; Kapadia, Bajan et al. 2000) and delays removal of the tracheostomy tube. There are no clear national or government guidelines or policies that direct how to clinically manage excessive pooled saliva, this being the main reason for the tracheostomy tube being in-situ, in order to clear aspirated saliva. As a result of requiring regular tracheal suctioning to remove aspirated saliva the tracheostomy tube cannot be closed-off and removed.
In everyday clinical practice, patients with swallowing difficulties who are at high risk of aspirating their own saliva and who have a tracheostomy tube in-situ are

referred to the speech and language therapist for assessment of swallowing and laryngeal function. These patients may be cared for in an intensive care setting or in a ward environment, where they continue to receive one-to-one nursing care to prevent secondary complications, such as airway occlusion, as a result of having a tracheostomy tube in-situ.

Patients admitted to The Wellington Hospital, London, with a tracheostomy tube in-situ are referred to the speech and language therapist for assessment and management of communication and swallowing. Following assessment by the speech and language therapist, recommendations may be made to the medical team to consider management options to reduce the flow of saliva to aid cuff deflation trials and to determine the suitability for safe decannulation. There is however no evidence of a clear decision making process to guide practice on how best to medically manage saliva in the tracheostomised patient and what implications this may have on commencing therapy with the aim of eventual successful decannulation. In a study by McGowan et al. (McGowan, Ward et al. 2014), they investigated the working practices of 106 speech and language therapists, with prior experience in tracheostomy management across various areas. In their study they wanted to determine the level of clinical consistency for speech and language therapy practice in adult tracheostomy care, including clinical patterns in relation to current scientific evidence and national guidelines. Their study concluded that there was a moderate to high consistency in a number of areas of clinical practice consistent with current research evidence (McGowan, Ward et al. 2014). These areas included the role of the speech and language therapists in swallowing assessment and management, increased utilisation of instrumental assessments such as fibreoptic endoscopic evaluation of swallowing (FEES), use of cuff deflation protocols in order to aid decision making in decannulation, increased use of speaking valves and use of manometers to measure cuff pressures during re-inflation. A highlighted area of concern for tracheostomy management was the feeling that care was not being provided in optimal team environments, despite the emerging evidence that working in such teams enhances patient outcomes (McGowan, Ward et al. 2014). Their data showed that there is a requirement for greater consistency in the speech and language therapy management of the tracheostomised patient

in order to enhance and optimise patient outcomes (McGowan, Ward et al. 2014).

However when considering the management of saliva in the tracheostomised patient and across other patient populations, there appears to be a lack of consistency or guidance and that decision making is not provided in an optimal team environment, despite emerging evidence that tracheostomy teams may enhance patient outcomes (McGowan, Ward et al. 2014).

The purpose of this study is to investigate the current medical practice and management of excessive pooled saliva in tracheostomised patients and to examine how this affects the reduction in saliva and subsequent need to perform tracheal suctioning and ultimate closure of the tracheostomy tube. Successful reduction in orally pooled saliva in patients with a tracheostomy tube decreases the frequency and amount of tracheal suctioning and can instigate the successful removal of the tracheostomy tube.

Saliva is a valuable oral fluid that is often taken for granted. Saliva is a clear, slightly acidic, watery and usually frothy substance produced in the mouths of mammals. Saliva is produced in and secreted by the salivary glands and is crucial to the preservation and maintenance of oral health. However, it is not until the quantity or quality changes from the normal range, either through an excess or diminished amount of saliva, that it becomes an area of concern. Too much saliva and the inability to control oral secretions, can lead to subsequent anterior and / or posterior drooling, which can be devastating and affect quality of life and health status. Drooling is not due to the excessive production of saliva, but is a problem in the coordinated control of the muscles of the oral cavity, face and tongue, usually due to impaired neurological control. This impaired control results in a dysfunctional swallow and may lead to an excessive accumulation of saliva in the oral cavity and unintentional loss of saliva from the mouth. Furthermore, the inability to swallow adequately also increases the risk of developing aspiration pneumonia, which can be life-threatening or even fatal.

Although a number of studies have investigated the management of drooling in different patient populations there are no formal guidelines detailing how to manage drooling or the build-up of saliva within the oral cavity, secondary to swallowing difficulties. Furthermore there are no licensed medications that are available to physicians that can be prescribed in order to assist patients who have problems in managing their saliva. Therefore medications for managing saliva are typically prescribed 'off-label', using medications, not specifically designed and not licensed for this use. 'Off-label' prescribing can potentially harm patients, and the harm is greatest when 'off-label' use lacks an evidence base.

Although the medicinal use of Botulinum Toxin and Scopolamine TTS® has been shown to be a safe and effective method for managing drooling and excessive saliva in people with Parkinson's disease and in children with Cerebral Palsy (Porta, Gamba et al. 2001; Banerjee, Glasson et al. 2006; Lagalla, Millevolte et al. 2006); to date there has been no reported studies investigating its use in patients who have a tracheostomy tube in-place. There is no evidence about the relative effectiveness, side-effect profiles or patient acceptability of one of the most commonly used medications - Hyoscine hydrobromide (Scopoderm® TTS), to manage saliva reduction in patients who have a tracheostomy tube in-situ. Consequently, there is no consensus or guideline to aid in clinical decisions about which drug to use.

In reviewing these case series investigating the clinical management of saliva in tracheostomised patients, the initial two chapters will provide a literature review beginning with saliva, and the clinical options in managing excess saliva.

Subsequent chapters will describe the methodology and results obtained in this study and discuss the findings. The final chapter will consider the wider implications this study has on current practice and will comment on future research options in order to add to the knowledge-base when investigating the clinical management of saliva in this patient population.

Chapter 1

1. Saliva

1.01 Saliva secretion and regulation

Saliva is produced in and secreted from salivary glands. The basic secretory units of salivary glands are clusters of cells called acini. These cells secrete a fluid that contains water, electrolytes, mucus and enzymes, all of which flow out of the acinus into collecting ducts.

Saliva is secreted into the mouth by three major pairs of salivary glands; the parotid, submandibular and sublingual glands, and by a number of minor mucous glands, such as the accessory parotid gland and glands within the tongue and palate (Humphrey and Williamson 2001). The parotid, submandibular and sublingual salivary glands account for approximately 90% of daily salivary production, whilst the minor glands present within the lips, buccal mucosa, posterior hard palate, soft palate, tongue and uvula produce about 10% (Figure 1).

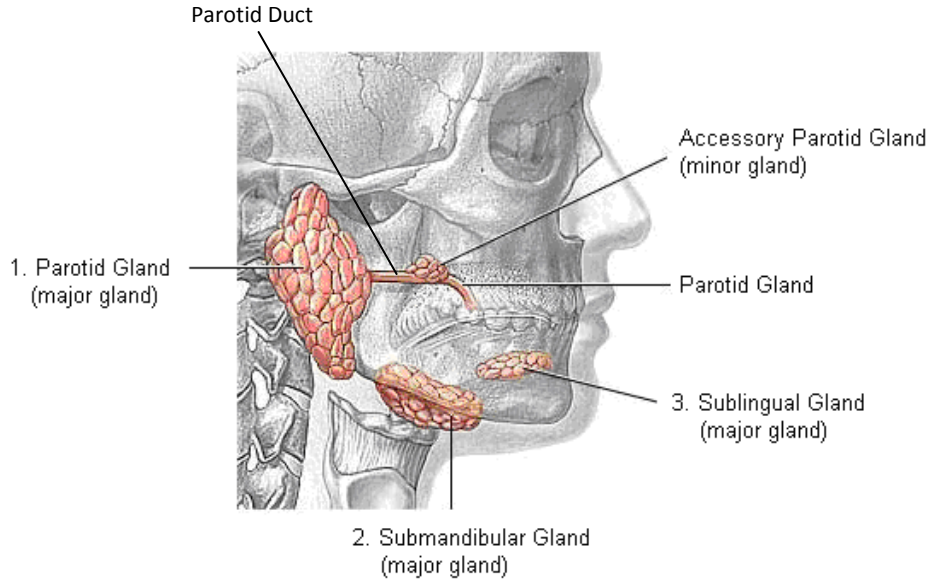

Figure 1 The major salivary glands, adapted from the website http://www.mdconsult.com/

The type of secretion produced by the different salivary glands is determined by the acinar cells, in which saliva is first secreted. The type of secretion can be classified into three categories; as serous, mucous or mixed (Humphrey and Williamson 2001). Serous secretions, which are produced mainly by the parotid glands, are watery secretions.

Mucous secretions are produced by the minor glands, whereas mixed serous and mucous secretions are produced by the sublingual and submandibular glands (Roth and Calmes 1981).

The origins of different salivary glands secreting saliva of differing composition can be understood by examining the glands histology, in which two types of acinar epithelial cells can be found; serous and mucous cells, which produce the corresponding secretion (Bailey 2013). The cells (stained pink here) are serous cells, whereas the white foamy cells are mucous secreting cells (Figure 2).

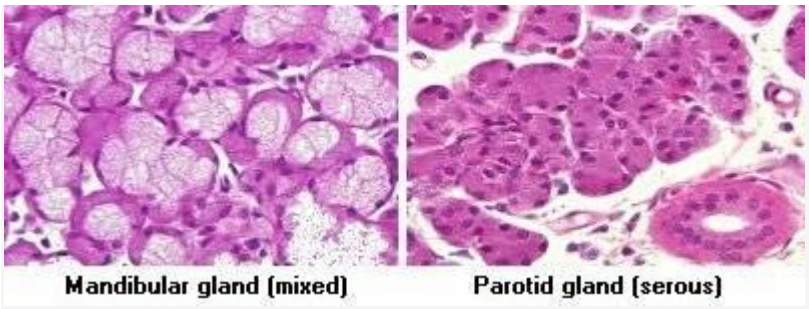

Figure 2 The histologic sections of canine salivary gland: the cells stained pink are serous cells, while the white, foamy cells are mucus-secreting cell (Bowen 2012)

Salivary production is principally under the control of the autonomic nervous system and modifications of the nervous system can be indirectly monitored by observing alterations in saliva production (Denniss, Schneyer et al. 1978). At rest, without stimulation, there is a small continuous salivary flow, referred to as the basal unstimulated secretion, which is present in the form of a film that coats and covers, moisturises and provides lubrication to the oral tissues. Stimulated saliva is produced as a result of some mechanical, gustatory, olfactory, or pharmacological stimulus, and contributes approximately 80% to

90% of daily saliva production. A healthy individual's mean daily salivary production is between 1 to 1.5 litres (Humphrey and Williamson 2001).

1.02 Salivary flow

In the unstimulated state, the parotid glands contribute 20% of the volume of saliva, whereas the submandibular contribute 65% and sublingual glands 7-8%. The minor salivary glands collectively contribute less than 10% (Humphrey and Williamson 2001). However in the stimulated state, saliva flow rates drastically change the percentage contributions from each gland, with the parotid gland contributing more than 50% of total salivary secretions (Edgar 1990), producing large volumes of serous secretions, in response to a stimulant.

Salivary flow does not occur evenly throughout the mouth and there are variations in intra-oral flow, which is site specific due to the contribution and location of the salivary glands, with the mandibular lingual area being a site of high volume and the maxillary anterior glands and interproximal glands being sites of low volume flow (Edgar 1990). These sites of high and low volume flow have been referred to as "salivary highways and byways" (Moss 1995). The regional clearance rate of acid produced by bacteria is directly influenced by regional flow rates within the mouth (Dawes and Macpherson 1993).

Measuring salivary flow is important because saliva is being studied extensively and used for risk assessment, diagnosis and monitoring disease progression. A variety of medical conditions and medications are associated with salivary gland dysfunction. Salivary gland hypofunction may result in a lack of salivary flow, which affects a person's quality of life by causing difficulties in speaking, eating, swallowing and tasting (von Bultzingslowen, Sollecito et al. 2007). Salivary gland hyperfunction may be attributed to medical conditions such as gastroeosophageal reflux disease, pancreatitis, liver disease, serotonin syndrome and oral ulcers.

The salivary flow index is a measure which enables stimulated and unstimulated saliva flow to be classified as normal, low or very low (Tenovuo

and Lagerlof 1994). In adults, the normal unstimulated salivary flow rate ranges from 0.25 to 0.35 millilitres per minute (ml/min), with low rates in the range of 0.1 to 0.25ml/min, whilst very low salivary flow is classified as less than 0.1ml/min (Tenovuo and Lagerlof 1994; Axelsson 2000). The normal total stimulated salivary flow ranges from 1 to 3ml/min, low ranges from 0.7 to 1.0 ml/min and very low salivary flow rate is characterised by less than 0.7 ml/min (Table 1). Despite this classification for the "normal" ranges given in the stimulated and unstimulated flow rates, there remain large variations. It is important that individual salivary flow is measured regularly as a base reference to avoid any variations associated throughout the day, in periods of stimulated and unstimulated states (Edgar 1990), and not classified and rated solely on one measurement, but rather measured a number of times to take account of this variation (Axelsson 2000). Ship et al (Ship, Fox et al. 1991) suggested that, if an individual's base rate has been established, then a 50% reduction in this rate should be considered as abnormal flow (Ship, Fox et al. 1991).

Table 1 Salivary flow rates in stimulated and unstimulated conditions (Tenovuo and Lagerlof 1994)

	Unstimulated	Stimulated
Normal flow rates	0.25 – 0.35 ml/min	1 – 3 ml/min
Low flow rates	0.1 – 0.25 ml/min	0.7 – 1.0 ml/min
Very-low flow rates	< 0.1 ml/min	< 0.7ml/min

Clinical reports of dry lips, dryness of buccal mucosa, absence of saliva in response to gland palpation, and a high number of missing, decayed or filled teeth have been put forward as an easily assessed set of clinical parameters for identifying most individuals with salivary gland dysfunction affecting salivary flow (Navazesh, Christensen et al. 1992). However, in a study investigating the relationship between gingival and periodontal health and salivary gland function, results suggested that there was no consistent relationship between the parotid salivary flow rates and gingival bleeding, tartar, tooth loss or severity of tooth loss (Crow and Ship 1995). The authors concluded that periodontal disease

was not an indicator of decreased salivary flow. As salivary glands age the acini cells decrease in number and are replaced with adipose and fibrotic tissues (Atkinson and Baum 1992). Despite this finding the impact these changes have on salivary output is disputed in the literature. Although more than 50% of elderly subjects, aged 65 years and older report occasional dry-mouth (Nahri, Meurman et al. 1999), studies researching salivary flow rates related to age and gender in the stimulated and in the unstimulated state, showed that there were no changes in the rate of salivary flow in the stimulated state related to age (Heft and Baum 1984; Percival, Challacombe et al. 1994). A few studies have suggested no significant differences in salivary flow rates between males and females (Billings, Proskin et al. 1996; Ghezzi, Lange et al. 2000), although the majority of studies report that flow rates are significantly higher in males (Percival, Challacombe et al. 1994; Bergdahl 2000; Fenoll-Palomares, Munoz-Montagud et al. 2004). In a study examining healthy volunteers and salivary flow rate Fenoll-Palomares et al. (Fenoll-Palomares, Munoz-Montagud et al. 2004), reported that the salivary flow rate in males was significantly greater (0.57 ml/min) than in females (0.42 ml/min). This may be explained by the variances in the sizes of salivary glands between males and females. Scott (Scott 1975) determined weighing of salivary glands and reported that male glands were larger than female glands by 50% on average. In a recent study by Smith et al (Smith, Boland et al. 2013), they collected whole stimulated saliva (which is a mixture of the secretions from all of the various salivary glands located in the mouth), in healthy volunteers in three age groups (young = 20-30; middle-aged = 40-50; older ≥ 70), and concluded that there was a significant reduction in saliva flow in the older participants when compared to the younger and middle-aged groups, but no difference between the young and middle-aged group (Smith, Boland et al. 2013). In their study there was no significant effect on gender or interaction of age and gender (Smith, Boland et al. 2013).

1.03 Circadian / Circannual rhythms in salivary flow rate

There are daily and annual peaks and troughs in saliva flow, with low flow occurring during sleep, and high flow occurring during high stimulation periods, such as presentation of food stimuli and olfactory stimulus (Dawes 1974). There are also annual (circannual) variations in saliva flow, with peak flow observed during winter and low flow rates during the summer (Edgar 1990). In a study by Shannon (Shannon 1966), he examined circannual rhythms in salivary flow rate in 3868 military recruits in the San Antonio region of Texas and concluded the peak flow rate was in December to January, when the mean temperature was10^0C and the minimum was in June to August, when the mean temperature was 29^0C. The lower flow rate was attributed by Shannon to the possible dehydration of recruits during the summer months (Shannon 1966). Kavanagh et al. (Kavanagh, O'Mullane et al. 1998) collected unstimulated saliva from 43 adolescents, on a monthly basis from September to June in North Wales. In their study they did not attempt to fit a rhythm to their data, but did report statistically significant higher salivary flow rates (0.87 ml/min) during the winter months than in the summer months (0.52 ml/min).

In a study by Kariyawasam and Dawes (Kariyawasam and Dawes 2005), examining unstimulated salivary flow rates in 46 healthy students. They collected unstimulated saliva during set times each month over a 12-month period and concluded that even a small change in ambient temperature (approximately 2^0C), may be enough to influence the unstimulated salivary flow rate (Kariyawasam and Dawes 2005).

1.04 Measuring salivary flow

Accurate measurements of salivary flow (sialometry) are required in clinical and experimental practice. In 1910, Carlson and Crittenden devised a two-chambered metal cup with two outlet tubes, one connected to a vacuum, which held the cup in place and the other connected to a collection receptacle (Stephen and Spiers 2012). This basic design has since been updated by Lashley, who subsequently has been credited with the original design now known as a ‘Lashley’ cup (Percival, Challacombe et al. 1994) (figure 3).

The design is made-up of two chambers, an inner and outer chamber, whereby the inner chamber is placed over the parotid duct and suction applied to the outer chamber to hold it in place (Stephen and Spiers 2012).

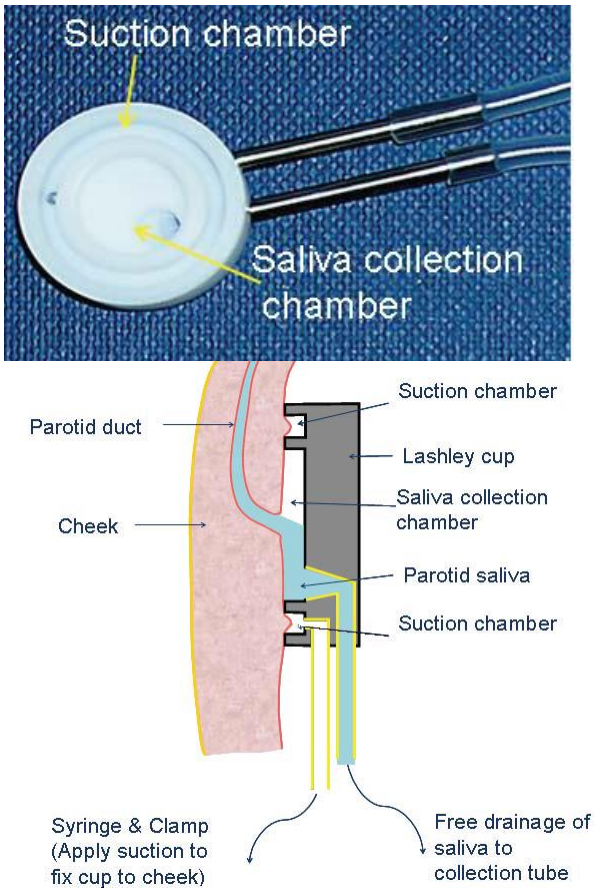

Figure 3 Method of saliva collection using a 'Lashley' cup illustration from http://news.ifr.ac.uk/wp-content/uploads/2012/01/AnthonyAshSETforBritain.pdf

Submandibular saliva collection can be collected using a design first described by Truelove et al. (Wolff, Begleiter et al. 1997). This is a 'V' shaped collector with two outer suction chambers and an inner collection chamber (Stephen and Spiers 2012).

In 1955, Schneyer described a 'segregator' device, which enables secretions from the right and left sublingual glands to be collected separately from the submandibular glands. This device has since been modified and does not

require suction to hold it in place, as they are individually made to fit each subject (Stephen and Spiers 2012). Measurements of the other major and minor salivary glands are not performed routinely, due to their relative inaccessibility.

Methods for measuring saliva are usually based on (i) draining the saliva collected into a receptacle, known as the 'draining' method, (ii) collection by aspiration, known as the 'spitting' method or (iii) measuring the increase in weight of an absorbent material that is chewed or placed in the mouth, known as the 'swab' method. A frequent and easy means of collection used in the swab method is the absorption of saliva by rolls of cotton. The weight of these cotton rolls is established before and after measurement. This method of collection has proved to be valid, reliable and sensitive (White 2007). However, some adverse effects of this procedure make it less desirable, such that it is always necessary to interrupt the experimental procedure by inserting and removing the dental rolls and the pressure of the rolls on the salivary glands may induce a salivary response, thereby affecting the experimental response (Nederkoorn, Wit et al. 2001). Suskind and Tilton (Suskind and Tilton 2002) however found that their patients either continually gagged or tried to swallow the rolls. Another technique is measuring the frequency of swallows, determined by counting peaks in the electromyographic activity of the diagastric muscle. This technique allows effects of timing on salivary response to be monitored and although it does not directly measure salivary flow, it does measure response to a given stimuli (Nederkoorn, Wit et al. 2001). Their study concluded subjects swallowed significantly more ($F\ 1,\ 12 = 50{\cdot}1$, $p<0{\cdot}001$), after being presented with a stimulus (tasting lemon juice) than when compared to a control (tasting still water) (Nederkoorn, Smulders et al. 1999).

Experiments have shown that the data collected using this technique correlated well with that of cotton rolls, providing that some precautions are taken against artificial movements, such as coughing (Nederkoorn, Smulders et al. 1999).

An alternative method for measuring salivation is via electrophysiological measurement of the activity of the parotid gland (Davis, Bauslaugh et al. 1996). In this procedure a recording electrode is placed on the cheek to lie over the

parotid gland and extends to the upper cheek, the joint action of the secretory and muscle cells in the gland produces a change in electrical potential over the gland, which can be recorded at the skin's surface. A peak in activity in response to lemon juice was reported, with a latency of 2.5 – 3 seconds, the highest peak around 3.5 – 7 seconds, and recovery between 13 – 25 seconds, when compared to a water control (Davis, Bauslaugh et al. 1996).

Nederkoorn (Nederkoorn, Wit et al. 2001) devised an experiment to test the three methods of collection (cotton rolls, electromyographic activity of the diagastric muscle and electrophysiological measurement of the parotid gland) and compared the results of each collection method. They presented four stimuli to 48 subjects in succession and concluded that electrophysiological measurement of activity of the parotid gland is not a reliable or valid method of measuring salivary response to stimulation with different foods. However, both the dental roll (swab) method and swallowing technique did differentiate between the stimuli (Nederkoorn, Wit et al. 2001).

Measurement of unstimulated saliva flow rates using the spitting or draining methods are thought to be unreliable in children of younger than 10 years of age, as these methods depend on the child being fully co-operative, when they have to sit still for some time (Ben-Aryeh, Fisher et al. 1990). Measuring saliva flow in young children or in those with physical or cognitive impairment can be challenging using the swab method, as it requires the individual to be compliant and remain in a static position. Measuring flow rates in these children is usually performed by measuring the amount of saliva spill (drooling) or counting the number of bibs saturated with saliva. Volumetric measurements to obtain absolute quantification of saliva spill or intra-oral pooling, using external collection devices or intra-oral suction hooks can assist and guide treatment and assess treatment outcomes. Counting the number of bibs changed in a day, despite being an objective quantitative measure, relies on care-giver observation and their judgement as to when a bib is sufficiently soaked to require changing.

An accurate evaluation of drooling is difficult because of variations between individuals, but also because drooling fluctuates throughout the day and between activities. Several systems have been devised and used by authors, either in isolation or in combination. Measurements can be objective and quantitative or subjective and qualitative.

Wilkie and Brody (Wilkie and Brody 1977) provided a classification of efficacy of therapeutic procedures for drooling into excellent, good, fair and poor. Most popular scales categorise drooling into dry, mild, moderate or frequent (Scully, Limeres et al. 2009). The clinical evaluation of drooling severity and frequency is difficult because of within-subject fluctuation during the day and a large between-subject variation. Several systems have been used and advocated for assessment of the extent of drooling. Since its introduction, various modifications of the Drooling Quotient (DQ) have been used (Rapp 1980; Jongerius, Van Limbeek et al. 2004). The Drooling Quotient is a validated, semi-quantitative, direct observational method; the presence or absence of drooling is assessed every 15 seconds during two 10-minute periods (40 observations in 10 minutes), separated by a 60-minute break (Rapp 1980; Jongerius, Van Limbeek et al. 2004). Although this is a validated method it may be very disruptive to an individual's routine and therefore unsuitable to use in certain environments. Furthermore it would need to take in to account stimulated and unstimulated periods of stimulation and record time at which it was rated.

DQ (%) = No. of drooling episodes / No. of observations in 10 mins x 100

Rating scales such as the Teacher Drooling Scale (TDS) (Camp-Bruno, Winsberg et al. 1989) have been designed to assess drooling severity and frequency. The TDS is a quantitative scale for periodic assessment of drooling (Nickel and Desch 2000) and rates the frequency of drooling on a score of 1 to 5 (Table 2). The difficulty with using this scale is the variance in inter-rater reliability and without any pre-training on the use of the scale, one rater may score an individual as 'infrequent drooling' and another rater score the same individual as 'occasional drooling', thus leading to inconsistencies in scoring in

the scale. This scale does not separate severity and frequency of drooling and may not be considered sensitive enough, as it does not explain all possible variations, such as an individual who may infrequently drool, but when they do may do so in large quantities, but this is not a given option within the scale.

Table 2 The Teacher Drooling Scale (Camp-Bruno, Winsberg et al. 1989)

1. No drooling
2. Infrequent drooling, small amount
3. Occasional drooling, on and off all day
4. Frequent drooling, but not profusely
5. Constant drooling, always wet

Thomas-Stonell and Greenberg (Thomas-Stonell and Greenberg 1988), described a drooling scale, using severity and frequency of drooling. The severity of drooling is rated on a scale of 1 to 5, with 1 being dry and 5, profuse wetness, whilst frequency is rated on a 1 to 4 scale, ranging from 1, never to 4, constant (Table 3).

Table 3 Drooling Severity and Frequency Rating Scale (Thomas-Stonell and Greenberg 1988)

Drooling severity

1. Dry – never drools
2. Mild – wet lips only
3. Moderate – wet lips and chin
4. Severe – damp clothing
5. Profuse – damp clothing, hands and surrounding objects

Drooling frequency

1. Never – no drooling
2. Occasionally
3. Frequently
4. Constantly

Another method of measuring drooling is the use of subjective questionnaires to record the views of the carer or patient (Van der Berg, Didden et al. 2007). If designed carefully in relation to content and construct validity, these can be sensitive to reflect the concerns of the patient and / or the carer and can assist in measuring clinical change. A valid and reliable questionnaire is the Drooling Impact Scale (Reid, Johnson et al. 2010) (Table 4) , which is composed of 10 items, rated on a scale of 1 to 10, which is completed by either the patient, their carer or someone who knows the individual well. The Drooling Impact Scale highlights the changes in drooling as perceived by the person completing the questionnaire.

Reid et al. (Reid, Johnson et al. 2010) commented that objective measures may be invasive, unsuitable and sometimes inaccurate and that the main aim of reducing drooling is to improve quality of life.

Table 4 Drooling Impact Scale (Reid, Johnson et al. 2010)

OVER THE PAST WEEK		
1. How frequently did your child dribble?		
Not at all	1 2 3 4 5 6 7 8 9 10	Constantly
2. How severe was the drooling?		
Remained dry	1 2 3 4 5 6 7 8 9 10	Profuse
3. How many times a day did you have to change bibs or clothing due to drooling?		
Once or not at all	1 2 3 4 5 6 7 8 9 10	10 or more
4. How offensive was the smell of the saliva on your child?		
Not offensive	1 2 3 4 5 6 7 8 9 10	Very offensive
5. How much skin irritation has your child had due to drooling?		
None	1 2 3 4 5 6 7 8 9 10	Severe rash
6. How frequently did your child's mouth need wiping?		
Not at all	1 2 3 4 5 6 7 8 9 10	All the time
7. How embarrassed did your child seem to be about his/her dribbling?		
Not at all	1 2 3 4 5 6 7 8 9 10	Very embarrassed
8. How much do you have to wipe or clean saliva from household items, e.g. toys, furniture, computers?		
Not at all	1 2 3 4 5 6 7 8 9 10	All the time
9. To what extent did your child's drooling affect his or her life?		
Not at all	1 2 3 4 5 6 7 8 9 10	Greatly
10. To what extent did your child's dribbling affect you and your family's life?		
Not at all	1 2 3 4 5 6 7 8 9 10	Greatly

There are also two specific assessments available to measure drooling and drooling related discomfort in patients who have Parkinson's Disease; found within subsection II, activities of daily living, number 6, of the Unified Parkinson's Disease Rating Scale (UPDRS), (Goetz, Tilley et al. 2008) (Table 5). This scale cannot be rated in isolation, but only as part of the wider rating system and within this population.

Table 5 Unified Parkinson's Disease Rating Scale (UPDRS), (Goetz, Tilley et al. 2008)

II. ACTIVITIES OF DAILY LIVING - No. 6 Salivation
0 = Normal.
1 = Slight but definite excess of saliva in mouth; may have night-time drooling.
2 = Moderately excessive saliva; may have minimal drooling.
3 = Marked excess of saliva with some drooling.
4 = Marked drooling, requires constant tissue or handkerchief.

The Visual Analogue scale (VAS), a semi-quantitative scale, is usually given to parents/primary caregivers. Scales of exactly 10cm without visible subdivisions, on which the average degree of drooling is marked, are given. A score of ten indicates severe drooling and a score of zero (0) indicates no drooling. An independent person then scores the VAS with a ruler in millimetres, resulting in a number ranging from 0 to 100 (Jongerius, Rotteveel et al. 2004).

In 2006, Perez et al (Perez, Piran et al. 2007) carried out a study to develop and validate a clinical scale for subjective evaluation of sialorrhea (drooling) in Parkinson's disease; the Sialorrhea Clinical Scale for Parkinson's disease (SCS – PD), (Perez, Piran et al. 2007). In Phase I of their study they established internal consistency and in phase II of their study they established scale validity. In their study the SCS-PD scores showed significant correlation with saliva volume and with total Unified Parkinson's Disease Rating Scale (UPDRS) scores. Sialorrhoea or drooling is known to affect 75–80 per cent of patients

with Parkinson's Disease (Mancini, Zangaglia et al. 2003). It has long been thought this was due to hypersecretion of saliva as a result of autonomic dysfunction. However, more recent research has suggested that, far from producing excess saliva, people with Parkinson's Disease actually tend to produce less saliva than matched controls (Bagheri, Damase-Michel et al. 1999; Proulx, de Courval et al. 2005). These studies suggest that, due to delayed swallowing disorders also common in Parkinson's Disease, patients are unable to swallow all their saliva as it is being produced; this then leads to an accumulation of saliva and the apparent drooling symptoms, due to weak oral musculature.

A variety of subjective and objective methods for assessment of excessive saliva and subsequent drooling have been described (Sochaniwskyj 1982). Assessment of the severity of drooling and its impact on quality of life for the patient and their carers is important as it helps establish a prognosis and to decide the therapeutic regimen.

1.05 Saliva Composition

Salivary fluid consists of approximately 99% water, containing a variety of electrolytes and proteins, in the form of enzymes (Young and Van Lennep 1979). Saliva is normally a colourless fluid with a pH value of approximately 6.64, but this varies depending on the level of carbon dioxide (CO_2) in the blood (Guyton 1996). When blood CO_2 level is raised, a higher proportion of CO_2 is transferred to the saliva and therefore salivary pH decreases. Conversely, if blood CO_2 levels fall, the salivary pH increases, as a result of minimal transfer of blood CO_2 to the saliva (Chicharro, Lucia et al. 1988). The two additional gases present within saliva are oxygen (O_2) and Nitrogen (N_2). Other components (of saliva) include maltese, serum albumin, urea, uric acid, creatinine, mucin, ascorbic acid (vitamin C), amino acids, lactate and hormones such as testosterone and cortisol (Chicharro, Lucia et al. 1988).

'Total' or 'whole' saliva describes the composite mixture of fluids from the salivary glands, oral mucosa and the mucous of the nasal cavity and pharynx. It

also contains blood cells and traces of medications or chemical products (Humphrey and Williamson 2001).

The mean concentrations of the main substances found in saliva are shown in Table 6. The salivary flow rate can significantly alter some of these values in that as it increases, sodium and bicarbonate levels and pH rise, while potassium, calcium, phosphate, chloride, urea and protein levels fall. Because salivary components are considered multifunctional and change depending on the intraoral environment, the development of an effective artificial saliva is a difficult task (Levine 1993). This is particularly important when considering patients who experience reported symptoms of 'dry-mouth' and prescribing artificial saliva, which cannot react to chemical changes intra-orally and help maintain chemical balance.

Saliva provides an easily available non-invasive diagnostic medium for a rapidly widening range of diseases and clinical situations (Mandel 1990). Saliva is a defensive factor in the mouth, and a reduction in its flow rate affects oral and dental health. A reduced or increased salivary flow may cause a variety of symptoms and so the establishment of patients' saliva flow is of primary importance.

Table 6 Saliva Composition (Rice 1984)

	Salivary Gland	
	Parotid	Submandibular
Substance	mEq*/ Litre	mEq/ Litre
Potassium	20.0	17.0
Sodium	23.0	21.0
Chloride	23.0	20.0
Bicarbonate	20.0	18.0
Calcium	2.0	3.6
Magnesium	0.2	0.3
Phosphate	6.0	4.5
mg/dl** mg/dl		
Urea	15.0	7.0
Proteins (mucins, MG1 & MG2)	250.0	150.0
Ammonia	0.3	0.2
Uric acid	3.0	2.0
Lysozymes	2.3	1.5
Glucose	<1.0	<1.0
IgA	4.0	2.0
Amylase	0.1	0.0025
Cholesterol	<1.0	unknown
pH	5.92	5.73

*mEq – molar equivalent; **milligrams per decilitre

1.1 Saliva Functions

The functions of saliva can be organised into five main actions that are necessary for the maintenance of oral health; (1) lubrication, binding and protection, (2) buffering action, (3) maintenance of tooth integrity, (4) antibacterial activity, and (5) taste and digestion (Moss 1995).

1.11 Lubrication, binding and protection

Saliva forms a covering that lubricates and protects the oral tissues against irritating agents (Stack and Papas 2001). These irritants may include, proteolytic and hydrolytic enzymes produced in plaque, potential carcinogens from smoking and exogenous chemicals and drying out of the mouth from mouth breathing (Grant, Stern et al. 1988). This effect of lubrication occurs due to the presence of mucins, which are proteins with high carbohydrate content, excreted from minor salivary glands, submandibular and sublingual glands. Mucins act as lubricants, providing protection against dehydration, and maintaining the elasticity and viscosity of saliva. These complex protein molecules are formed from polypeptide chains that stick together and have properties of low solubility, high viscosity, high elasticity and strong adhesiveness. In addition, the lubricant effects of these proteins also aid in mastication, speech and swallowing (Humphrey and Williamson 2001; Amerongen and Veerman 2002). The mucous in saliva is highly effective in binding masticated food into a slippery bolus that can then easily be passed through the oesophagus, without causing damage to the mucosa. Saliva also coats the oral cavity and oesophagus, and food never directly touches the epithelial cells of these tissues (Bailey 2013).

1.12 Buffering action

Saliva acts as a buffering and clearance system through the following components: bicarbonate, phosphate, urea and amphoteric proteins and enzymes. Bicarbonate is the most important buffering system and it diffuses into plaque and acts to neutralise acids (Humphrey and Williamson 2001). In addition it generates ammonia to form amines, which also acts as a buffer by neutralising acids (Mandel 1989). Urea another buffer present in saliva, releases ammonia after being metabolised by plaque and thus increases the pH of plaque (Johnson 1987). In summary saliva buffers and protects the mouth in two ways: 1) It prevents the colonisation of potentially pathogenic microorganisms by preventing the optimal environmental conditions that they require to thrive (Nagler 2004); 2) Saliva neutralises and cleans the acids produced by microorganisms, thereby preventing enamel erosion (Almeida, Gregio et al. 2008). The buffering action of saliva works most efficiently at times of stimulated high flow rates, but is almost ineffective during periods of low flow, with unstimulated saliva (Edgar 1990). The pH of saliva is not necessarily an important measure for buffering action on caries, as it changes depending on the pH of plaque. (Roth and Calmes 1981). The resting pH of plaque, after approximately 2 to 2.5 hours after consumption of carbohydrates is 6 to 7 (Edgar 1990). The pH rises during the first 5 minutes of food intake. The pH then falls to its lowest level, to 6.1 or lower, approximately 15 minutes after food intake, unless there is further consumption of fermentable carbohydrates, the pH of plaque then gradually returns to its resting value of 6 to 7 (Edgar 1976).

1.13 Maintenance of tooth integrity

Saliva has a fundamental role in sustaining the physical-chemical integrity of tooth enamel, by regulating re-mineralisation and demineralisation. Tooth enamel demineralisation is triggered by an increase in the acidity of bacterial plaque, which initiates the caries process (Fejerskov and Kidd 2008). Demineralisation occurs when acid diffuses through enamel and the pellicle. The pellicle is a layer of salivary glyco-proteins that forms on the tooth surface,

which protects against caries, as it slows the diffusion of calcium and phosphate ions away from the tooth surface.

Crystalline dissolution occurs at a pH of 5 to 5.5, which is the critical pH range for the development of caries (Edgar 1990). The main factors controlling the stability of enamel are the high salivary concentrations of calcium, phosphate and fluoride, and the normal salivary pH value of approximately 6.6 (Axelsson 2000). Statherin, a salivary peptide, aids the stabilisation of calcium and phosphate solutions and serves as a lubricant to protect the tooth from wear (Dowd 1999). The presence of fluoride in saliva, even at low levels is essential for stabilising dental minerals and is dependent on fluoride in drinking water and in other sources, such as pastes, liquids or powders used to help maintain good oral hygiene (dentifrices) and other products used in the prevention of tooth decay (caries). It has also been identified that fluoride reduces the production of acids in the saliva and speeds up crystal precipitation, forming a coating more resistant to caries than the original tooth structure (Humphrey and Williamson 2001). The presence of fluoride in saliva speeds up crystal precipitation, forming a fluorapatite-like coating more resistant to caries than the original tooth structure. It has been suggested that small amounts of demineralisation are therefore advantageous for the tooth (Edgar 1990).

1.14 Antibacterial activity

The salivary glands secrete fluid containing immunologic and non-immunologic agents for the protection of teeth and mucosal surfaces. Immunologic contents of saliva include immunoglobulin A (IgA), immunoglobulin G (IgG), and immunoglobulin M (IgM). Non-immunologic contents of saliva include selected proteins, mucins, peptides and enzymes. Secretory IgA is the largest immunologic constituent of saliva and is produced by plasma cells in connective tissues and is transported and located within the duct cells of both major and minor salivary glands. IgA whilst active on the mucosal surface, also works to neutralise viruses, acts as an antibody to bacterial antigens by isolating and clumping harmful bacteria, and inhibits their adherence to oral tissue (Dowd 1999). MG2, the low molecular-weight mucin and IgA bind mucosal pathogens

with greater affect, than either MG2 or IgA alone (Biesbrock and Levine 1991). Non-immunologic antibacterial contents such as proteins, mucins, peptides and enzymes, all products of acinar gland cells, help protect the teeth against chemical, physical and micro-organism attack (Rudney 1995). Lactoferrin is a protein produced in the salivary ducts; it acts to binds ferric iron in saliva and thereby makes ferric iron unavailable as a food source for microbes, which require iron to work successfully (Roth and Calmes 1981). This process of starving bacteria of vital nutrients is called 'nutritional immunity' (Mandel 1976). Other proteins such as glycoproteins, statherins, agglutinins, histadine-rich proteins, and proline-rich proteins work to aggregate bacteria and 'clump' them together, thereby reducing the ability of bacteria to adhere to hard or soft tissue of the intraoral surfaces and thus controls bacterial, fungal and viral colonisation (Mandel 1989). These proteins assist in reducing bacterial growth and protect the teeth.

1.15 Taste and digestion

The chemical substance responsible for taste is released in the mouth and comes in to contact with a nerve cell, which activates the cell by changing specific proteins in the sensory cell (Institute for Quality and Efficiency in Health Care 2012). This change causes the sensory cell to transmit messenger substances, which then activate further nerve cells. These nerve cells then pass on information for a particular perception of flavour on to the brain (Institute for Quality and Efficiency in Health Care 2012). Numerous wart-like bumps on the mucous membrane of the tongue are where the substance producing taste is transformed into nerve signals. These bumps are called taste papillae and contain many sensory cells including taste buds. Most of the taste buds are on the tongue, but there are also cells that detect taste in the back of the throat, epiglottis, the nasal cavity and in the upper part of the oesophagus (Institute for Quality and Efficiency in Health Care 2012). Based on the information that is transported from the tongue to the brain, there are thought to be at least five basic qualities of taste. The basic tastes are sweet, sour, salty, bitter and savoury all of which can be sensed by all parts of the tongue (Institute for Quality and Efficiency in Health Care 2012).

Saliva is responsible for the initial digestion of starch and aids in the formation of the food bolus (Ten Cate 1998). This occurs primarily because of the presence of the digestive enzyme amylase, a major component of parotid saliva, which initially begins the breakdown of starch (Mandel 1987; Moss 1995). The involvement of saliva in the break-down of starch is limited as most of the digestion of starch results from pancreatic amylase, and not salivary amylase (Grant, Stern et al. 1988). The presence of amylase is thought to be a good indicator of properly functioning salivary glands (Enberg, Alho et al. 2001), contributing 40% to 50% of the total salivary enzyme produced by the glands. Salivary enzymes also initiate the digestion of fats (Valdez and Fox 1991).

1.2 Xerostomia, drooling and its management

Saliva is required in order for the mouth to be able to work properly. Saliva keeps the mouth moist, and it helps to break down food and helps with swallowing. It is constantly present around the mouth and teeth, fighting decay and helping to keep the teeth clean. Dry mouth or ‘xerostomia' is a condition in which individuals report a feeling of dry-mouth.

Drooling, also known as ptyalism can be defined as salivary incontinence or the spillage of saliva over the lower lip. It may reflect a disturbance of the oral phase of deglutition which is associated with inefficient, uncoordinated swallowing and poorly synchronised lip closure. It is frequently associated with abnormal tone of the muscles that open the mouth. Individuals who drool have difficulty managing normal salivary flow; sialorrhea, which some use interchangeably with drooling, indicates an increase in salivary flow, which can be due to inflammation in the oral cavity, such as teething, dental caries, or due to medications such as antiepileptic or antipsychotic drugs, alternatively due to certain conditions, such as gastroeosophageal reflux, which can all also lead to drooling. In either case a feeling of dry-mouth or drooling can be distressing for individuals.

1.21 Xerostomia

Xerostomia is a reported complaint of feelings of dry mouth and is highly prevalent in the elderly population (Billings, Proskin et al. 1996). Its prevalence ranging from 10% to 38% (O'Grady 1990; Locker 1995). Xerostomia can occur due to severe reduction in salivary flow (Sreebny 1987), even where there appears to be normal salivary gland function (Fox, van der Ven et al. 1985; Sreebny 1987). The most common reason for xerostomia is Sjogren's syndrome (van der Berg, Pijpe et al. 2007); a condition where the body's immune system malfunctions and begins to attack healthy tissue (an autoimmune condition). In Sjogren's syndrome the immune system usually targets the tear and saliva glands, leading to a reduction in the production of saliva and tears (van der Berg, Pijpe et al. 2007), which results in the perception of dry-mouth. In the past, complaints of dry mouth were often thought to be as a result of aging. However it is now generally accepted that salivary function is preserved throughout life in healthy individuals (Matear and Barbaro 2005) and aging is not an associated factor with xerostomia. However, the use of medications or presence of systemic disease (Fox, van der Ven et al. 1985) can be a causal factor and explain the reason for the salivary hypofunction in older individuals.

Cystic fibrosis affects all of the exocrine glands to varying degrees (Ferguson 1999). The most noticeable change is that in the composition of saliva, in which there are reported changes in elevation in calcium (Ca) and proteins which reduce the flow rate of minor salivary glands to virtually zero. Normally the flow rate of a single labial gland is 0.1 µl/min (microlitres per minute) (Ferguson 1999). This phenomenon can be used as a diagnostic test by measuring the flow from labial glands of the lower lip (Mandel 1990). The sodium (Na) and potassium (K) concentrations of saliva are markedly affected by corticosteroids, especially aldosterone. The Na / K ratio of stimulated whole saliva can be used

in diagnosing and monitoring ‘Cushing’s syndrome’ and ‘Addison’s disease’ (Mandel 1990). Investigators have also demonstrated the diagnostic value of Na / K ratio in primary aldosteronism, a type of hormonal disorder that leads to high blood pressure (Wotman, Goodwin et al. 1969). In several clinical settings salivary analysis has provided valuable diagnostic information. This includes digitalis toxicity, affective disorders, stomatitis in chemotherapy, specific secretory IgA deficiency, smoking, ovulation time, relation of dietary factors to cancer and chronic pain syndromes (Mandel 1990).

Another frequent cause of dry mouth is medication (Nahri 1994), which can affect aspects of salivation and saliva flow rate. Some of the medications associated with dry mouth include anti-convulsion, anti-hypertensive, anti-psychotic, anti-depressant, anti-Parkinsonian and sedative drugs (Laclede 1999); the intake of these drugs have a dryness-inducing (xerogenic) effect. A number of diseases, conditions and treatments can also cause dry mouth, such as diabetes, Parkinson’s Disease, thyroid disorders and head and neck radiation therapy (Laclede 1999), due to the symptoms they produce, such as dehydration in diabetes and excessive sweating as sometimes seen in individuals who have an overactive thyroid gland (Laclede 1999).

Symptoms of dry mouth may include an itching or burning sensation of the oral mucosa and the tongue, difficulties with speech, eating and swallowing (Sreebny and Valdini 1988), as well as taste impairments (Spielman 1990). Other causes of dry mouth include wearing dentures and malnutrition (Laclede 1999). The condition of xerostomia is known to seriously damage the quality of life among the affected individuals (Gerdin, Einarson et al. 2005).

Because saliva plays a vital role in lubricating and protecting the mouth from infection, it has a critical role in daily oral functioning. Without adequate amounts of saliva, normal oral function is compromised. Individuals who present with xerostomia can be highly prone to the development of dental decay, since saliva has buffering properties which increase the intra-oral pH level to a neutral value, assisting in the reduction of dental decay.

1.22 Drooling

Currently there is no generally accepted existing definition for the term ‘drooling’. Drooling is also sometimes described as ‘dribbling’, or ‘saliva loss’. It is important to distinguish the differences between anterior and posterior drooling in relation to aetiology and clinical impact (Reddihough, Erasmus et al. 2010). Saliva spilled from the mouth, which can be visibly seen, is known as anterior drooling (Reddihough, Erasmus et al. 2010). Posterior drooling is where saliva is spilled through the faucial isthmus (Reddihough, Erasmus et al. 2010), leading to a risk of aspiration (Smith 2008). Posterior drooling occurs in individuals who present with oropharyngeal dysphagia (Jongerius, Van Hulst et al. 2005). Blasco’s definition of drooling is often used, describing it as ‘the unintentional loss of saliva and contents from the mouth’, (Blasco and Allaire 1992). This is not due to excessive saliva production (hypersalivation or sialorrhea), but is more commonly a problem in coordinating the control mechanisms of the oral-facial and palatolingual muscles, associated with a neurological disturbance (Blasco and Allaire 1992). Studies have shown that patients who produce less saliva (e.g. patients with Parkinson’s Disease), (Bagheri, Damase-Michel et al. 1999; Proulx, de Courval et al. 2005) can also have difficulties with drooling. Impairments in neurological control leads to difficulties with the swallowing function; this results in excessive pooling of saliva in the anterior part of the oral cavity and subsequently causes unintentional loss of saliva from the mouth, due to impaired lip-seal. Drooling is a normal finding in healthy infants, but usually ceases by about the age of 18 months as oral motor and sensory ability improves. Drooling is considered as abnormal if it persists beyond the age of 4 years (Crysdale and White 1989).

Anterior drooling (Reddihough, Erasmus et al. 2010) can be extremely distressing for patients and their caregivers, with the possibility of social rejection, continuous wetness of clothing and physical distress adding to the special care and attention they require. Anterior drooling has been found to be a significant impediment to socialisation, building interpersonal relationships and

integrating into society for individuals with disabilities (Tahmassebi and Curzon 2003). The presence of pooled saliva may cause articulatory imprecision, resulting in communication breakdown. In addition there may be associated posterior drooling (Reddihough, Erasmus et al. 2010), due to an inability to swallow effectively leading to an increased risk of aspiration pneumonia.

1.23 Prevalence of drooling

The most common cause of drooling in children is cerebral palsy. It has been estimated that drooling abnormally persists in 10-38% of individuals with cerebral palsy (Johnson and Scott 1993), although it has been reported to exceed 50% (Tahmassebi and Curzon 2003). In a study by Morales et al. (Morales, Grollmus et al. 2008), 50 individuals with Cerebral Palsy comprising of both children and adults were evaluated and it was concluded that 58 % presented with drooling. In adults, Parkinson's disease is the most common cause. Approximately 45% of Parkinsonian patients complain about drooling, which in 15% of cases is detected in the early phases of the disease (Volonte, Porta et al. 2002). However a study by Molloy suggested that drooling occurs in 70-80% of patients with Parkinson's disease (Molloy 2007). Drooling is also commonly associated with other neurological conditions such as stroke, pseudobulbar palsy, or bulbar palsy, where it is seen in almost 30% of patients (Sullivan, Lambert et al. 2000).

1.24 Drooling and reduced level of consciousness

Teasdale and Jennett (Teasdale and Jennett 1974) published the Glasgow Coma Scale (GCS) an aid in the clinical assessment of post-traumatic unconsciousness. It was devised as a formal scheme to overcome the ambiguities that arose when information about comatose patients was presented and groups of patients compared. The GCS evaluates three components: eye (E), verbal (V) and motor (M) responses to external stimuli (Teasdale and Jennett 1974). The scale consists of 15 points and is used to predict the progression of a person's condition (figure 4). Clinicians use the scale to rate the best eye opening response, the best verbal response, and the

best motor response an individual makes. The final GCS score is the sum of these numbers.

Best Eye Response (4)

1. No eye opening
2. Eye opening to pain
3. Eye opening to verbal command
4. Eyes open spontaneously

Best Verbal Response (5)

1. No verbal response
2. Incomprehensible sounds
3. Inappropriate words
4. Confused
5. Orientated

Best Motor Response (6)

1. No motor response
2. Extension to pain
3. Flexion to pain
4. Withdrawal from pain
5. Localising pain
6. Obeys Commands

Figure 4 Glasgow Coma Scale (Teasdale and Jennett 1974), illustration from http://www.trauma.org/archive/scores/gcs.html

A GCS of 8 or less indicates severe injury, one of 9-12 a moderate injury, and a GCS score of 13-15 is obtained when the injury is minor. The lowest score for each category is 1; therefore the lowest score is 3, where there is no response to pain, no verbalisation and no eye opening, sometimes termed as vegetative state (McPherson and Stephens 2012). Patients with a reduced conscious level are unable to clear their own secretions and cannot protect their own airway. A Glasgow Coma Scale of 8/15 or below is often considered the threshold at which intubation is necessary (McPherson and Stephens 2012). Patients with

reduced conscious level are at risk of aspiration (McPherson and Stephens 2012).

1.25 The management of drooling

Management of excess pooled saliva, which may result in drooling, ranges from the conservative, such as postural changes, oral motor therapy and biofeedback, to the more aggressive such as medication, radiation and surgical intervention. This section investigates and describes the different ways of managing drooling and the efficacy of these techniques.

Oral motor therapy

Oral motor training can be used to attempt to normalise muscle tone, stabilise the positions of the body, head and jaw, reduce tongue thrust, increase lip closure and promote swallowing, but can be time-consuming, and requires motivation. Harris and Dignam (Harris and Dignam 1980) showed that through training programmes, mirrors, games and positive reinforcement with children with Cerebral Palsy, they were able to reduce drooling and achieve an appropriate anterior oral lip seal (Harris and Dignam 1980). Stonell and Greenberg (Thomas-Stonell and Greenberg 1988), offered three conservative treatment approaches in reducing drooling: no direct intervention, feeding / oral stimulation programmes and finally behavioural modification programmes. They concluded that 66% of participants who received conservative treatment showed an effective reduction in the severity or frequency of drooling (Thomas-Stonell and Greenberg 1988). However in their study they assigned individuals to each of one of the three treatment groups following initial multidisciplinary team assessment, rather than random allocation, which may have introduced a selection bias, for example participants were allocated to the no direct intervention group, if further neurologic maturation was anticipated, but these individuals may have had severe drooling and therefore altered the outcomes by assigning them to a given treatment intervention.

Behavioural modification

Koheil (Koheil, Sochaniwsky et al. 1987) reported on the success of a training programme using auditory electromyography (EMG) biofeedback, using electrodes placed on the muscles surrounding the lips, conditioning the patient to swallow at the sound of an auditory stimulus. However the study concluded that patients had to have intact communication skills and intellectual function, present only with a moderate drooling difficulty and be reasonably well motivated. Consequently, these techniques were not used in clinical practice (Koheil, Sochaniwsky et al. 1987). Stonell and Greenberg (Thomas-Stonell and Greenberg 1988), offered behaviour modification programmes in their study and found that 73% of participants who engaged in this programme showed an improvement in their drooling control (Thomas-Stonell and Greenberg 1988).

Drug therapy

Studies have shown that the use of medications, such as glycopyrrolate and scopolamine, are effective in reducing drooling, but have many adverse side effects, such as excessive dry mouth, constipation, urinary retention, decreased sweating and skin flushing (Bachrach, Walters et al. 1998; Meir, Bachrach et al. 2000; Hockstein, Samadi et al. 2004). A systematic review by Jongerius (Jongerius, van Tiel et al. 2003), investigated the efficacy of anticholinergic drugs in the treatment of drooling in children with multiple disabilities, they found only seven articles. From their review they suggested that at least some of these medications are effective, but were unable to conclude which one drug is preferable (Jongerius, van Tiel et al. 2003). In a further study by Jongerius et al. (Jongerius, Rotteveel et al. 2004), 45 children who experienced severe drooling, were recruited to a controlled clinical trial. Using a within-subject design each participant received treatment with transdermal scopolamine and then treatment with single-dose botulinum toxin injections in the submandibular glands. Measurements on the drooling quotient (DQ), teacher drooling scale

(TDS) and visual analogue scale (VAS) all showed that drooling was reduced during scopolamine application as well as after botulinum toxin injections. However 71.1% of the patients had moderate to severe side effects as a reaction to scopolamine, and in comparison only non-severe, incidental side effects were reported from the use of botulinum toxin. Side effects of the scopolamine application included xerostomia, restlessness, drowsiness, blurred vision and confusion, whereas a mild temporary disturbance in swallowing was reported in one individual who received botulinum toxin injections, but did not require any additional intervention. The botulinum toxin injections were given under general anaesthesia, which also has potential risks, but when weighed against the possible adverse effects encountered when using scopolamine for a longer period, was deemed acceptable (Jongerius, Rotteveel et al. 2004). Walshe et al. (Walshe, Smith et al. 2012) conducted a review to examine the effectiveness and safety of interventions with the objective of reducing or eliminating drooling in children with cerebral palsy. In their review they identified two studies, using pharmacological treatments which although did not fully meet their inclusion criteria of age and included some children without cerebral palsy, did include these as they were the only studies to describe the use of glycopyrrolate and benztrophine intervention, which is commonly prescribed in this population (Walshe, Smith et al. 2012). They concluded that the pharmacological intervention only took into account immediate change and did not measure longer-term effects, and whilst there was some evidence available for short-term benefits, no conclusions could be reached on the efficacy and safety of either of these two treatments, due to the methodological quality and variations in the designs of the studies (Walshe, Smith et al. 2012).

Radiotherapy

Studies using radiation therapy, with radiation doses targeting the submandibular and sublingual salivary gland tissue, have shown initial satisfactory responses in the management of sialorrhea, with up to 80% success rate, although there were some reported side effects, including oral candidiasis and mild skin reactions amongst participants (Borg and Hirst 1998). Due to the risk of malignancy, xerostomia, mucositis, radiation caries and

osteoradionecrosis, it has been advised that radiotherapy be avoided in young children (Borg and Hirst 1998). Conversely, in elderly patients who may have a limited life expectancy, these long-term side effects would not be expected to develop. Following a review of their results Borg and Hirst (Borg and Hirst 1998) concluded that the desired response in controlling drooling, with minimal discomfort, can be expected by controlling the amount of radiation exposure to both the parotid and submandibular glands (Borg and Hirst 1998). In a study of 18 patients with amyotrophic lateral sclerosis and severe drooling Anderson (Anderson, Gronberg et al. 2001) showed that irradiation of the larger part of the parotid salivary glands and the posterior part of the submandibular glands reduced drooling without producing permanent xerostomia in all but of one of their patients.

Surgical salivary duct and gland procedures

Three studies involving the surgical management of drooling have investigated parotid duct relocation from the buccal vestibule to the area of the maxillary second molar and the tonsillar fossa, along with bilateral removal of the sub-mandibular gland. The aim of duct relocation is to redirect the saliva to the posterior part of the mouth, in order to initiate the swallowing reflex and prevent drooling. Some studies of surgical management have reported good outcomes, showing a success rate of 86%, showing good to excellent results in 58 patients who have undergone surgical resection of the sub-mandibular gland with bilateral parotid duct ligation. (Dundas and Peterson 1979; Brundage and Moore 1989; Shott, Myer et al. 1989). However more recent research has shown the long-term efficacy of intra-oral surgery for the management of sialorrhea to be minimally effective and that over two-thirds of patients had a recurrence of drooling following surgery and additional medication or surgical intervention was required (Martin and Conley 2007). Scheffer et al. (Scheffer, Erasmus et al. 2010) studied 19 children and young adults (15 children diagnosed with bilateral cerebral palsy, three with unilateral cerebral palsy, and one with non-progressive developmental delay), and compared the use of Botulinum Toxin injections versus submandibular duct ligation for the management of severe drooling. In their study they used the drooling quotient

and measured this at eight-weeks and then again at 32-weeks. Each participant first underwent botulinum toxin injections and then surgical re-routing of the submandibular duct, at least six months after having had the injections. Compared with a baseline value of 28, the mean drooling quotient 8 weeks post-surgery was 10, and 32 weeks post-surgery was 4 ($p<0.001$). Among the group treated with botulinum toxin, the drooling quotient showed a significant reduction from a baseline value of 30 to 18 after 8 weeks ($p=0.02$), and an ongoing but diminished effect after 32 weeks drooling quotient score of 22 ($p=0.05$). They concluded that both methods were effective in reducing drooling, but surgical relocation had a larger and longer-lasting effect (Scheffer, Erasmus et al. 2010).

Injection of botulinum toxin

Many studies have investigated the management of drooling in both patients with Parkinson's Disease and in children with Cerebral Palsy, using botulinum toxin injected into the salivary glands (Jongerius, Joosten et al. 2003; Caline, Rodrigues et al. 2007; Scheffer, Erasmus et al. 2010). Several studies report on the use and efficacy of ultra-sound guided injection versus direct 'blind' injection into the salivary gland or glands (Dogu, Apaydin et al. 2004; Caline, Rodrigues et al. 2007; Contarino, Pompili et al. 2007). These studies concluded that 'blind' injections are as effective as ultra-sound guided injections, when solely injecting into the parotid gland. When injecting into both the parotid and submandibular glands, the use of guided injections during administration is superior and that this technique is safe and effective in the treatment of sialorrhea (Porta, Gamba et al. 2001; Dogu, Apaydin et al. 2004). In their study Porta et al. (Porta, Gamba et al. 2001) injected the parotid and submandibular glands of 10 patients with neurological disorders with botulinum toxin-A, using ultrasound guidance. Prior to injection, the baseline rate of salivation was assessed using a visual analogue scale. Post-injection, assessments were repeated at regular intervals for up to 1year. They concluded that nine out of the ten (90%) reported a subjective reduction in salivation post-treatment and one patient (10%) found no improvement. Visual analogue scale scores showed a reduction of 60.8% for the nine respondents who reported a reduction. There were no reported serious

side-effects or procedural-related difficulties reported within their study (Porta, Gamba et al. 2001).

Dogu et al (Dogu, Apaydin et al. 2004) investigated the efficacy and safety of intra-parotid botulinum toxin-A injections into parotid gland using ultrasound-guided versus non-guided techniques for the treatment of sialorrhea in patients with Parkinson's Disease. Fifteen patients with Parkinson's Disease were allocated to one of the two groups and saliva secretion was assessed quantitatively at baseline and at weeks 1, 4, and 12. Patients and / or caregivers also assessed the saliva secretion using visual analogue scale (VAS). All patients except one reported subjective improvement in sialorrhea after one-week. Comparisons of quantitative saliva assessments at each follow-up visit showed that ultrasound-guided injections were superior to blind injections for saliva reduction. The VAS scores showed an improvement in the mean rate of saliva secretion in each group at first week ($P<0.05$). Two of the 15 patients suffered from dry mouth, which was described mild in severity, lasting 1 month. They concluded intra-parotid botulinum toxin injections using ultrasound guidance may be an effective, easy, and safe treatment for Parkinsonian sialorrhea (Dogu, Apaydin et al. 2004). In a review by Walshe et al (Walshe, Smith et al. 2012) to evaluate the effectiveness and safety of interventions for drooling in children with cerebral palsy, they performed a comprehensive search of databases from inception through to December 2010, and also included searches for ongoing clinical trials. In their review they only selected randomised controlled trials and controlled clinical trials and found a total of six trials that were eligible for inclusion. Of these six trails, four studies examined the effectiveness of botulinum toxin A, They found that all studies differed in the products used, how these products were made-up and dosages, injection sites and number of injections administered and how the dosage was determined and anaesthesia administered (Walshe, Smith et al. 2012). Their findings also reported that the control interventions differed and that outcomes were examined medium term at three to 18 months, but none of the studies reviewed outcome beyond this time (Walshe, Smith et al. 2012). Walshe et al reported that no conclusions could be reached on the efficacy and safety of the use of botulinum toxin A in the treatment of drooling in children with cerebral palsy (Walshe, Smith et al. 2012).

Optimal treatment options

The treating physician may feel confused with so many different causes of drooling, different pathogenic mechanisms and so many treatments available. However it is important to be aware that a team including at least an otolaryngologist, neurologist, dentist, speech and language therapist, occupational therapist and physiotherapist is recommended (Blasco 2002). The initial step is to correct the many situational factors that may worsen the drooling, such as head positioning, airway difficulties, unnecessary medications, malocclusion, and significant dental disease and where possible to actually correct the underlying cause (Meningaud, Pitak-Arnnop et al. 2006). Following the consideration of situational factors, it is thereafter important to offer physiological treatment options, such as oral-motor therapy and behaviour modification. If this is not possible, or unsuccessful, it is appropriate to suggest drug therapy. When these means have been shown to be ineffective, or are seen to be detrimental, due to the number of associated side-effects, more aggressive treatments may be indicated. However, when considering more aggressive treatment options preference should be given to the more reversible treatments like botulinum toxin, over the non-reversible surgical and radiological options available (Meningaud, Pitak-Arnnop et al. 2006).

Chapter 2

2. The Clinical Management of Saliva in Tracheostomised Patients

The clinical management of saliva in tracheostomised patients is either botulinum toxin or the prescription of medications 'off-label', or a combination of both. Both interventions aim to reduce saliva production and reduce the amount of pooled saliva in the oral cavity, which may fall into the airway, secondary to swallowing difficulties. In addition, patients with a tracheostomy tube, who have difficulties in swallowing their saliva, are assisted in saliva clearance by using tracheal or oral suctioning in order to remove pooled saliva orally and / or within the airway. This chapter will discuss the use of botulinum toxin in the management of excessive pooled saliva and how it affects saliva production, its side-effects and how botulinum toxin has been used in some studies to manage drooling. The chapter will discuss the reasons for tracheostomy tube insertion, why tracheal suctioning is required and associated complications with having a tracheostomy tube in place. It will detail clinical knowledge and skills in the management of tracheostomised patients and current practice and perceptions of patients that have a tracheostomy tube. The final section will comment on the use of medications that are prescribed 'off-label' for the management of saliva, national guidelines that relate to prescribing medications 'off-label' and informed consent and decision making when prescribing these medications.

2.1. Use of anticholergenic medications to reduce saliva flow

A systematic review for evidence of efficacy of anticholinergic drugs to treat drooling concluded benztropine, glycopyrrolate, and benzhexol hydrochloride, as being effective in the treatment of drooling (Jongerius, van Tiel et al. 2003), but all have adverse side-effects and none of the drugs were identified as being superior (Jongerius, van Tiel et al. 2003). Jongerius et al (Jongerius, van Tiel et al. 2003) performed an in-depth review of the literature in order to carry-out a

meta-analysis, but due to limitations within the studies only identified a total of seven. They concluded that due to methodological drawbacks within the studies, no general conclusions could be made about the efficacy or average effect of anticholergenic medications to treat drooling (Jongerius, van Tiel et al. 2003).

Anticholinergic medications block the parasympathetic innervation of the salivary glands. Several studies (Lawrence and Klingbeil 1991; Lewis, Fontana et al. 1994; Blasco and Stansbury 1996; Meir, Bachrach et al. 2000; Robb, Lee et al. 2008) involving the use of glycopyrrolate and scopolamine (Scopoderm TTS® patches) has shown them to be effective in the management of drooling. The anticholinergic medications most commonly used are atropine, benztrophine, glycopyrrolate bromide, benzhexol hydrochloride and scopolamine. These medications are administered in a number of different ways and can be given orally, intravenously, applied topically as patches, injected, and via nebulisation (Nair and Hunter 2004).

2.11 Glycopyrrolate

Studies (Meir, Bachrach et al. 2000; Robb, Lee et al. 2008) have shown 70-90% response rates but with a high rate of side effects. Approximately 20% of patients choose to discontinue due to unacceptable side effects such as excessive dry mouth, urinary retention, decreased sweating, skin flushing, irritability and behavior changes (Meir, Bachrach et al. 2000). In a study by Mier et al. (Meir, Bachrach et al. 2000) they reported glycopyrrolate to be effective in the control of excessive sialorrhea in children with developmental disabilities. In their placebo-controlled, double-blind, crossover study 39 children with developmental disabilities and excessive sialorrhea, were given glycopyrrolate in doses of 0.10mg/kg. They concluded that administering glycopyrrolate in these dosages (0.10mg/kg) was effective in controlling sialorrhea, however found approximately 20% of children given glycopyrrolate experienced substantial adverse effects, enough to require discontinuation of the medication

(Meir, Bachrach et al. 2000). In addition to this Mier et al. found that 25 out of 36 participants (69%) reported side-effects, which included behavioural changes, such as hyperactivity and irritation, also reported were diarrhoea, dry mouth, constipation, dehydration, urinary tract infection and retention, headache, fever, drowsiness, dizziness, disturbed vision, facial flushing, rash, nasal congestion, vomiting dehydration, deterioration of epilepsy and thickened secretions in a child who had a tracheostomy in-situ (Meir, Bachrach et al. 2000). In another study (Robb, Lee et al. 2008) glycopyrrolate was used for the treatment of clozapine induced sialorrhea in three adolescents. Three adolescent participants (aged 13-16), who developed sialorrhea secondary to clozapine treatment, for psychotic illness were given glycopyrrolate (4-8 mg), whilst inpatients. In their study Robb et al (Robb, Lee et al. 2008) concluded that the symptom of sialorrhea was improved in all three cases with all participants reporting a decrease, which was also confirmed by staff observations. However one participant reported constipation, which improved with symptomatic treatment and another participant complained of dry mouth, which was improved with a reduction in the dose of glycopyrrolate (Robb, Lee et al. 2008).

2.12 Scopolamine (Scopoderm TTS®) Transdermal Patches

Studies (Lawrence and Klingbeil 1991; Mato, Limeres et al. 2010) have reported a positive effect in the use of Scopoderm TTS® transdermal patches at reducing drooling. Scopoderm TTS® transdermal patches are prescribed in 1.5mg circular patches and applied behind the ear, releasing scopolamine through the skin into the bloodstream. One single patch application is considered to render a stable serum concentration for 72 hours at which point it will require replacement (ASHP 2013).

In a prospective, randomised, double-blind, crossover, placebo-controlled clinical trial Mato et al. (Mato, Limeres et al. 2010) investigated the management of drooling in disabled patients using scopolamine. They studied

30 disabled patients (age range 12–58 years), who presented with persistent drooling, which was determined subjectively by means of interviews with the carers and medical staff and by direct observation. The frequency of drooling was estimated using the number of bibs used each day and drooling was quantified using the Thomas-Stonell and Greenberg scale (Thomas-Stonell and Greenberg 1988). They reported a significant reduction in drooling ($P < 0.005$) in the scopolamine group in and the mean number of bibs/day decreased during the scopolamine phase from 6 bibs per day at baseline to 3 bibs per day (Mato, Limeres et al. 2010). Four patients (13.3%) dropped out because of moderate scopolamine side-effects: one case of irritability, one case of agitation and two cases of skin reaction. In conclusion, Mato et al. suggested that transdermal scopolamine is an effective and safe therapeutic option to control drooling in severely disabled patients, however it requires appropriate patient selection and is not free from adverse side-effects and the long-term efficacy is unknown (Mato, Limeres et al. 2010).

In a study to control drooling in a child of two-years of age, with severe spastic quadriparetic cerebral palsy and developmental delay, Lawrence and Klingbeil (Lawrence and Klingbeil 1991) provided treatment using transdermal scopolamine patches (1.5mg). They reported the child responded well to scopolamine therapy, with a reduction in drooling, which also resulted in secondary reduction in respiratory distress and frequency of suctioning with no significant side-effects reported (Lawrence and Klingbeil 1991).

2.13 Benzatrophine

Benzatropine, also known as benztropine is an anticholinergic drug which is used in patients to reduce the side effects of antipsychotic treatment, such as Parkinsonism and dystonia. Benztropine is an anticholinergic and works by decreasing the effects of acetylcholine, a chemical in the brain. This results in decreased tremors or muscle stiffness. Some of the adverse side effects may include dry mouth, visual disturbances, cognitive difficulties, constipation,

urinary retention, tachycardia (fast heart rate) and possible psychosis (in overdose) (Ogbru 2010).

In a study by Camp-Bruno et al (Camp-Bruno, Winsberg et al. 1989), they examined the efficacy of benztropine therapy for drooling. They administered benztropine to 20 developmentally-disabled participants with severe drooling to see if there was a reduction in salivary flow and also monitored the incidence of side-effects in these cases. They used a double-blind, placebo controlled, crossover design and found a statistically significant difference in salivary flow ($p < .001$), between patients on placebo and those taking benztropine immediately post-intervention. In their study they used the Teacher Drool Scale (TDS), to measure changes in drooling and found a statistically significant difference between both placebo and intervention in the frequency and severity of drooling immediately post-intervention ($p \leq 0.001$) (Camp-Bruno, Winsberg et al. 1989). The incidence of side-effects was so severe in three participants that they were excluded from the study. The side-effects included increased irritability, lethargy, vomiting, insomnia, dilated pupils, disorientation, facial-flushing, stomach-ache and dry-mouth. Although they reported that minor problems, such as dry-mouth were eradicated by adjusting the dose of benztrophine in other participant (Camp-Bruno, Winsberg et al. 1989).

2.14 Contraindications for the use of anticholinergic medications

Anticholinergic medications are contraindicated in patients with glaucoma, obstructive uropathy, gastrointestinal motility disorders, and myasthenia gravis. Furthermore these medications are poorly tolerated in elderly patients who present with multiple comorbidities (Mintzer and Burns 2000).

The two main interventions for the clinical management of saliva in tracheostomised patients at The Wellington Hospital is primarily through the use of either anticholinergic medications and/ or with the use of intraglandular injections of botulinum toxin into the salivary glands. When considering which intervention to assign in the management of saliva in tracheostomised patients, it is usually the primary consultant who makes the decision and prescribes the

course of intervention. The need for management of saliva is raised to the primary consultant by the multidisciplinary team caring for the patient. It is also highlighted and documented by the hospital's tracheostomy team, who perform ward-rounds, at least once-a–week, with every patient who has a tracheostomy tube in-situ. The tracheostomy team, which primarily consists of a nurse, speech and language therapist, physiotherapist and ear, nose and throat (ENT) specialist, determines through rounding which patients have copious amounts of saliva, difficulties with management of their saliva and therefore requiring regular tracheal suctioning. Following team discussion recommendations are made to the primary consultant to consider treatment options to assist in the management of saliva in their patient. The prescription of treatment modality is then determined solely by the consultant.

2.2 Tracheostomy tubes and tracheal suctioning

2.21 What is a tracheostomy tube?

A tracheostomy tube is a small tube designed to be placed directly into a patient's windpipe (trachea) through the neck (Figure 1), via a tracheotomy procedure. The tracheotomy can be performed in the operating room or at the patient's bedside, typically requiring only minimal anaesthesia. The tracheostomy tube can be inserted in one of two ways; the open technique or the percutaneous technique. The open technique involves a small incision made in the lower part of the neck just above the trachea (Weller 2000). Subsequently, an incision is made in the trachea and the tracheostomy tube is inserted. The percutaneous technique involves the formation of a small opening in the trachea that is gradually dilated to the size of the tracheostomy tube.

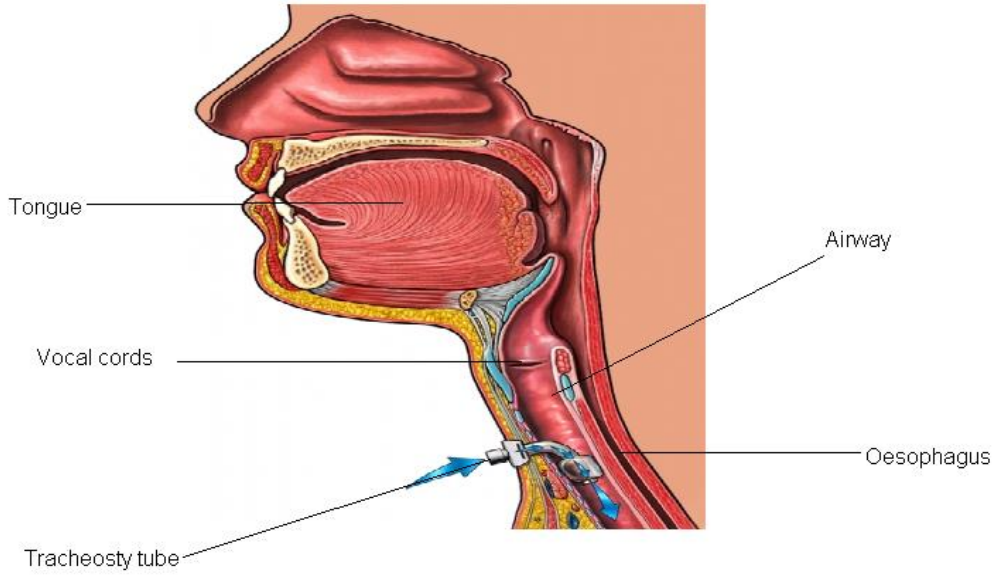

Figure 1 Lateral view of a tracheostomy tube, adapted from https://www.vivature.com/

2.22 Why is a tracheostomy tube needed?

A tracheostomy tube may be needed for patients who are unable to breathe independently, require long-term mechanical ventilation, are unable to cough effectively to clear their secretions, or have an obstructed or blocked airway. Mechanical ventilation is a method to mechanically assist or replace spontaneous breathing, using a machine called a ventilator.

The decision to insert a tracheostomy tube often follows the use of a breathing (endotracheal) tube (Dikeman and Kazandjian 1995). Tracheostomy tubes are commonly inserted in patients who require long-term ventilation, and play a vital role in maintaining a clear airway, allowing access for bronchial toileting and weaning from ventilation (Serra 2000; Choate and Barbetti 2003; The Intensive Care Society 2008).

2.23 Incidence of tracheostomy tubes

Tracheostomy care has traditionally been specific to specialised areas, such as ear, nose and throat (ENT) departments and intensive care units (ICU) (Heafield, Karnik et al. 1999). The number of tracheostomy tubes inserted internationally is increasing (Parker, Shylan et al. 2007), evidence indicating that both ventilation time and time in the intensive care unit (ICU) setting are reduced when a tracheostomy is performed early and this service and flow efficiency also results in patients being moved out of ICU making way for other patients (Arabi, Haddad et al. 2004). This is particularly true in the intensive care unit settings (The Intensive Care Society 2008), where as many as a third of patients will need a tracheostomy tube to assist in mechanical ventilation (Casserly, Lang et al. 2007). In a UK survey it was indicated that approximately 50 – 200 tracheostomy tubes are inserted annually in ICUs, although this figure varied according to location (Veenith, Ganeshamoorthy et al. 2008).

Most tracheostomised patients are decannulated, whereby the tracheostomy tube is successfully removed, prior to discharge from ICU (Stelfox, Crimi et al. 2008), but some patients continue to require the tracheostomy tube after their acute episode of care in order for secretion and airway management (Barnett 2008), whereby they are unable to swallow or clear their saliva safely and are dependent on tracheal suctioning to be performed to clear aspirated saliva. As a result an increased number of people are now being nursed on general hospital wards and within the community (Haines and Coad 2001), requiring staff in these settings to be able to provide safe and effective care for these individuals (Russell 2005). Despite increased international literature and care guidelines in tracheostomy tube care (Littlewood 2005), some health care professionals continue to lack the specialist skills, knowledge and confidence to provide this care (Parker, Shylan et al. 2007).

2.24 Types of tracheostomy tubes

A tracheostomy tube is a curved tube that is inserted into a tracheostomy (a hole made in the neck and trachea). There are different types of tracheostomy tubes that vary in certain features for different purposes. These are manufactured by different companies. However a specific type of tracheostomy tube will be the same no matter which company manufactures them.

A commonly used tracheostomy tube consists of three parts: outer cannula with flange (neck plate), inner cannula, and an obturator. The outer cannula is the outer tube that holds the tracheostomy open. A neck plate extends from the sides of the outer tube and has holes to attach cloth ties or velcro strap around the neck. The inner cannula fits inside the outer cannula. It has a lock to keep it from being coughed out, and it is removed for cleaning. The obturator is used to insert a tracheostomy tube. It fits inside the tube to provide a smooth surface that guides the tracheostomy tube when it is being inserted.

There are different types of tracheostomy tubes available and the patient should be given the tube that best suits his / her needs. The different types of tubes, indications for use and limitations are outlined in Table 4.

Table 1 Types of tracheostomy tubes, indications for use and limitations

Tube type and description	Indications for use	Risks and limitations
Cuffed tracheostomy tubes have a balloon (cuff) surrounding the distal end of the tube, which inflates in an attempt to seal the airway.	A cuffed tube allows for positive pressure ventilation and it reduces the risk of aspiration (Russell 2005).	Over-inflation of the balloon can cause damage to the mucosal wall of the trachea and necrosis (Serra 2000). If the lumen is occluded with the balloon (cuff) inflated the individual will not be able to breathe.
Uncuffed tracheostomy tubes do not have a balloon (cuff) that can be inflated.	This tube is used for patients who can breathe independently, who are able to swallow safely (Russell 2005).	The individual requires an effective cough reflex to protect them from any potential aspiration.
Fenestrated tracheostomy tubes have openings in the tube that allows air to pass through. They require a non-fenestrated inner cannula (with no opening), to allow for suctioning and to make sure the suction catheter does not go through the opening.	Air movement allows the patient to speak with placement of a special speaking-valve (Russell 2005). These tubes are sometimes used in patients weaning-off ventilation (The Intensive Care Society 2008).	Granulated tissue can develop around the fenestrations (Conlan and Kopec 2000). This type of tube may increase airway resistance if positioned incorrectly (The Intensive Care Society 2008).
Adjustable-flanged tracheostomy tubes are longer than the standard tubes and have outer flanges that secure the tube, which can be adjusted.	This type of tube is used where a standard length tube will not fit properly (Russell 2005).	There is increased risk of discomfort or movement of the tube whilst mobilising.
Silver tubes / long-term tracheostomy tubes, with no need for repeated cleaning (Serra 2000).	These tubes have an in-built speaking valve system, with no need to have an additional attachment of a valve (Russell 2005).	This type of tube should only be used for long-term tracheostomy care. These tubes tend to be expensive and are heavy.

2.25 Complications with tracheostomy tubes

Complications with the insertion and management of tracheostomy tubes include haemorrhage, aspiration and an increased risk of infection (Beards and Nightingale 1994). Law (Law, Barnhart et al. 1993) indicated that 58% of patients who had a long-term tracheostomy tube developed tracheal granuloma, a growth of inflammatory tissue, which is caused by the irritation of the airway by the tracheostomy tube (Law, Barnhart et al. 1993). They concluded that removal of the tracheal granuloma, even in asymptomatic tracheostomised patients, resulted in successful decannulation in 20 out of 25 patients. They suggested that for a large number of patients with a long-term tracheostomy tube in-situ, tracheal granulomas were a significant complication and impacted on the patient's airway (Law, Barnhart et al. 1993). Mucosal trauma is another complication, as a consequence of rigorous suctioning technique. The use of excessive or prolonged negative pressure can result in tearing of the mucosal lining, as the suction catheter touches the surface (Dikeman and Kazandjian 1995).

Tracheomalacia is where there is a softening of the cartilaginous structure of the trachea, and is caused by erosion of the tracheal rings. This is usually secondary to any trauma to the tracheal walls that exposes cartilage and thus leads to tissue breakdown (Dikeman and Kazandjian 1995). Another complication associated with longer-term tracheostomy tubes is tracheal stenosis, which is a narrowing that occurs when the tracheal rings begin to heal following trauma (Dikeman and Kazandjian 1995). Tracheal stenosis can occur at the tracheal stoma and the cuff site.

2.26 Tracheal suctioning

If the patient is unable to clear saliva or other material effectively from the airway, these need to be removed manually, using suctioning, before potentially resulting in an airway obstruction. Tracheal suctioning involves the removal of secretions from the trachea or bronchi, by inserting a catheter through the tracheostomy tube. In addition to assisting in the removal of saliva, tracheal suctioning also stimulates a cough reflex. This procedure helps maintain a

patent airway to allow optimal exchange of oxygen and carbon dioxide and minimises the risk of the development of aspiration pneumonia, which results from saliva that has fallen into the airway. Tracheal suctioning requires a strict aseptic technique and can be performed as is required, dependent on patient need. According to the American Association for Respiratory Care guidelines (AARC 1993), prior to suctioning the patient needs to be hyper-oxygenated with 100% oxygen for 30 seconds. The duration of the suction should not exceed 10 to 15 seconds and should adopt a sterile technique. The negative pressure used during suctioning should ideally be kept to a minimum, but enough to allow sufficient clearance of saliva pooled within the trachea. Finally, following removal of the suctioning catheter from the airway, the patient should receive hyper-oxygenation once again for up to a minute (AARC 1993).

Airway suctioning is associated with clinically significant complications, such as hypoxia microatelectasis (alveolar damage), laryngospasm and tracheal wall damage (Fiorentini 1992; Kapadia, Bajan et al. 2000). Hooper (Hooper 1996) suggested that the presence of a tracheostomy tube may cause irritation, resulting in the increased production of sputum (Hooper 1996). Despite the hazards associated with tracheal suctioning there is little evidence to show how well it is performed in everyday practice. Day (Day, Farnell et al. 2002) observed 28 nurses to investigate nursing practices in endotracheal suctioning. Using non-participant observations and structured observations from three acute and high dependency wards within a large teaching hospital in the United Kingdom, she investigated knowledge and competence in performing tracheal suctioning. She concluded that both knowledge and practice were poor, with no significant relationship between the two (Day, Farnell et al. 2002). Day (Day, Farnell et al. 2002) reported on these results in three sections, a) prior to suctioning; b) during suctioning and, c) post suctioning. She found that prior to suctioning there were incorrect procedures relating to chest auscultation and although a large number (n=19) indicated that suctioning should be performed after auscultation in actual practice only 2 subjects did. In practice only 2 out of the 28 subjects provided pre-oxygenation prior to suctioning, although 10 indicated knowledge to do so. Finally there were errors relating to infection control prior to suctioning, with only two subjects carrying-out correct hand-

washing prior to undertaking tracheal suctioning. During suctioning Day (Day, Farnell et al. 2002) discovered that in practice only nine subjects chose the correctly-sized catheter and only two used the correct negative pressures whilst suctioning, whilst all other subjects used higher pressures than those recommended. Following suctioning only one of the 28 subjects performed auscultation post suctioning; although a greater number (n=17) performed correct post-suction hand-washing, 11 subjects failed to do so (Day, Farnell et al. 2002).

Patients have reported sensations of pain, pressure, crushing, choking and gagging, whereas in the hands of a skilled practitioner, suctioning may not be more than a discomfort (Feber 2000). In a descriptive study by Arroyo-Novoa (Arroyo-Novoa, Figueroa-Ramos et al. 2008) almost half of 755 patients reported moderate to severe pain intensity during tracheal suctioning.

2.27 Why perform tracheal suctioning?

Tracheal suctioning is usually performed to maintain a clear airway and maximise respiratory function (Dougherty and Lister 2004). It is carried out when a patient with an artificial airway such as a tracheostomy or endotracheal tube cannot cough and remove pulmonary secretions. When a tracheostomy tube is in place, inspired and expired air bypass the normal humidification and warming processes that occur during passage through the upper airway. This may cause the drying of secretions and reduce the efficiency of muco-ciliary transport in the removal of secretions. The presence of a tracheostomy tube also impedes the ability to cough, a mechanism that requires glottic closure to generate the necessary high air flow and speed. While some patients may be able to clear their saliva via a tracheostomy tube independently, many will require assistance in the form of tracheal suctioning.

The Joanna Briggs Institute for evidenced based nursing and midwifery produced a best practice information sheet on “Suctioning Adults with an artificial Airway”, following a systematic review of research (Thompson 2000).

This identified six main clinical indicators for performing tracheal suctioning, which were coarse breath sounds, noisy breathing, increased or decreased pulse, increased or decreased respiration, increased or decreased blood pressure and prolonged expiratory breath sounds. In daily practice nursing staff at the Wellington Hospital use a recording sheet to document the reason why tracheal suctioning is performed on individual patients (Appendix A).

2.28 Tracheostomy tubes and patient perceptions

The presence of a tracheostomy tube may lead to significant mental and emotional morbidity. It causes disfigurement of the anterior neck and is associated with reduced body image perception, and may lead to anxiety and depression (Bronheim, Strain et al. 1991). Gilony et al. (Gilony, Gilboa et al. 2005) explored the quality of life after tracheostomy tube insertion by measuring its impact on well-being and body image perceptions. In their study they asked three groups of patients; cannulated, decannulated and non-cannulated patients to complete 3 conventional questionnaires. The questionnaires were; 1) Satisfaction-with-life scale; 2) Personality traits: neuroticism and extroversion; and 3) Body cathexis scale

They concluded that patients with a tracheostomy tube had significantly reduced life-satisfaction and body-image perceptions. Patients who had their tracheostomy tube removed showed slight improvement in their body-image perception, but still had reduced life-satisfaction scale scores (Gilony, Gilboa et al. 2005).

In a study investigating patients who had a temporary tracheostomy tube in-situ Sherlock et al. (Sherlock, Wilson et al. 2009) conducted semi-structured interviews with eight patients to gain an understanding of their experiences. Their interviews covered four main themes; physical sensations, understanding, information, and experiences following removal of the tracheostomy tube.

They concluded that the experience of having a tracheostomy tube in-situ is a complex mixture of physical sensations and emotions. They found that most

patients reported the physical and psychological effects more disturbing than they expected (Sherlock, Wilson et al. 2009). Their research also suggested that the information given to patients may be insufficient and not tailored to individual needs. Following removal of the tube patients still reported fears and feelings of discomfort, which suggested that they still required further support in order to cope (Sherlock, Wilson et al. 2009).

2.3 Off-label use of medications

The management of saliva in tracheostomised patients is often through the pharmacological methods, by prescribing medications which have an adverse effect of reducing saliva. However none of these medications are licensed for this treatment and therefore are given ‘off-label’ (UK Medicines Information 2012).

The “off-label usage” of a medication is commonly used; however, no standardised statutory definition is available. Off-label prescribing of medications relates to prescribing a registered medicine for a use that is not within or is disclaimed within the product information (Turner 1999). The term refers to the practice of issuing prescriptions or ordering a medication for a use that is not recognised as an official indication by a national licensing authority, e.g., the Medicines Healthcare Regulations Authority in the United Kingdom and Food and Drug Administration in the United States.

Once a licensing authority has undertaken a review of the manufacturer’s data of a medication, the medication may be approved for one or more indications, directed by specific dosages and administration requirements. The approved indication or indications then become part of the official “label” for the product. Once approved and licensed for market, the medication can be made available to use as a clinical tool and is not necessarily restricted to use in only the licensed (approved) indications, but for use outside the licensed indication and as such termed “off-label”.

Off-label use is legal and does not necessarily mean that the medication is being used inappropriately (Gazarian, Graudins et al. 2006). Many physicians prescribe a medication off-label as they believe it is the best treatment for a

specific condition, although it may not yet have been formally tested for use in that condition (Gazarian, Graudins et al. 2006; Meadows and Hollowell 2008). Some views suggest that off-label prescribing may actually push the frontiers of clinical knowledge and lead to improvements in care (Torres 1994).

2.31 National Licensing Authorities

In all industrialised countries, a dedicated governmental agency, department or ministry has the authority to review scientific data and make decisions regarding the eligibility for introducing a medicinal or therapeutic product into a specific national market. The name commonly given to this authority is product licensing. There are a number of similarities in the licensing process.

United Kingdom

In the United Kingdom (UK), prescription medications are licensed for marketing by the Medicines and Healthcare products Regulatory Agency (MHRA). The MHRA is an executive agency of the Department of Health. There seems to be no specific parliamentary declaration that corresponds to allowing off-label prescribing. However the MHRA has a statement relating to off-label prescribing in the UK which reads;

"Advice for prescribers:

Consider…

Before prescribing an unlicensed medicine, be satisfied that an alternative, licensed medicine would not meet the patient's needs

Before prescribing a medicine off-label, be satisfied that such use would better serve the patient's needs than an appropriately licensed alternative

Before prescribing an unlicensed medicine or using a medicine off-label:

a) be satisfied that there is a sufficient evidence base and/or experience of using the medicine to show its safety and efficacy

b) take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring and follow-up

c) record the medicine prescribed and, where common practice is not being followed, the reasons for prescribing this medicine; you may wish to record that you have discussed the issue with the patient

Communicate: best practice is that…

You give patients, or those authorising treatment on their behalf, sufficient information about the proposed treatment, including known serious or common adverse reactions, to enable them to make an informed decision

Where current practice supports the use of a medicine outside the terms of its licence, it may not be necessary to draw attention to the licence when seeking consent. However, it is good practice to give as much information as patients or carers require or which they may see as relevant

You explain the reasons for prescribing a medicine off-label or prescribing an unlicensed medicine where there is little evidence to support its use, or where the use of a medicine is innovative

Report suspected adverse reactions…

Healthcare professionals have a responsibility to help monitor the safety of medicines in clinical use through submission of suspected adverse drug reactions to the MHRA and CHM via the Yellow Card Scheme. Such reporting

is equally important for unlicensed medicines or those used off-label as for those that are licensed" (MHRA 2009).

The Yellow Card Scheme, run by the MHRA and the Commission on Human Medicines (CHM), is used to collect information from both health professionals and the general public on suspected side effects. It allows the on-line reporting of suspected side effects (also known as adverse drug reactions) to a medicine, vaccine, herbal or complementary remedy (MHRA 2009).

USA

In the United States (US), medicated prescriptions are licensed by the federal Food and Drug Administration (FDA). The FDA has no policy that confines the use of medications for off-label purposes. However the FDA periodically releases statements and guidance to assist health-care providers in understanding prescribing limitations. Recently the FDA has released an information sheet relating to off-label use of investigational drugs, which states;

"Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgement. If Physicians use a product for an indication not in the approved labelling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence, and to maintain records of the product's use and effects. Use of a marketed product in this manner when the intent is the "practice of medicine" does not require the submission of an Investigational New Drug Application (IND), Investigational Device Exemption (IDE) or review by an Institutional Review Board (IRB). However, the institution at which the product will be used may, under its own authority, require IRB review or other institutional oversight" (Food and Drug Administration 2011).

European Union

In the European Union (EU), licensing of prescription medications is authorised by the European Medicines Authority – European Medicines Evaluation Agency (EMEA). The EU does not have legislation against the use of off-labelling

prescribing and there are not any specific statements from the European Medicines Authority to limit the use of licensed medicines to only labelled uses.

2.32 Off-label prescribing

The practice, called "off-label" prescribing, is entirely legal and very common (Blum 2002; Kelly, Gazarian et al. 2005), and may sometimes be clinically appropriate (e.g. exceptional use in an appropriately informed patient with a serious disease, when there are no other alternatives and where the potential benefits outweigh the potential risks), (American Academy of Pediatrics 2002), it can be associated with a number of clinical, safety and ethical issues (Neubert, Dorman et al. 2004). Furthermore some long established off-label uses have been shown to be either ineffective or harmful, when they've undergone extensive evaluation, (e.g. deaths associated with the use of propofol medication, in the sedation of patients in paediatric intensive care), (Schreiner 2003). There is a large amount of literature about the extent and consequences of off-label prescribing, yet there is no specific and little guidance to help clinicians attempting to make decisions about the appropriateness of such prescribing. Radley et al. reported on off-label prescribing in office-based US medical practitioners (Radley, Finkelstein et al. 2006). In their study they collected data on the top 100 prescribed medications in 2001 and also on another 60 randomly selected medications from a database of prescribed medications. They concluded that the most frequently prescribed classes of off-label medications were for cardiac and anticonvulsant conditions and formed 46% of prescriptions (Radley, Finkelstein et al. 2006). They found that the individual medications most commonly prescribed off-label were gabepentin (83%) and amitriptyline (81%), but they did not report on the most common off-label uses for these medications (Radley, Finkelstein et al. 2006). However Radley et al did report that the off label uses for gabapentin had minimal or no scientific support in 66% of uses, and off-labelling prescription for amitriptyline, had minimal or no scientific support in 60% of uses (Radley, Finkelstein et al.

2006). In a study by Chen et al, they surveyed 1199 physicians' knowledge of FDA-approved medications for commonly prescribed medications (Chen, Wynia et al. 2009). The Physicians were presented with 14 drug-indication pairs and asked whether the pair had FDA licensing approval. One of these pairs was the medication gabapentin for use in diabetic neuropathy. Their study showed that although diabetic neuropathy was an off-label use of gabapentin, it was considered to be a labelled indication by 45% of all surveyed physicians (Chen, Wynia et al. 2009). In the 1960s, John Vane found that aspirin, a drug that was used for many years for primarily relieving minor pain and fevers, could disrupt a pathway needed for platelet aggregation. Further studies in the 1980s showed that this effect can be used in the prevention of heart attacks and stroke. Despite the evidence, the Food and Drug Administration (FDA) prevented manufacturers from advertising this information until more convincing clinical trials of aspirin's anticoagulant properties were completed. However doctors were still allowed to prescribe aspirin for this use and it was not until 1998 that the FDA finally approved aspirin for the prevention of cardiovascular events (Jeffreys 2004).

2.33 Informed consent and shared decision-making when prescribing "off-label"

Informed consent is the principle that is observed to ensure that patient autonomy is conserved, requiring that competent patients are made fully aware and adequately understand the intended benefits and potential risks of a proposed treatment to be undertaken, in order to then make an informed decision (Riley and Basilius 2007). Doctors are legally bound to fully inform their patients of risks. The fact that there may be little evidence or research for off-label use should be considered a risk to the patient. Physicians should follow legal standards that require them "to obtain informed consent from a person, prior to performing a test or carrying-out a specified treatment, especially where a treatment may involve some uncertainty" (Wilkes and Johns 2008). Doctors are encouraged to engage with an approach known as shared decision making, a model that promotes enhanced patient-physician relationships. This shared decision approach requires that both the physician and the patient share

information and work together in order to decide on a treatment plan (Wilkes and Johns 2008). Therefore withholding the intent to prescribe a medication for off-label use fails to honour this decision making process. Anytime a physician prescribes a medication for use that is not approved by the national licensing body, the physician can be seen as essentially carrying-out experimental research on the patient. The division between off-label use and research is important, because the national licensing authority closely regulates the sale, manufacture and licensing of medications. These regulations include development and clinical investigations using a medicinal product. Clinical investigations of medicines on human patients require obtaining approval from the MHRA in the United Kingdom and ethical approval, prior to beginning a study, as well as close oversight by local review boards. The licensing authority's primary focus is to protect human subjects involved in clinical drug trials. However they do not regulate practice of medicine, and physicians are allowed to prescribe approved drugs for off-label uses, as long as such prescriptions do not qualify as "research".

The General Medical Council produced a supplementary guidance on good practice in prescribing medicines (General Medical Council 2008), and expects doctors to comply with the standards of good practice set out in the guidance. It states that when prescribing medicines for use outside the terms of their licence (off-label);

"You may prescribe medicines for purposes for which they are not licensed. Although there are a number of circumstances in which this may arise, it is likely to occur most frequently in prescribing for children. Currently, pharmaceutical companies do not usually test their medicines on children and as a consequence, cannot apply to license their medicines for use in the treatment of children. The use of medicines that have been licensed for adults, but not for children, is often necessary in paediatric practice" (General Medical Council 2008).

When prescribing a medicine for use outside the terms of its license you must:

i) “be satisfied that it would better serve the patient’s needs than an appropriately licensed alternative
ii) Be satisfied that there is a sufficient evidence base or experience of using the medicine to demonstrate its safety and efficacy; the manufacturer’s information may be of limited help, in which case the necessary information must be sought from other sources
iii) take responsibility for prescribing the medicine and for overseeing the patient’s care, monitoring and any follow up treatment, or arrange for another doctor to do so
iv) make a clear, accurate and legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing the medicine in the patient’s notes” (General Medical Council 2008).

2.34 Evidence levels to guide off-label prescribing

The National Institute for Health and Clinical Excellence (NICE) identifies that off-label medicines are invaluable in the care of certain patients in the absence of any other suitable licensed medicines which meet their needs. The information available for healthcare professionals and patients to decide whether these off-label medicines are safe and effective, and when they’re most likely to give good outcomes, can be difficult to find. Therefore NICE have provided the first nationally available source of information for healthcare professionals and patients called ‘Evidence summaries for unlicensed / off-label medicines’ (ESUOMs) (National Institute of Health and Care Excellence 2013). ESUOMs are intended to provide information for clinicians and patients to inform their decision-making and support the development and updating of local medical formularies. The strengths and weaknesses of the relevant evidence are critically reviewed within each ESUOM.

The key activities involved in the production of each ESUOM are:

- “identifying, prioritising and selecting the topic

- summarising the published evidence
- critically reviewing the strengths and weaknesses of the evidence
- placing the evidence in the context of the wider evidence base for the management of the condition for which the unlicensed or off-label use is being considered, particularly NICE guidance, if available
- highlighting any potential implications for local decision-making or clinical practice
- producing a summary for patients for each ESUOM
- identifying any new evidence relevant to published ESUOMs through scanning the literature, reviewing and, if necessary, updating or withdrawing an ESUOM" (National Institute of Health and Care Excellence 2013)

The American Medical Association have suggested that we divide potentially appropriate off-label prescribing into three evidentiary categories: supported, suppositional and investigational (Largent 2009). Each of these categories is differentiated by the level of certainty obtained through objective assessment of existing evidence that a patient will experience a net health gain from the treatment. Supported off-label use relates to moderate to high level of certainty in net health benefit, whereas suppositional off-label use correlates with a low level of certainty. Investigational off-label use corresponds with a very low level of certainty. The US Preventative Services Task Force (USPSTF) (Sawaya, Guirguis-Blake et al. 2007) have developed such an approach and propose that judgements of evidence include consideration of the number and size of clinical trials, study design and conduct and the consistency of the results. By rigorously evaluating a piece of evidence in this manner, a judgement can be arrived as to the level of certainty for the net health benefit that can be gained from a particular intervention.

Unfortunately physicians do not always have the skills or time to perform their own systematic review of the evidence on potential risks and benefits of off-label prescribing. They should therefore access the most rigorous evidence that is readily available and take an objective approach to judgment (Largent 2009). Where available, professional body recommendations or guidelines should be

sought as they often reflect a thorough assessment of the available evidence, beyond the capability of any individual physician, and therefore can play a vital role in determining the physician's level of certainty when prescribing (Largent 2009). Although it can be argued that professional group recommendations may have conflicts of interest, these professional body recommendations are still likely to signify a greater understanding and reflection on the evidence, than that of an individual physician (Sox 2009).

Gazarian et al. developed a practical and clear approach to guide clinicians, policymakers and funders of health care in systematically evaluating the appropriacy of medicines recommended for off-label use (Gazarian, Graudins et al. 2006). They established a working party from the New South Wales Therapeutic Advisory Group (NSW TAG), which is an independent state government-funded organisation whose aim is to promote quality use of medicines. The working party was founded by identifying areas of expertise considered relevant to address the issue of off-label prescribing and to develop recommendations in order to guide practice. They provided a systematic process for evaluating the appropriacy of any proposed off-label use and a decision algorithm with explanatory notes was developed (Figure 3). This provides recommendations to support prescribers in determining off-label use that is supported by high-quality evidence, its use in pioneering therapy that is justified in individual clinical circumstances or that which should be pursued in a research environment (Gazarian, Graudins et al. 2006).

Figure 2 Assessing appropriateness of off-label medicines use, (Gazarian, Graudins et al. 2006)

The algorithm provides guidance to clinicians who are considering off-label usage of a particular medicine and essentially in answering the question, “Is there high-quality evidence supporting its use?” (Gazarian, Graudins et al. 2006).

Prescribing medicines for off-label use makes patients vulnerable and compromises evidence-based practice. Clinical trials and other formalised studies attempt to fill in the evidentiary gaps, but currently there are no formal

guidelines on the off-label use of medications and clinical practitioners, manufacturers, patient advocates and professional organisations need to collaborate on systematic gathering of evidence to assist and justify off-label uses of medicines. It is also important that practitioners involve the patient in shared decision making and gain informed consent when prescribing off-label. Physicians should be encouraged that their prescriptions for off-label uses are; (1) made in conjunction with the patient's knowledge that the medicine is being prescribed as off-label use; (2) primarily motivated by a desire to diagnose, treat or benefit the patient; (3) based on the physician's own expert opinion; (4) supported by peer-reviewed literature, that reflects scientific evidence; and (5) in general supported by the views of the physicians colleagues.

2.4 Purpose and aims of this study

The management of saliva ranges from conservative (postural changes and biofeedback) to more aggressive such as pharmacological, surgical and radiological intervention. Studies using medications such as glycopyrrolate and scopolamine, have shown them to be effective in reducing drooling, but may have adverse side effects; excessive dry mouth, constipation, urinary retention, decreased sweating and skin flushing (Bachrach, Walters et al. 1998; Meir, Bachrach et al. 2000; Hockstein, Samadi et al. 2004). Other investigations have studied the management of drooling in patients with Parkinson's Disease and in children with Cerebral Palsy, using injections of botulinum toxin into the salivary glands, which showed positive outcomes in the management of drooling with minimal, transient (swallowing difficulties) or no adverse effects (Jongerius, Rotteveel et al. 2004; Banerjee, Glasson et al. 2006; Lagalla, Millevolte et al. 2006). However other reviews have reported that the efficacy and safety of botulinum toxin injections to the salivary glands is inconclusive (Walshe, Smith et al. 2012) and much more work is required to ascertain the benefits and longer-term adverse effects of the intervention (Reddihough, Erasmus et al. 2010). Given the wide-range of clinical competencies necessary for the safe and effective administration of tracheal suctioning (AARC 1993) any

pharmacologically induced benefit could attenuate the incidence of secondary complications associated to performing tracheal suctioning.

This prospective interrupted time-series experimental design was used to investigate the medical management of saliva in tracheostomised patients at The Wellington Hospital, in London, UK. The study wanted to determine the medical interventions which are prescribed in the management of pooled saliva, secondary to neurological impairment in this patient population and how effective this treatment was in reducing saliva.

This study aimed to address the following questions;

1) Whether treatment intervention resulted in a reduction in saliva in participants who had a tracheostomy tube in-situ
2) Whether there is a reduction in the need to perform tracheal suctioning in these participants as a result of the intervention
3) To determine participant and/or carer perceptions on saliva, tracheal suctioning and social well-being using a visual analogue scale and patient survey
4) To determine the one-to-one nurses perceptions on saliva and frequency of tracheal suction required, using a visual analogue scale and nurse survey

This interrupted time-series design had two phases, the first prior to intervention (baseline), followed by the second phase, with introduction of the intervention. All observations obtained subsequent to the introduction of the intervention condition, also continued throughout the second phase (the intervention-phase). The major purpose of this design was to evaluate the possible differential performance under the two conditions (pre and post intervention) of the time series. There are no other documented studies that have investigated the medical management of saliva in this patient population and this is the first study of its kind to do so.

Chapter 3

Methods Chapter

3 Ethics and the process of gaining approval for the study

The following chapter describes the processes and outcomes involved in applying for ethical approval for the study involving a medicinal product. It explains the procedures that were undertaken in order to register the study with the Medicines Healthcare Regulations Authority (MHRA) and considers local requirements and stipulations made by the Clinical Trials Office (CTO), which is a division of the Hospital Corporation of America (HCA) group, which owns The Wellington Hospital, where the study was undertaken. It details the process in how approval was obtained for the study and why participant numbers were limited following an audit of patients admitted to the service with a tracheostomy tube in-situ during a four-year period.

3.1 The Clinical Trials Office (CTO)

The Clinical Trials Office (CTO) is a department within Hospital Corporation of America (HCA), which was set-up in 2009 to oversee and manage any research undertaken at any of its HCA facilities within the United Kingdom. HCA Inc. is the world's largest private hospital group. HCA's private hospitals in London are the company's overseas division and are made up of a total of six hospitals; The Harley Street Clinic, The Lister Hospital, London Bridge Hospital, The Portland Hospital, The Princess Grace Hospital and The Wellington Hospital.

Prior to embarking on any research within one of its facilities, a protocol of the study must be submitted to the Head of the CTO, who would, in turn, meet with the Clinical Governance Committee and members of the CTO. The initial protocol for this study was titled "A randomised placebo controlled trial to explore the effectiveness of Botulinum Toxin injection at reducing oral

secretions and frequency of tracheal suctioning in tracheostomised patients". This protocol can be found in Appendix B.

The CTO employs a specialist Pharmacist who is responsible for overseeing pharmacovigilance in any studies using medicinal products, for supporting the process of completing the 'IRAS' ethics application form and procedures required to make an application to the Medicines Healthcare Regulatory Authority (MHRA).

3.2 Is the product an investigational medicinal product (IMP) or a non-investigational medicinal product (NIMP)?

The decision as to whether a product is an IMP or a NIMP depends on the product being used and the design of the study. The MHRA have designed an algorithm which allows investigators to determine whether their research is a clinical trial using a medicinal product, which then determines the need to gain MHRA approval (Appendix C). Therefore, to classify a "medicinal product" as an "investigational medicinal product" a sponsor must consider both its intended use and the objectives of the study. For example, if it is to be used as the test substance or reference substance (active comparator or placebo) in a study it would meet the first criteria of an IMP. However, if the study is not intended to discover or verify: (a) its clinical, pharmacological and/or other pharmacodynamic effects or (b) to identify any adverse reactions associated with its use or (c) to study its absorption, distribution, metabolism and excretion; with the objective of ascertaining its safety or efficacy, it would fail the second test. It would therefore not be classified as an IMP (European Commission 2011). Medicinal products with a marketing authorisation (MA) are classified as IMPs when they are to be used as the test substance or reference substance in a clinical trial.

3.3 Clinical Trials and Legal Framework

The undertaking of Clinical Trials occurs in a highly regulated environment, requiring compliance at numerous local and international levels. In 1964, the World Medical Association (WMA) developed the "Declaration of Helsinki" (World Medical Organization 1996), a statement of ethical principles for medical

research involving human subjects, including research on identifiable human material and data. It was primarily established as a framework for physicians. However the Declaration was subsequently amended and is now a worldwide-agreed policy for guiding the conduct of Clinical Trials and the protection of subjects. The requirement of ethical and scientific review of the trial protocol expressed in the Declaration is implemented in the national legal conditions for the conduct of Clinical Trials.

In 1996, the International Conference on Harmonisation (ICH) (ICH Expert Working Group 1996)
adopted the Guideline for Good Clinical Practice (GCP), which explicitly refers to the ethical
standards of the Declaration of Helsinki. It defines GCP as an international quality standard for
clinical trials in human subjects in ethical and scientific respects, clinical trials should be scientifically sound, and described in a clear, detailed protocol and trials should be conducted in
compliance with the protocol that has received prior institutional review board (IRB)/independent
ethics committee (IEC) approval/favourable opinion (ICH Expert Working Group 1996).

Adherence to the guideline should assure the protection of the rights, safety and wellbeing of the subjects as well as the reliability of the data generated in the Clinical Trial. The International Conference on Harmonisation (ICH)-guidelines and therefore also the Declaration of Helsinki are implemented in national law in the three ICH regions, the European Union, Japan and in the United States (ICH Expert Working Group 1996).

As well as these guidelines, further national requirements have to be taken into account, which do not address the conduct of Clinical Trials but address the involved parties such as the investigator, manufacturer and pharmaceutical companies.

Therefore before submitting to Ethics ('IRAS') and the MHRA the proposal to conduct a clinical trial using an Investigational Medicinal Product GCP training had to be undertaken, by the primary investigator and a Consultant Neurophysiologist (Dr. Peter Misra), who was originally listed as an investigator in the study. Both investigators were enrolled to complete this GCP training and were successful in gaining GCP certification.

Good Clinical Practice training ensures that the investigators are aware of legislation, guidance and good practice relating to the ways in which clinical trials using medicinal products are conducted. The MHRA's Good Clinical Practice (GCP) (MHRA 2013) Inspectorate is part of the Inspection, Standards and Enforcement Division of the MHRA. It assesses the compliance of organisations conducting clinical trials using investigational medicinal products with UK and EU legislation (MHRA 2013).

GCP training includes issues relating to the;

- Protection of subjects in clinical trials through
    - Adherence to the Declaration of Helsinki
    - Risk assessment based on toxicological results
    - Protection of confidential personal data
    - Approval processes by ethics committees and competent authorities
    - Informed consent of the subjects and special provisions for those not able to give legal consent
- Harmonisation of regulatory requirements in all European Union – Member States
- Competitiveness and effectiveness of European research taking into account the requirements of pharmaceutical industry and non-commercial researchers
- Transparency and moral responsibility to both the study participants and society to share results and assist in the development of further research

involving improved trial design, fewer patients and thereby avoiding unnecessary duplication. This means that information about clinical trial methodologies and outcomes is collected prospectively and is made available to healthcare professionals and the public.

- Pharmacovigilance (via EudraVigilance), the process and science of monitoring the safety of medicines and taking action to reduce the risks and increase the benefits of medicines. EudraVigilance is a data processing network and management system for reporting and evaluating suspected adverse drug reactions (ADRs) during the development, and following the marketing authorisation of medicinal products in the European Economic Area (EEA).

- Verification of compliance with GCP by inspections, which are performed in order to verify protection of the rights and well-being of trial participants, compliance with the provisions of Good Clinical Practice and the quality of data generated within clinical trials.

3.31 EudraCT

Following attendance at GCP training and as part of the Ethics (IRAS) application a EudraCT number was applied for from the MHRA, along with payment[1] in support of the application. In order for an application to be considered as valid by the MHRA, a submission should contain a file for each of the following documents:

- Covering letter
- Clinical Trial Application
- Protocol
- Investigators Brochure (IB) or document replacing the IB
- Investigational Medicinal Product Dossier (IMPD) / simplified IMPD
- Non-IMP Dossier (if required)

[1] £3600.00

- Scientific advice - A summary of scientific advice from any Member State or the European Medicines Agency (EMA) with regard to the clinical trial (if available).
- European Medicines Agency (EMA) Decision - A copy the EMA's Decision on the decision of the Paediatric Investigation Plan and the opinion of the Paediatric Committee (if applicable).
- The content of the labelling of the IMP (or justification for its absence)
- Proof of payment
- Manufacturer's authorisation or Importer's authorisation plus Qualified Person (QP) declaration on Good Manufacturing Practice (GMP) for each manufacturing site.

A EudraCT number was successfully obtained on 27/02/2009 (2009-011204-27).

3.4 The Sarah Cannon Research Institute (SCRI) UK

Sarah Cannon Research Institute (SCRI) is a global strategic research organisation focusing on advancing therapies and accelerating drug development. It is one of the largest clinical research programmes, conducting community-based clinical trials in oncology and cardiology through affiliations with a network of more than 700 physicians in the United States and United Kingdom. Additionally, SCRI offers management, regulatory and other research support services to drug development sponsors and strategic investigator sites.

SCRI participates in both industry-sponsored and investigator-initiated clinical trials and conducts phase 1 through to phase 3 and outcomes-based clinical trials. SCRI's academic partnerships with Yale Cancer Center, Peggy and Charles Stephenson Cancer Center at The Oklahoma University and University College London, enables SCRI to provide academic and collaborative leadership.

Sarah Cannon Research UK is a unique standalone trial facility that collaborates and works closely with clinical investigators to develop new and

innovative therapies for patients. Sarah Cannon Research UK is part of the Hospital Corporation of America (HCA) network, which comprises six central London hospitals. They specialise in the development of novel therapies and provide a clinical research option for patients in London and the United Kingdom. All clinical trials conducted via the Sarah Cannon Research UK goes through a rigorous process of research governance which includes approval by an independent Research Ethics Committee and the Medicines and Healthcare Products Regulation Agency (MHRA).

Following two unsuccessful applications to the Ethics Committee, a meeting was convened by the Head of SCRI UK and the SCRI research team and it was concluded that the study should be revised to examine and research the current practice and management of saliva in patients who have a tracheostomy tube in-situ. It was also determined that ethical approval was no longer required, following the MHRA's algorithm guiding whether a study is research, audit or evaluation, which determined that the study was a service evaluation of current practice. (Appendix F). Approval for this revised study was obtained from the Wellington Hospital's Executive Board and HCA's Clinical Governance Board.

It was suggested that in order to increase the potential number of participants in this evaluation, patients could be recruited from a number of hospitals within the HCA International Ltd. group. This proposal was presented to two of The Wellington Hospital's sister hospital boards (The Harley Street Clinic and The London Bridge Hospital), but although initially agreed, was subsequently withdrawn, as the consultants in charge of the patients within the intensive care units at these hospitals felt they could not wholly commit to the study and could not fulfil data collection. Therefore participant recruitment was restricted to the Wellington Hospital.

3.5 The phases of clinical-outcome research

Robey (Robey 2004) suggested an adaptation of a five-phase model of clinical-outcome research as a means for structuring forms of clinical research throughout audiology and speech-language pathology. He suggests that the sequence of research tasks are; Phase I for identifying treatment protocols, justifying the enormous expense of extensive clinical testing; Phase II for making all of the preliminary tests and preparations necessary for testing the protocol in a clinical trial; Phase III for conducting a clinical trial to test efficacy; and Phase IV for testing the effectiveness of efficacious treatments. For treatment protocols proving effective, an additional phase of research is required: Phase V for testing the worth of a treatment (i.e., does the obtained value justify the cost of achieving that value?). This interrupted times-series evaluation would constitute a Phase II study (Robey 2004), whereby the research is exploring the dimensions of the therapeutic effect and making the necessary preparations for conducting a clinical trial. In 2010 the CONSORT (Consolidated Standards of Reporting Trials) (Schultz, Altman et al. 2010) statement updated guidelines for reporting parallel group randomised trials as a result of inadequate reporting and developed a 25 item check list to provide guidance for reporting all randomised control trials (Schultz, Altman et al. 2010). This CONSORT 2010 (Schultz, Altman et al. 2010) aims to assist authors in writing reports of randomised controlled trials, editors and peer reviewers in reviewing documents for publication, and assisting readers in critically appraising published articles. Although this study can be considered to be a Phase II study (Robey 2004), elements from the evidence based approach used for CONSORT 2010 can be used to guide reporting in other studies that are not randomised controlled trials (Schultz, Altman et al. 2010).

3.6 Identification of patient population and referral trends

3.61 Wellington Hospital Tracheostomy Team Service Review from 2009 to 2011

The Wellington Hospital Tracheostomy Team is primarily a therapy led team comprising a Specialist Speech and Language Therapist and Senior Physiotherapist responsible for the co-ordination of patient tracheostomy tube management. All patients on the intensive care, rehabilitation and acute (medical / surgical) wards who have a tracheostomy tube in-situ are referred to the service. The service reviews patients on a weekly basis with the aim of ensuring an appropriate weaning plan is in place, referring to specialist services as appropriate (e.g. ENT and respiratory physicians) trouble shooting for complex patients and ensuring safety standards are maintained.

A retrospective review within the Rehabilitation Unit at the Wellington Hospital for the years 2009 to 2011 was undertaken to evaluate the number of referrals, service demands and the outcomes for patients on the acute wards.

3.62 Review Findings

There were a consistently high number of referrals to the Tracheostomy Team within acute service areas (149 patients between 2009 and 2011) in comparison to the Rehabilitation Unit (78 patients between 2009 and 2011,) (Figure 1). There has been a decline in referral numbers year on year across both service areas but this decline is more significant in the Rehabilitation Unit, with a 19% drop in referral numbers between 2009 and 2010, and a 12% drop between 2010 and 2011.

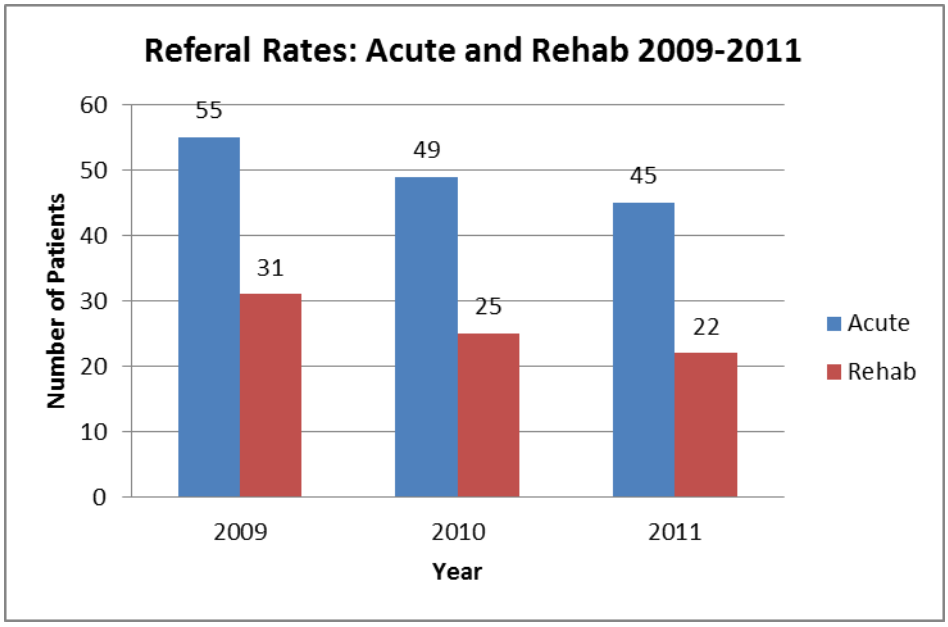

Figure 1 Acute and Rehabilitation Tracheostomy Team referrals at The Wellington Hospital from 2009 to 2011

The largest group of patients referred to both services were those with a diagnosis of stroke (35% acute, 44% rehabilitation), followed by those who had sustained a traumatic brain injury (17% acute, 24% rehabilitation) (Figures 2 and 3).

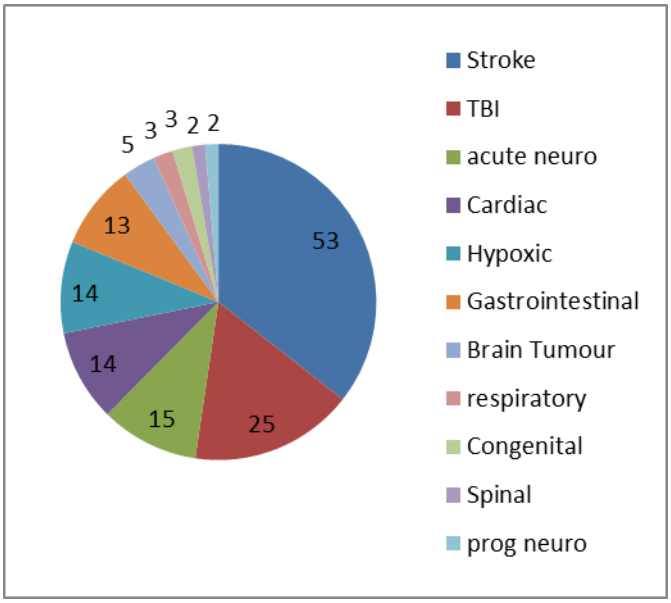

Figure 2 Number of Acute referrals by aetiology, The Wellington Hospital from 2009-2011

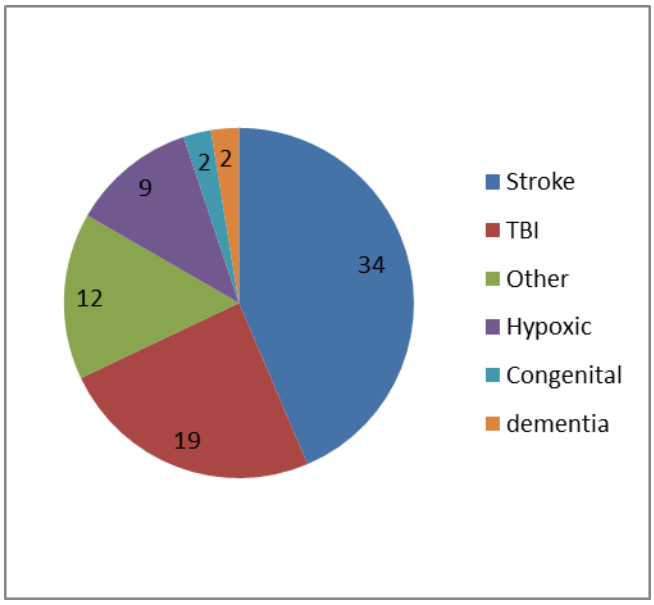

Figure 3 Number of Rehab referrals by aetiology, The Wellington Hospital from 2009-2011

Sixty three percent of rehabilitation patients were successfully decannulated (had their tracheostomy removed) during their admission. Of the 37% who were not decannulated, 66% were discharged with a weaning (removal process) plan in place, 17% were discharged with no plan to wean and 17% died (Figure 4).

In the acute service, 17% of patients were decannulated. Of the 83% who were not decannulated, 59% were discharged from the acute services with a weaning plan in place, 16% were discharged with no plan to wean and 25% died (RIP) (Figure 4).

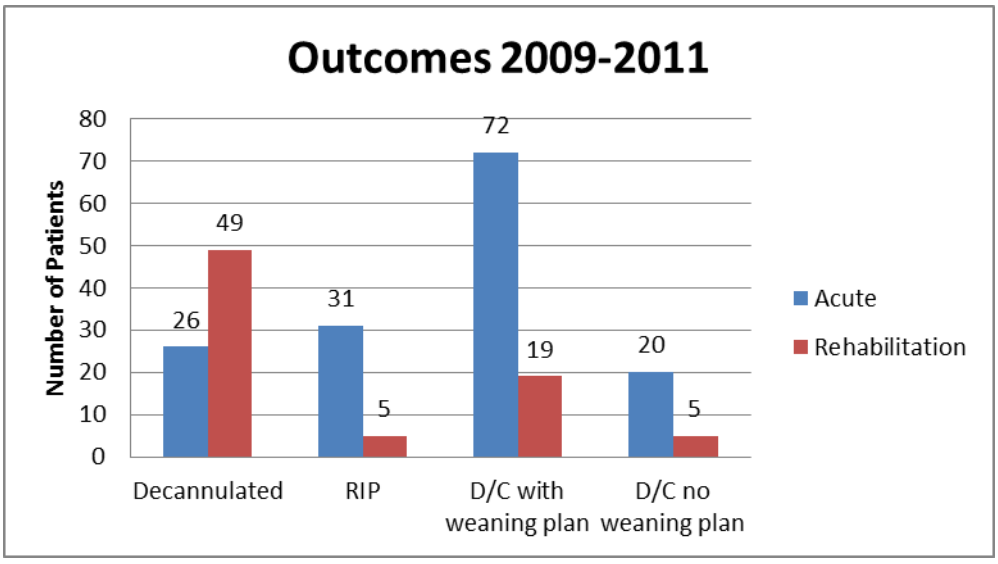

Figure 4 Tracheostomy tube outcomes for acute and rehabilitation services, at The Wellington Hospital from 2009 to 2011

The successful removal of the tracheostomy tube involves a number of graded stages, from tolerating tracheostomy tube cuff deflation, to eventual closing-off /capping-off of the tube and subsequent removal (decannulation). This process is known as “weaning”. Within the acute intensive care setting, patients are typically capped for 24 hours or less before decannulation of the tracheostomy tube. On the Rehabilitation Unit the patients were typically capped for more than 48 hours prior to decannulation (Figure 5). This is primarily due to there being a medical intensivist doctor available 24-hours a day, 365 days a year within the intensive care unit, who is able to decannulate the patient, whereas in comparison a reduced medical presence of a consultant who is able to decannulate the patient at a ward level (rehabilitation setting), where the Ear, Nose and Throat (ENT) consultant visits only at the request of the primary neurologist, which can potentially delay the process of decannulation.

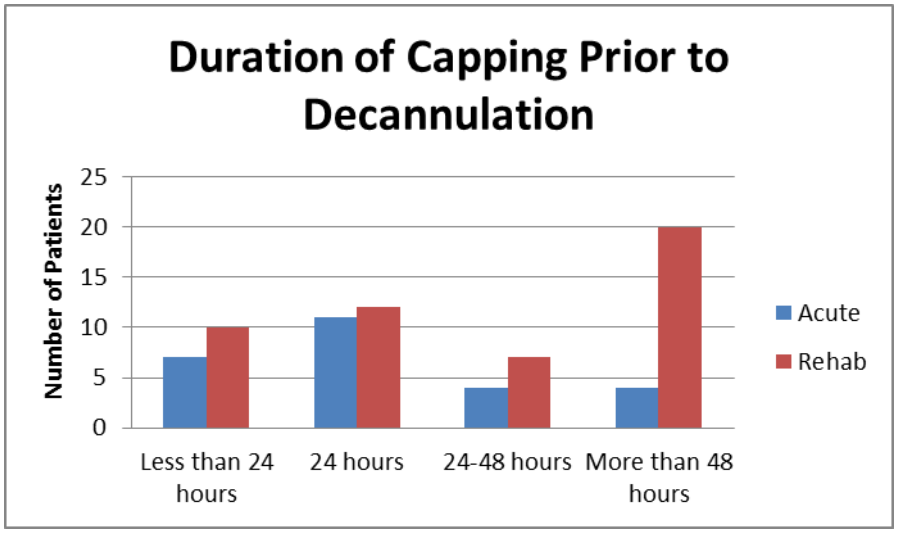

Figure 5 Duration of tracheostomy tube capping prior to decannulation

The duration of the tracheostomy tube weaning programme is significantly longer in the rehabilitation setting compared to the acute setting (Figure 6). The range of the duration of tracheostomy weaning in the acute setting is as follows; 2-32 days (2009), 4-48 days (2010) and 1-24 days (2011). In comparison, the

range of the duration of tracheostomy weaning in the Rehabilitation service is as follows; 12-148 days (2009), 36-152 days (2010) and 8 -148 days (2011). The primary difference is explained by the fact that patients admitted to the Rehabilitation Unit had a number of pre-existing co-morbidities, such as chronic obstructive pulmonary disease, difficulties with the tracheostomy tube, such as tracheal stenosis (narrowing of the tracheal cartilage) and tracheomalacia (weakness of tracheal cartilage).

During the period of 2009-2011 there were two failed decannulations on the Rehabilitation Unit, due to tracheomalacia in one patient and due to gastroparesis in the second patient therefore being dependent on the tracheostomy tube, due to risk of aspiration from gastric contents. There was one failed decannulation on the acute wards as this patient's vocal cords were in an adducted position and therefore dependency on the tracheostomy tube for breathing.

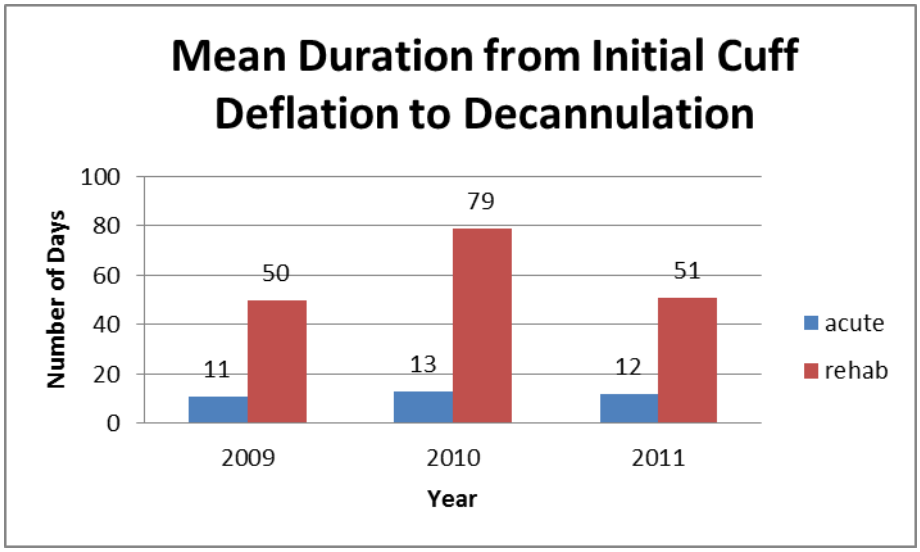

Figure 6 Mean duration from initial cuff deflation to decannulation

3.7 Referrals to the Tracheostomy Team at The Wellington Hospital in 2012

Comparing referral trends from the previous three years against those received in 2012, there was a dramatic decline in the number of referrals for patients with a tracheostomy tube within both the acute and rehabilitation service areas (Figure 7). The average number of referrals received per year was 72 compared to the 28 referrals received during 2012. This was due to the reduced number of patients admitted to the hospital (acute and rehabilitation service areas) who had a tracheostomy tube in-situ.

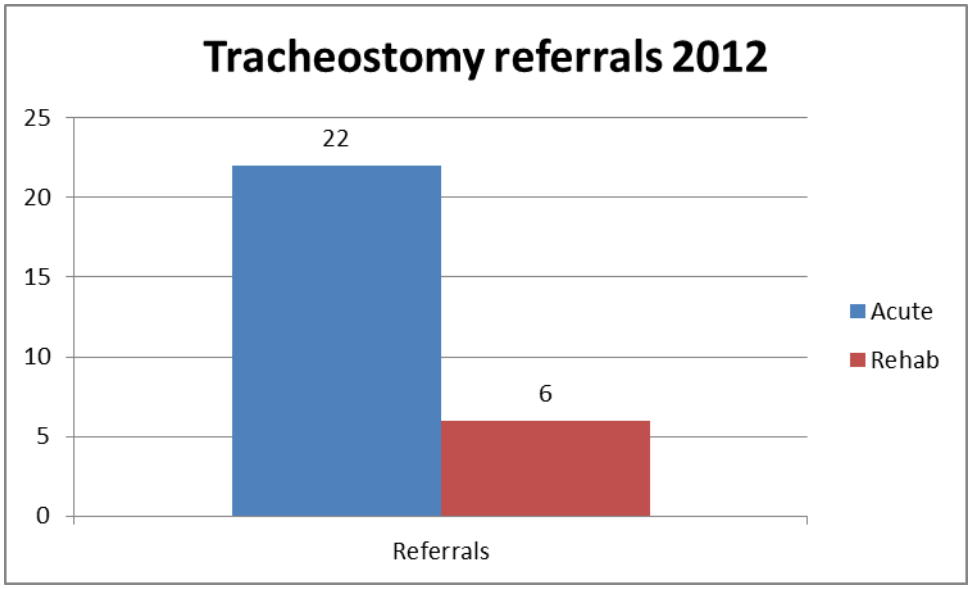

Figure 7 Acute and Rehabilitation Tracheostomy Team referral rates at The Wellington Hospital in 2012

Five of the six (83%) rehabilitation patients were successfully decannulated during their hospital stay. One was not decannulated due to ongoing vomiting, as a result of diabetic gastric paresis and therefore could not have the tracheostomy tube cuff deflated. Because of continuing vomiting, a weaning programme could not be established.

In acute services, 36% of patients were decannulated. Of the 64% who were not decannulated, 7% were discharged from the acute services with a weaning

plan in place, 57% were discharged with no plan to wean, due to their dependency on the tracheostomy tube for ventilation, and poor prognosis and 36% died (RIP) (Figure 8).

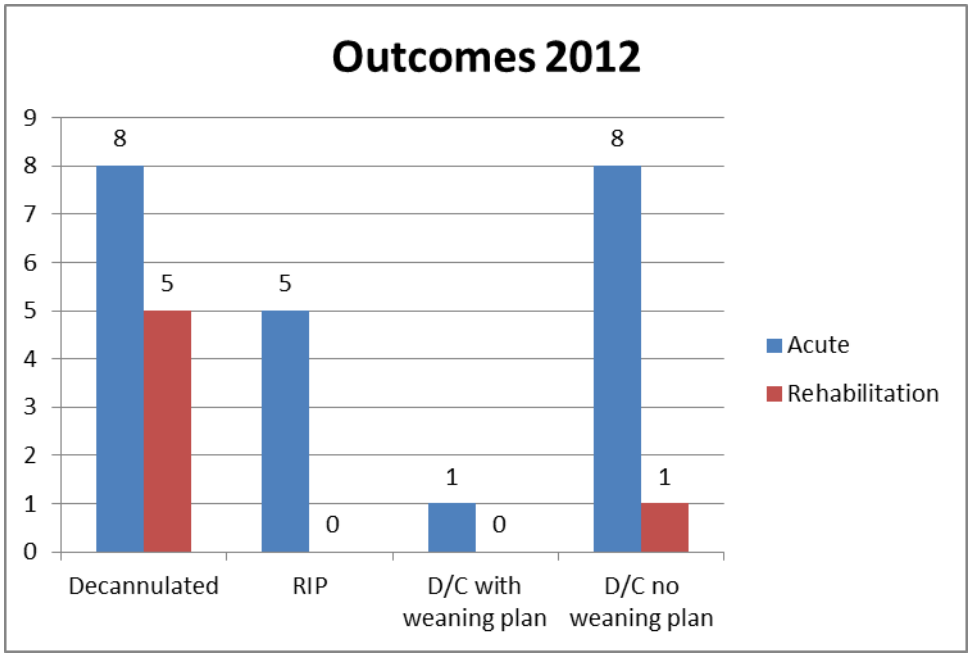

Figure 8 Tracheostomy tube outcomes for acute and rehabilitation referrals in 2012

Of the total of 28 referrals received to the acute and rehabilitation services, nine (32%) were discharged with no weaning plan and decannulation was not considered an option, due to sepsis, requirement of continuous ventilation and poor prognosis, due to comorbidities, as determined by the primary Consultant (Figure 9).

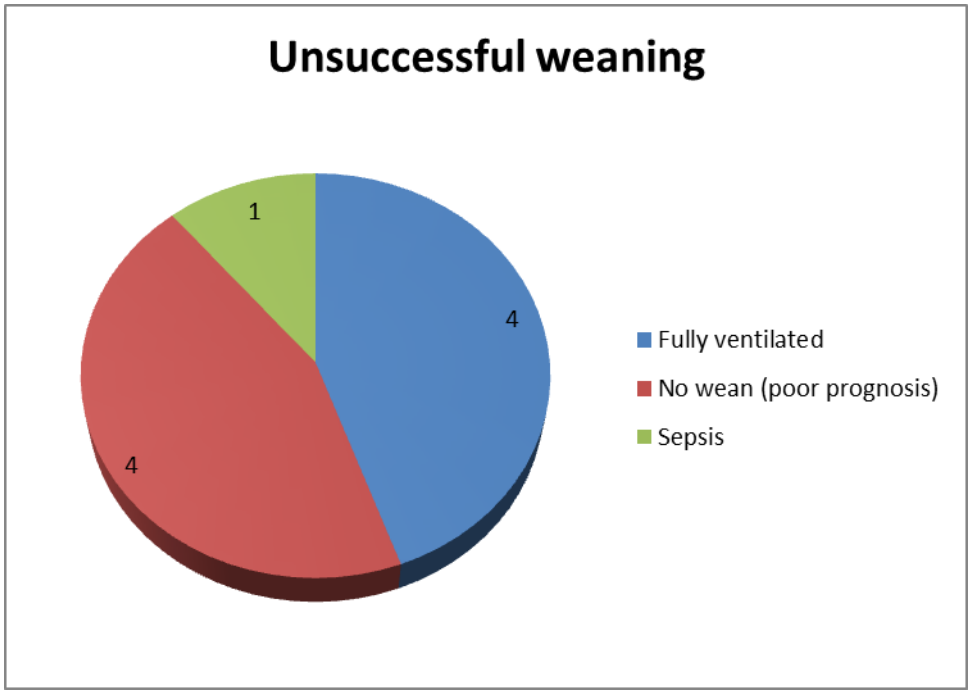

Figure 9 Reasons for unsuccessful weaning from the tracheostomy tube in nine patients

3.71 Reasons for reduced referral rates of tracheostomised patients

Patients admitted to the acute and rehabilitation wards of the Wellington Hospital are accommodated in private rooms, behind closed doors, with the exception of those in intensive care. For those patients with a tracheostomy tube in-situ in a private room a one-to-one 24-hour nurse is essential, especially when the patient is unable to swallow safely and/or clear saliva that has fallen into the airway. Therefore this one-to-one nurse is required to provide tracheostomy tube care, including tracheal suctioning as and when required. The decrease in overall referral rates may have been as a result of the withdrawal of funding, by the funding Embassy or funding body, for this one-to-one nursing care within the rehabilitation service. Subsequently patients who, in the past, would have been transferred to the rehabilitation wards, have remained in the acute service areas, including intensive care, where funding for one-to-one nursing continued to be provided.

Over the past four years there has been a decline in the number of referrals made to the Tracheostomy Team as the Wellington Hospital has received fewer patients who have a tracheostomy tube in-place. This decline is particularly observed in 2012. The referrals that were received in 2012 were for acutely unwell patients who presented with multiple co-morbidities and high dependency on mechanical ventilation, and therefore not suitable for rehabilitation or weaning from their tracheostomy tube. Having conducted an investigation as to why there had been a decline in the number of referrals received from overseas referral sources, it was discovered that a number of local hospital facilities had been established in the countries of origin from which the patients came and these new hospitals were able to care for tracheostomised patients. For example, within the United Arab Emirates (UAE) the Al Rahba Hospital (John Hopkins is now within easy reach for patients from Abu Dhabi and Dubai). In Abu Dhabi, the Berlin Medical and Neurological Rehabilitation Center and The Sheikh Khalifa Medical City, managed by the Cleveland Clinic, USA, are now also able to take tracheostomised patients. All these facilities recruited internationally qualified and experienced staff that had experience in tracheostomy tube care and management. Patients who sustained injuries in these countries and who required a tracheostomy tube placement were no longer being sent overseas to the UK, but were being managed locally, rather than being transferred overseas for treatment.

This significant decline in admission of patients who had a tracheostomy tube in-situ resulted in smaller numbers of patients who met the inclusion criteria and could be recruited into this study. Consequently the study design was changed, in agreement and in consultation with Sarah Cannon Research (SCR) UK, The Wellington Hospital and HCA's Clinical Governance Board, to a case study design, using an interrupted time series design (Appendix G).

3.8 Patients and Methods

This case series study is a prospective interrupted time-series design, involving patients who have been identified as having difficulties in managing their secretions and thus requiring a tracheostomy tube for dependency on tracheal suctioning to clear secretions from within the airway.

3.9 Overview

Across a consecutive 12-18 month period, participants that fulfilled the study inclusion criteria at The Wellington Hospital, London were enrolled in this study. Participants were eligible for the study if following a clinical bedside swallowing examination by the speech and language therapist, they were reported to have a tracheostomy tube in-place, exhibited difficulties in managing their saliva. They were dependent on tracheal suctioning in order to clear saliva that had fallen into the airway and who therefore required active treatment to manage their saliva. Also participants, who at time of enrolment, were dependent on alternative tube feeding to maintain their nutrition and hydration, as defined by the functional oral intake scale (FOIS) in table 1 (Crary, Mann et al. 2005). They also had to meet all inclusion criteria as listed below (section 3.114).

Table 1 Functional oral intake scale (FOIS) (Crary, Mann et al. 2005)

TUBE DEPENDENT (levels 1 - 3)

Level 1 - No oral intake
Level 2 - Tube dependent with minimal / inconsistent oral intake
Level 3 - Tube supplements with consistent oral intake

TOTAL ORAL INTAKE (levels 4 - 7)

Level 4 - Total oral intake of a single consistency
Level 5 - Total oral intake of multiple consistencies requiring special preparation
Level 6 - Total oral intake with no special preparation, but must avoid specific foods or liquid items
Level 7 - Total oral intake with no restrictions

3.10 Ethical Approval

This service evaluation has been approved by both HCA's Clinical Governance Team, Sarah Cannon Research (SCR) UK and The Wellington Hospitals' Clinical Audit and Executive Board.

3.11 Participants

All eligible participants were asked to participate and given an information sheet relating to the service evaluation. They were given 24-hours in which to decide whether they wished to participate, following which, if they agreed, they were asked to consent in participation. Participants were given a tracheostomy tube self-perception survey (Appendix H), which was created for the purpose of this study and developed with feedback obtained from the speech and language therapy department and the Wellington Hospital's Tracheostomy Team. The tracheostomy tube self-perception survey asked participants and/or their carers questions relating to their tracheostomy tube, tracheal suctioning, reports on saliva and management and social aspects of having a tracheostomy tube in-situ. The survey asked respondents to rate a statement relating to their tracheostomy tube, saliva management, suction and social well-being, using a 'Likert' rating scale, rating from 1 ("always") to 5 ("never"). Patients were asked to complete and return the survey to their designated speech and language therapist. Patient's characteristics, including their level of consciousness, using the Glasgow Coma Scale (Teasdale and Jennett 1974) and their oral intake status using the functional oral intake scale (FOIS) (Crary et al. 2005) is shown for each participant (case) in table 2. Table 3 shows the tracheostomy tube size and type and routine nursing and therapy interventions with the tracheostomy tube.

Table 2 Patient characteristics, with Glasgow Coma Scale (GCS) score (Teasdale and Jennett 1974) and functional oral intake score (FOIS) (Crary, Mann et al. 2005)

Patient	Sex (M/F)	Age	Primary Diagnosis	GCS[1]	FOIS[2]
Case 1	M	69	Cerebral Vascular Accident	11/15	Level 2
Case 2	M	18	Hypoxic Brain Injury	8/15	Level 1
Case 3	M	22	Head Injury	5/15	Level 1
Case 4	M	68	Cerebral Vascular Accident	12/15	Level 2

[1] Glasgow Coma Scale (GCS) score

[2] Functional Oral Intake Scale (FOIS)

Table 3 Tracheostomy tube characteristic for each participant and intervention status

Patient	Tracheostomy Tube		Tracheostomy Tube Cuff Status	Routine Nursing care	Therapy Intervention
	Size	Type			
Case 1	Size 8	Cuffed, unfenestrated	Cuff fully inflated	Tracheal suctioning, as required; oral hygiene care	Swallow stimulation programme
Case 2	Size 6	Cuffed, unfenestrated	Cuff fully inflated	Tracheal suctioning as required; oral hygiene care	Sensory stimulation / oral desensitisation programme. Swallow stimulation programme
Case 3	Size 6	Cuffed, unfenestrated	Cuff fully inflated	Tracheal suctioning as required; oral hygiene care	Sensory stimulation / oral desensitisation programme. Swallow stimulation programme
Case 4	Size 6	Cuffed, unfenestrated	Cuff fully inflated	Tracheal suctioning as required; oral hygiene care	Swallow stimulation programme

Of the initial four participants who enrolled within the study only full sets of data were recorded for three participants as one participant (case 4) withdrew.

3.111 Case 1

A 69-year-old man who had a cerebral vascular accident (CVA) on 05/12/2011, who presented awake and alert with a Glasgow Coma Scale score of 11 out of 15 (E4, V2, M5) (Teasdale and Jennett 1976). He was non-mobile and had difficulties in following commands and in expressing his needs or wants. He had a size 8, cuffed, tracheostomy tube inserted on 05/12/2011. The cuffed tracheostomy tube blocked any air from flowing around the tube and assured that the patient was well oxygenated for ventilation purposes and also minimised the amount of saliva that fell into the airway by attempting to make a seal between the tube and the airway. The tracheostomy tube was initially inserted for the purpose of providing ventilation assistance, as he had difficulties in maintaining oxygen saturation levels whilst breathing on room air, and thereafter, once weaned from ventilation, for management of saliva falling into his airway due to severe oral and pharyngeal stage swallowing dysfunction. He had a 24-hour one-to-one (1:1) nurse to provide tracheostomy tube care and tracheal suctioning and set-up and delivery of alternative percutaneous endoscopic gastrostomy (PEG) tube feeding. He was prescribed transdermal patches of Scopoderm TTS® five days post insertion of the tracheostomy tube, due to copious amounts of pooled saliva within his oral cavity, which subsequently was falling into his airway necessitating tracheal suctioning at least every hour.

3.112 Case 2

An 18 year old male was admitted to the Wellington Hospital on 12/11/2012 having sustained a closed head injury on 30/07/2012, resulting in hypoxic brain damage. He was in a low-awareness state, unresponsive with a Glasgow Coma Scale score of 8 out of 15 (E4, V1, M3) (Teasdale and Jennett 1976). He was fully dependent on 24-hour one-to-one (1:1) nursing to provide all his daily care,

including positioning and meeting his alternative feeding and hydration needs, via a percutaneous endoscopic gastrostomy (PEG) feeding tube. He also presented with a bite-reflex, which was triggered by placement of a swab or tongue depressor against his teeth or on his tongue, which made it difficult to perform oral hygiene or clear pooled saliva from within the oral cavity. He had a size 6, cuffed tracheostomy tube which was inserted in August 2012 for the management and clearance of copious amounts of saliva falling into his airway, secondary to severe oral and pharyngeal stage swallowing difficulties. The tracheostomy tube was replaced with a size 6, cuffed, 'Tracoe-twist' tracheostomy tube on 14/11/2012. He was commenced on treatment of Scopoderm TTS® transdermal patches for management of his saliva on 05/02/2013.

3.113 Case 3

A 22 year old male was admitted to the Wellington Hospital on 03/04/2013 in a low-awareness and unresponsive state, with a Glasgow Coma Scale score of 5 out of 15 (E2, V1, M2) (Teasdale and Jennett 1976), having sustained a closed head injury, following a road traffic accident on 07/02/2013. He was fully dependent on 24-hour one-to-one (1:1) nursing to provide all daily care, including positioning, meeting alternative feeding and hydration needs via a percutaneous endoscopic gastrostomy (PEG) feeding tube and oral hygiene care, which were made difficult due to the presence of a bite-reflex and inaccessibility to the tongue and floor of the mouth. He initially had a size 7, cuffed tracheostomy tube which was inserted in February 2013, for the management and clearance of copious amounts of saliva falling into the airway due to severe oral and pharyngeal stage swallowing difficulties. The tracheostomy tube was replaced with a size 6, cuffed, tracheostomy tube on 08/04/2013. He was commenced on treatment of 'Scopoderm TTS®' transdermal patches for management of his saliva on 25/04/2013.

3.114 Inclusion Criteria

Participants had to meet all of the following criteria to be enrolled in this study:

- Males or females over the age of 18 years
- Participants who had a tracheostomy tube in-situ
- Breathing on room air, without the need for any mechanical ventilation
- Requiring tracheal suctioning in order to clear saliva from within the airway
- Requiring pharmacological intervention to manage their saliva
- Participants who were able to consent, or included as part of their treatment evaluation, as agreed with their carer / next-of-kin and primary consultant
- Participants who were 'Nil-By-Mouth' (NBM) , receiving alternative tube-feeding at the time of recruitment, scoring levels 1 – 3 on the functional oral intake scale (FOIS) (Crary, Mann et al. 2005)
- Participants who were not on any prescribed medications that are known to induce hypersalivation or inhibit saliva flow

3.12 Measurements

3.121 Collection of unstimulated whole saliva

Unstimulated whole saliva was collected using the 'swab' method, which involved the placement of three absorbent cotton dental rolls intra-orally, placed by the primary investigator, for duration of 5 minutes, before being removed. The weights of the cotton dental rolls were established before and after measurement. All data collection for saliva was made by the primary investigator. A protocol for collection was used, whereby three dry dental rolls were placed and sealed within a clear sterile bag and then weighed to gain the dry-weight of the bag and rolls; this dry-weight reading was recorded to a sensitivity of 1/100 of a gram (0.01g). Prior to data collection participants were positioned as close to a 90^0 seated position as possible, by their 1:1 nurse and the previously weighed dry dental rolls were removed from the sterile bag and placed intra-orally by the primary investigator, using sterile tweezers into the

oral cavity (one in the anterior sulcus, behind the lower front lip, between the lip and gum and one-each in the lateral sulci, between the cheek and lower gum). The patient was not given any other stimuli, such as oral hygiene care or therapy intervention prior or during data collection, to avoid any potential stimuli that might physically cause an increase in saliva flow, however continued to follow any regimes in relation to therapy intervention relating to the tracheostomy tube, such as placement of the speaking valve onto the end of the tracheostomy tube or trials of closing-off (capping) the tracheostomy tube at times of data collection. The dental rolls were left in place for a total of five minutes, monitoring that they had not dislodged in this duration of time, by the primary investigator. At the end of the five minute placement period, the dental rolls were removed by the primary investigator, using sterile tweezers and were replaced into the clear sterile bag from which they had been removed and were re-weighed and the wet-weight was recorded to a sensitivity of 1/100 of a gram (0.01g), within one to two minutes after collection, by the primary investigator. The dental roll dry and wet weights were recorded by the primary investigator, using the 'Shimadzu TXB222L' electronic weighing scales, which are scales with an in-built calibration and levelling function. The differences in the weight of the dry versus the wet dental rolls were recorded to a sensitivity of 1/100 of a gram (0.01). Readings of the weights were taken across three equally spaced time intervals: early morning (10:00am), midday (1:00pm) and late afternoon (4:00pm), for three consecutive days, and an average reading was obtained. These data readings were repeated throughout the inpatient stay by the primary investigator at the following time intervals: one-week prior to treatment; one-week, two weeks, four weeks, eight weeks and at 12 weeks post treatment.

3.122 Determination of the frequency and reasoning of tracheal suctioning

The frequency of tracheal suctioning performed across a 12-hour period, from 8:00am to 8:00pm, was recorded using the patient's tracheostomy nursing care chart (Appendix I), along with the primary reasoning for performing tracheal suctioning (Appendix A), which were listed as; 1) secretions audible; 2) ventilator shows high peak pressures; 3) increased peak inspiratory pressures associated with volume control; 4) audible or visible secretions; 5) increased

work of breathing; 6) deteriorating oxygen saturations; 7) routine; and 8) other. The nurse caring for the patient on each 12-hour (day) shift was the same nurse, who was present for the duration of their inpatient stay and their consistent 1:1 nurse whilst the patient was a participant within the study. This nurse was asked to record (via tally) on a tracheostomy nursing care chart each time a catheter was passed via the tracheostomy tube in order to perform tracheal suctioning. At the same time the nurse was also asked to document on another sheet, which listed the main reasons for performing the tracheal suctioning (Appendix A). The measurements of frequency of tracheal suctioning were calculated across the twelve-hour period for three consecutive days and an average was obtained. The 3 day cycle of measurements were made at one-week prior to treatment and then again at five time points post treatment: at one week, two weeks, four weeks, eight weeks and at 12 weeks post treatment.

3.123 Participant / primary carer self-perceptions on tracheal suctioning/saliva flow

The responses from the participants and/or the same primary carer reports of the amount of saliva, frequency of tracheal suctioning and perceptions of having a tracheostomy tube in-situ, using a tracheostomy tube self-perception survey (Appendix H) were also recorded at the same time intervals: one-week prior to treatment, one week, two weeks, four weeks, eight weeks and at 12 weeks post treatment. This survey used a series of statements, asking participants or their carers to rate from 1 (‘always’ / ‘very much true’) to 5 (‘never’ / ‘not at all true’), using a ‘Likert’ rating scale, relating to their tracheostomy tube, tracheal suctioning, saliva management and well-being (Appendix H).

3.124 Nursing perceptions on tracheal suctioning/saliva flow

Nursing staff perceptions on the amount of saliva and the frequency of tracheal suctioning required by participants were also recorded by the same 1:1 nurse carer (Appendix J). Saliva was rated on a visual analogue scale (0 – 100) and frequency of tracheal suctioning on a 'likert' scale from a score of 1 ("very much true") to a score of 5 ("not true at all"). These scores were recorded at the same time intervals: one-week prior to treatment, one week, two weeks, four weeks, eight weeks and at 12 weeks post treatment.

3.13 Treatments

The current medical treatment interventions used at the Wellington Hospital for saliva management include injections of botulinum toxin to the salivary glands or placement of Scopoderm TTS® transdermal patches. The treatment to be prescribed is the decision of the primary consultant, thus assignation to the intervention is the sole decision of the consultant. The need for management of saliva is raised to the primary consultant by the multidisciplinary team caring for the patient. It is also highlighted and documented by the hospital's tracheostomy team, who perform ward-rounds, at least once-a–week, with every patient who has a tracheostomy tube in-situ. The tracheostomy team, which primarily consists of a nurse, speech and language therapist, physiotherapist and ear, nose and throat (ENT) specialist, determines through rounding which patients have copious amounts of saliva, difficulties with management of their saliva and therefore requiring regular tracheal suctioning. Following team discussion recommendations are made to the primary consultant to consider treatment options to assist in the management of saliva in their patient.

All patients within this series evaluation underwent treatment using placement of Scopoderm TTS® transdermal patches.

3.131 Intervention using Scopoderm TTS® transdermal patches

Scopoderm TTS® transdermal patches of 1.5mg dosages were placed behind one ear. Each patch released 1mg of Hyoscine across a 72 hour period. Each Scopoderm TTS® transdermal patch was replaced every 72 hours and was discontinued if the patients no longer had difficulties in managing their saliva and were able to clear orally pooled saliva, either by expectorating it independently or swallowing their saliva. The treatment was also discontinued if there were any identified adverse reactions to the treatment, such as evidence of visual disturbances, skin irritation, dryness of the mouth, drowsiness or confusion and hallucinations, as described in the products summary of characteristics.

3.132 Speech and Language Therapy intervention and routine care provided

Whilst engaged within this study each participant continued to receive daily speech and language therapy intervention, for tracheostomy tube assessment and treatment, treatment for severe oral and pharyngeal stage swallowing difficulties and communication difficulties. In addition two participants (case 2 and 3) who were in a low-awareness, unresponsive state had therapy to treat the presence of a bite-reflex. Patients received a range of therapy interventions, which incorporated a global sensory stimulation programme, including oral desensitisation for the patients who presented with hypersensitivity and bite reflex (cases 2 and 3) and swallowing stimulation, using differing flavoured swabs and ice-chips. In case 1, where the participant was awake and alert, instrumental diagnostic assessment of his swallow was performed and this confirmed he could be commenced on small amounts of controlled oral trials of a modified diet (pureed diet) with the speech and language therapist only**.**

These participants were at high risk of oral health complications, due to a combination of factors, which included reduced level-of-awareness, inability to participate in self-care and inability to effectively clear oral saliva. This may cause pathogens to colonise in the oral cavity, which if aspirated may contribute

to serious respiratory complications, such as aspiration pneumonia. All participants within this study received regular oral hygiene care, which was performed primarily by the one-to-one nurse, this involved 2-4 hourly brushing and debriding with the use of a suction toothbrush / swab system, antiseptic mouthwash, non-foaming toothpaste and mouth moisturiser.

As all participants were self-ventilating, breathing on room air and not requiring additional oxygen therapy and were routinely prescribed with 4-6 hourly saline nebulisers, which was administered by the one-to-one nurse. Saline nebulisation was prescribed in order to loosen and thin secretions, to prevent atelectasis and sputum consolidation within the airway and promote clearance via coughing and/or assisted tracheal suctioning. Saline nebulisers were given outside of data collection times and did not interfere with the placement of the dental rolls within the oral cavity.

All data collection was structured around therapy and nursing interventions, so as to minimise the effect of external stimuli and treatments, which may have inadvertently caused a change in saliva flow.

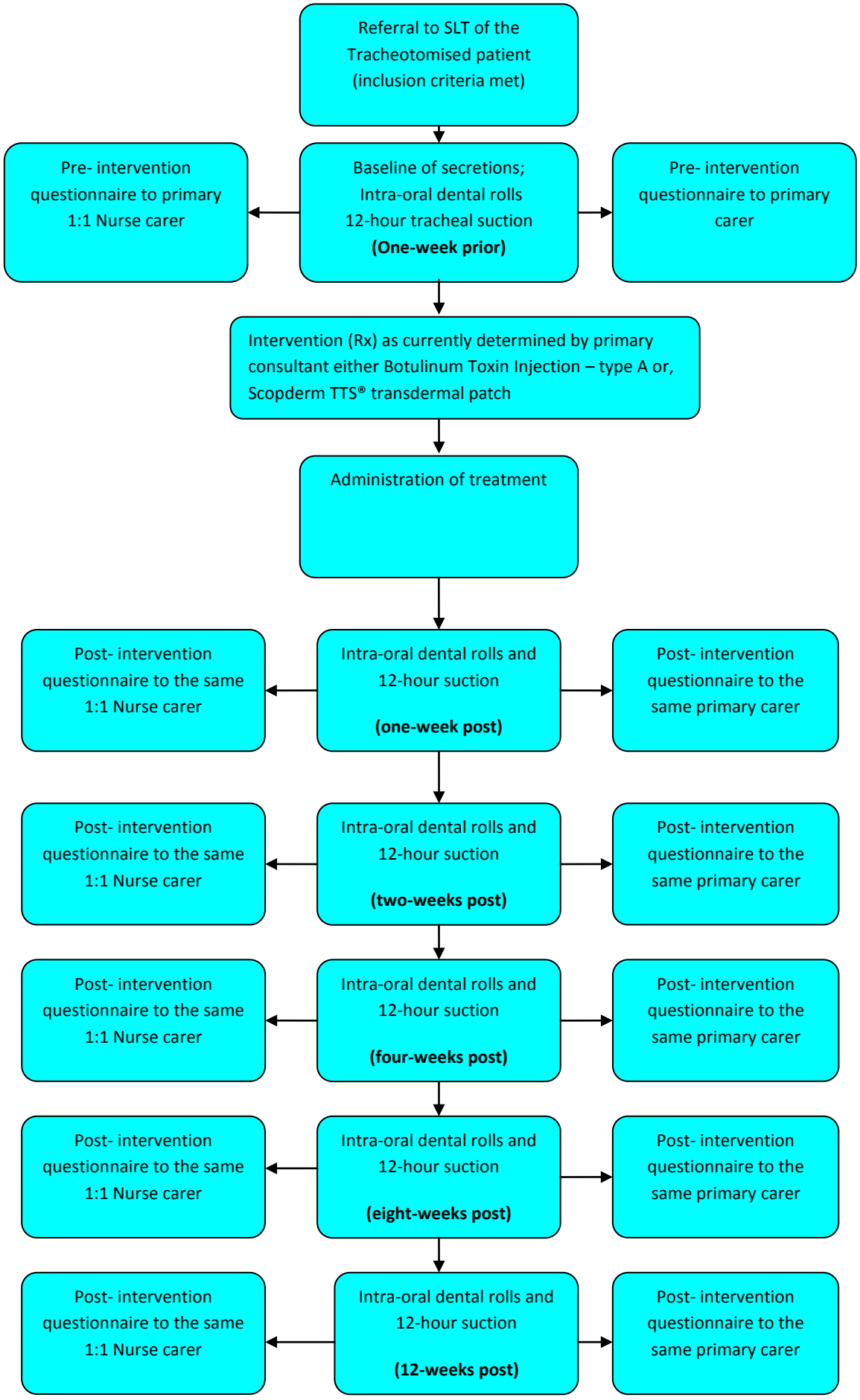

Figure 10 Schedule of data collection in each participant (case). All dental roll readings made by the primary investigator. All nurse/carer questionnaires completed by the same nurse/same carer.

3.14 Equipment

‘Shimadzu TXB222L Series’ electronic balance scales (220g in 0.01g intervals)

‘Nu-Care Products Ltd’; Dental Rolls D882, Size No. 2

Sterile tweezers

Sterile clear plastic bags

Tracheostomy nursing care chart (Appendix I)

Reasons for performing tracheal suctioning chart (Appendix A)

Tracheostomy tube self-perception survey (Appendix H)

Nurse-rating saliva perception scale (Appendix J)

3.15 Statistical Analysis

Linear regression analysis was used to analyse the relationship between salivary flow rate pre and post treatment and a P value of 0.05 or less was considered statistically significant.

The data was analysed using linear regression once all assumptions required for linear regression analysis were met, namely;

1) The two variables were measured at a continuous level
2) There was a linear relationship between the two variables, which was seen once the data was displayed in a scatterplot graph
3) There were no significant outlying data readings observed, when the data was plotted on a scatterplot
4) There were independence of observations, which was checked using the ‘Durbin-Watson’ statistic
5) The data showed homoscedasticity, in that the variances along the line of best fit remained similar, whilst moving along the line

6) Finally, that the residuals (errors) of the regression line are approximately normally distributed, which was checked by plotting a histogram with a superimposed normal curve

The data collected met all assumptions required in order to proceed with linear regression analysis, which was performed in each case pre and post intervention and further follow-up tests were carried-out comparing the dental roll weights pre intervention and at each time-point post intervention (at one, two, four, eight and 12 weeks post intervention) for each participant (case).

A Chi-Square test was performed analysing the frequency of tracheal suctioning performed by the same primary nurse caregiver for all participants. Further follow-up analyses using Chi-Square Goodness of Fit tests were performed for each case for tracheal suctioning performed across time and are shown under each case. In order to avoid type I errors (false positive errors) in the analyses, the significant level was taken from P=0.05 to p=0.01, which was calculated by dividing 0.05 by the number of tests, which were 5 (α=0.05 / 5), giving a p value = 0.01.

The data was entered into a Statistical Package for the Social Sciences (SPSS) software (version 22) and linear regression analysis was used to determine the relationship between dental roll weights over time, pre and post treatment and a Chi-Square test and Chi-Square Goodness of Fit tests were performed to analyse the frequency of tracheal suctioning.

The results from the primary caregiver questionnaires were analysed to provide a qualitative review on caregivers' perceptions on the tracheostomy tube, saliva and social consequences of having a tracheostomy tube in-place. The results of frequency of tracheal suctioning and reasoning for suctioning as recorded by the same 1:1 nurse was also analysed (quantitatively and qualitatively) in each case and nursing perceptions on saliva ratings were also recorded and reported in the results.

Chapter 4

4 Results

Of the four participants within this study, three full sets of data were obtained (cases 1–3) and one participant (case 4) withdrew one week post intervention. This participant withdrew one-week post intervention, after being re-advised of the potential side-effects of the Scopoderm TTS® transdermal patches, despite no adverse side-effects being recorded or reported in this participant. The three full sets of data were analysed and results presented in each case below. There were no documented adverse reactions or side-effects in any of the patients who received treatment using transdermal patches of Scopoderm TTS®.

4.1 Case reports

4.11 Case 1

Using linear regression analysis there was a significant reduction in the amount of oral secretions pre and post treatment, (P <0.001, F= 27.252, df= 1, 52). The most significant change in oral secretions occurred post one-week of intervention (P<0.001, F= 153.532, df= 1, 16). The average weights of the wet dental rolls at each time point are shown in table 1.

Table 1 Average wet weights of dental rolls at pre and post intervention time-points (case 1)

Time	Weight in grams
One-week prior treatment	4.02
One-week post treatment	2.65
Two-weeks post treatment	2.78
Four-weeks post treatment	2.87
Eight-weeks post treatment	2.73
Twelve-weeks post intervention	2.68

Figure 1 shows the weights of the wet dental rolls for each observation for this individual (Appendix K).

The visual analogue scale (VAS) score for saliva ranged from 100 (copious amounts of saliva) to 0 (no difficulties with saliva). In case 1 the primary one-to-one nurse rated the saliva score at 80 out of 100, prior to treatment, suggestive of large amounts of saliva presence and at 10 out of 100 at 12-weeks post treatment, suggestive of minimal amounts of saliva presence (Appendix K).

The VAS score for saliva was rated at 100 out of 100 by the patient's primary carer pre-treatment intervention, suggestive of large amounts of saliva presence and at 12-weeks post intervention by the same carer at 10 out of 100, suggestive of minimal amounts of saliva presence (Appendix K).

The primary one-to-one nurse reported that pre-treatment the patient was requiring tracheal suctioning as 'very much true' and at 12-weeks post treatment intervention requiring tracheal suctioning as being rated as 'not at all true' (Appendix K). Tracheal suctioning was performed on average 13 times during a 12-hour period pre-treatment and on average six times during a 12-hour period, post one-week intervention and to once a day, during a 12-hour period post 12-weeks intervention (Figure 2; Appendix K). Analysis of the frequency of tracheal suctioning performed across time, using The Chi-Square Goodness of Fit test, showed a significant reduction in the frequency of tracheal suctioning performed, at two weeks post intervention, $p=0.007$.

The primary reason for performing tracheal suctioning was documented by the one-to-one nurse as audible or visible secretions in the tracheostomy tube (Appendix K). One-week after data collection ceased the tracheostomy tube was successfully removed and the patient was breathing on room air, without the need for any further tracheal suctioning.

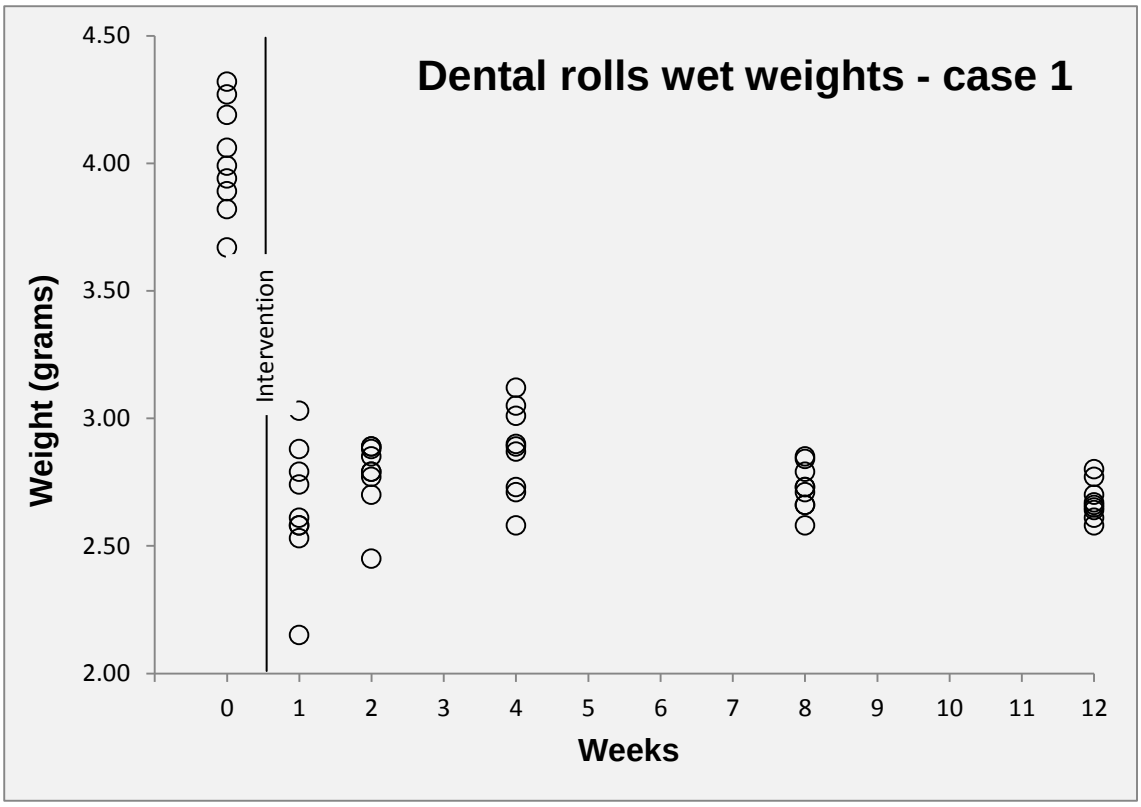

Figure 1 Dental rolls wet weights in grams, at pre and post intervention time-points (case 1)

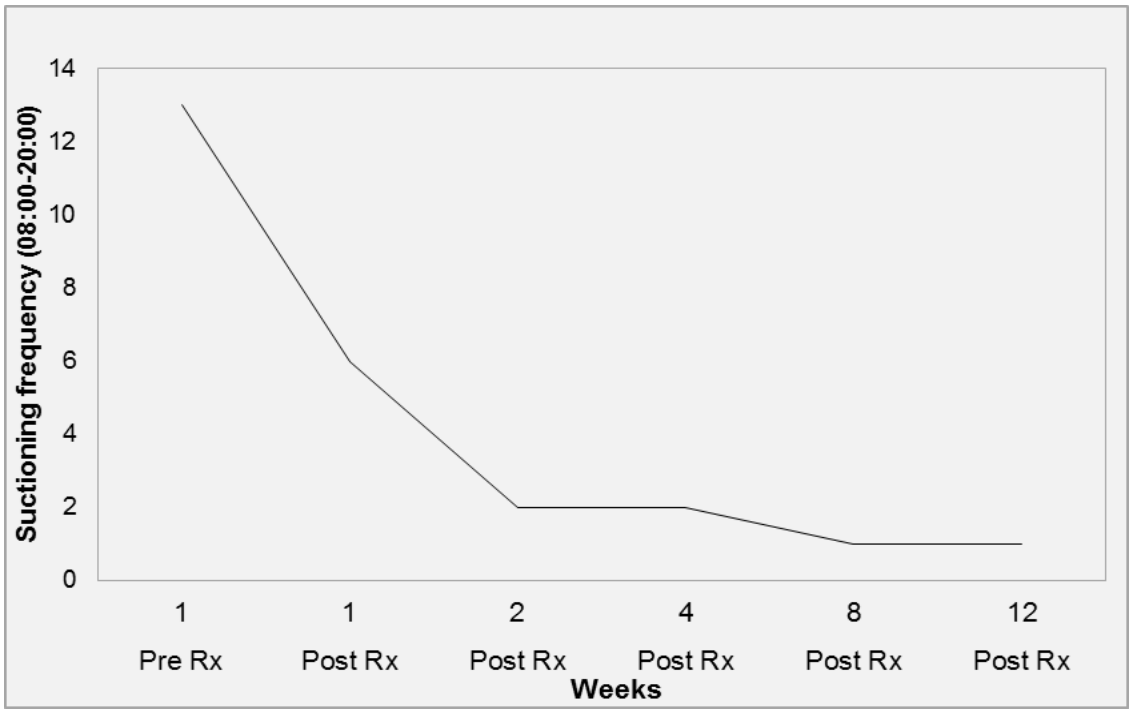

Figure 2 Average suctioning frequency (12-hour period), pre and post treatment (Rx) (case 1)

4.12 Case 2

Using linear regression analysis there was a significant reduction in the amount of saliva pre and post treatment, (P <0.001, F= 11.622, df= 1, 52). The most significant change in saliva occurred post one-week of intervention (P<0.001, F= 138.573, df= 1, 16). The average weights of the wet dental rolls at each time point are shown in table 2.

Table 2 Average wet weights of dental rolls at pre and post intervention time-points (case 2)

Time	Weight in grams
One-week prior treatment	6.07
One-week post treatment	4.52
Two-weeks post treatment	3.86
Four-weeks post treatment	4.30
Eight-weeks post treatment	4.40
Twelve-weeks post intervention	4.84

Figure 3 shows the weights of the wet dental rolls for each observation for this individual (Appendix L).

The visual analogue scale (VAS) score for saliva was rated at 100 out of 100 by the primary one-to-one nurse, prior to treatment intervention, suggestive of large amounts of saliva presence and at 12-weeks post intervention by the same nurse carer at a score of 40 out of 100, suggestive of moderate amounts of saliva presence (Appendix L).

The VAS score for saliva was rated at 100 out of 100 by the patient's primary caregiver pre-treatment intervention, suggestive of large amounts of saliva presence and at 12-weeks post intervention by the same caregiver at 50 out of 100, suggestive of moderate amounts of saliva presence (Appendix L).

The primary one-to-one nurse rated that pre-treatment intervention the patient was requiring tracheal suctioning as ‘very much true’ and at 12-weeks post treatment intervention requiring tracheal suctioning as being rated as ‘somewhat true’ (Appendix L). Tracheal suctioning was performed on average 10 times during a 12-hour period pre-treatment intervention and on average 10 times during a 12-hour period, post one-week intervention and an average of six times a day, during a 12-hour period post 12-weeks intervention (Figure 4; Appendix L).

Analysis of the frequency of tracheal suctioning performed across time in this case, using The Chi-Square Goodness of Fit test, did not show any significant changes at any time-point, when comparing pre and post intervention tracheal suctioning.

The primary reason for performing tracheal suctioning was documented by the one-to-one nurse as audible or visible secretions in the tracheostomy tube (Appendix L).

Post data collection the patient continued to require tracheal suctioning and the tracheostomy tube continued to be in-situ for this purpose, although there were short-periods throughout the day when a one-way valve was placed onto the end of the tracheostomy tube to allow airflow to be directed across the larynx. Three-weeks after data collection ceased the tracheostomy tube was successfully removed and the patient was breathing on room air, without the need for any further tracheal suctioning.

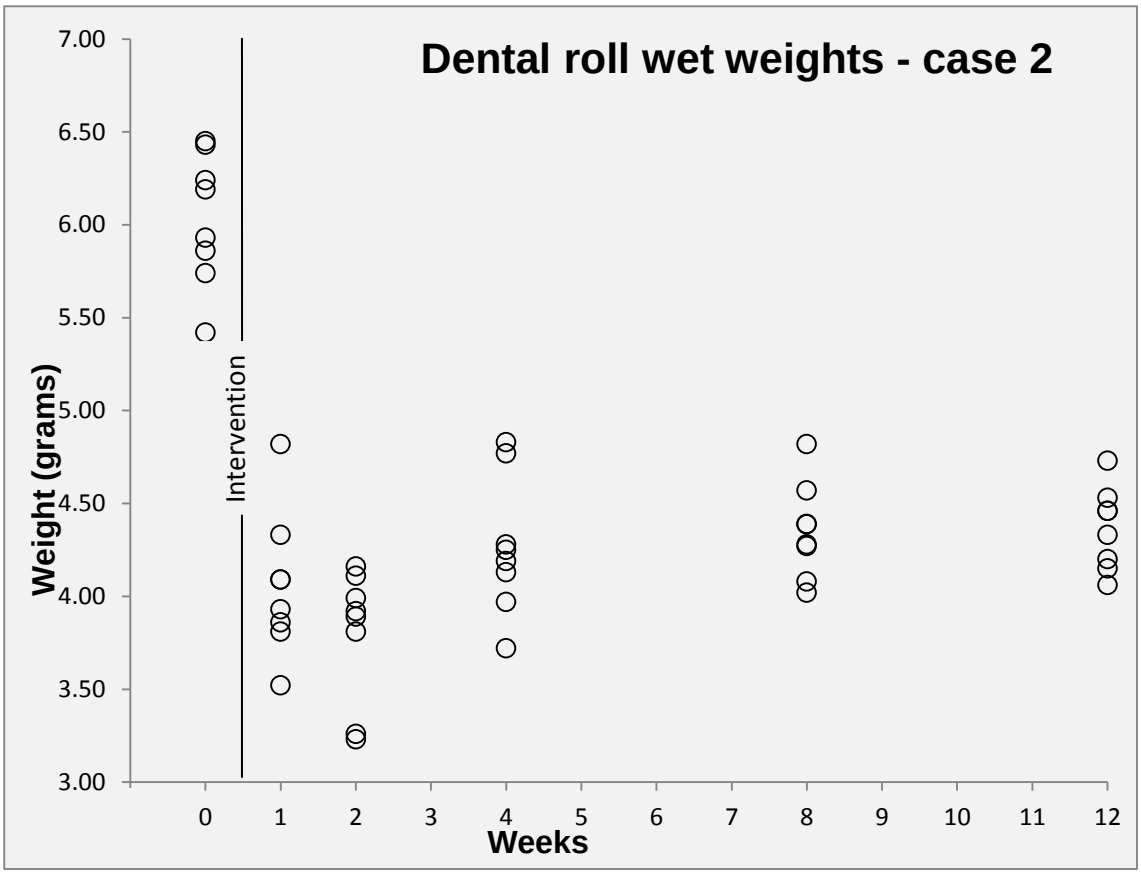

Figure 3 Dental rolls wet weights in grams, at pre and post intervention time-points (case 2)

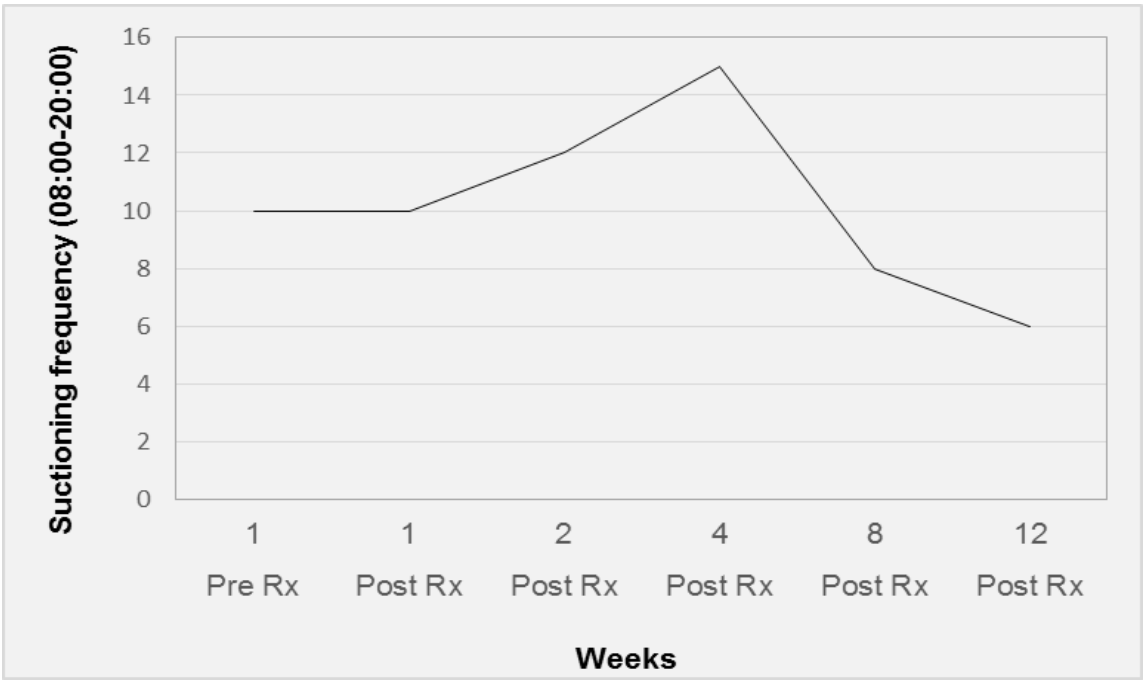

Figure 4 Average suctioning frequency (12-hour period) pre and post treatment (Rx) (case 2)

4.13 Case 3

Using linear regression analysis there was a significant reduction in the amount of saliva pre and post treatment, (P <0.001, F= 159.314, df= 1, 52). The most significant changes in saliva occurred in the periods one-week, two-weeks and at four-weeks post intervention (P<0.001, F= 54.379, df= 1,16; P<0.001, F= 22.098, df= 1,16 and P<0.003, F= 12.312, df= 1,16). The average weights of the wet dental rolls at each time point are shown in Table 3.

Table 3 Average wet weights of dental rolls at pre and post intervention time-points (case 3)

Time	Weight in grams
One-week prior treatment	4.91
One-week post treatment	4.45
Two-weeks post treatment	4.20
Four-weeks post treatment	4.06
Eight-weeks post treatment	4.01
Twelve-weeks post intervention	3.97

Figure 5 shows the weights of the wet dental rolls for each observation for this individual (Appendix M).

The visual analogue scale (VAS) score for saliva was rated at 100 out of 100 by the primary one-to-one nurse, prior to treatment intervention, suggestive of large amounts of saliva presence and at 12-weeks post intervention by the same nurse at a score of 20 out of 100, suggestive of minimal amounts of saliva presence (Appendix M).

The VAS score for saliva was rated at 100 out of 100 by the patient's primary caregiver pre-treatment intervention, suggestive of minimal amounts of saliva presence and at 12-weeks post intervention at 20 out of 100 suggestive of minimal amounts of saliva presence (Appendix M).

The primary one-to-one nurse rated that pre-treatment intervention the patient was requiring tracheal suctioning as 'very much true' and at 12-weeks post treatment intervention requiring tracheal suctioning as being rated as 'a little true' (Appendix M). Tracheal suctioning was performed on average 15 times during a 12-hour period pre-treatment intervention and on average nine times during a 12-hour period, post one-week intervention and an average of three times a day, during a 12-hour period post 12-weeks intervention (Figure 6; Appendix M). Analysis of the frequency of tracheal suctioning performed across time, using The Chi-Square Goodness of Fit test, showed a significant reduction in the frequency of tracheal suctioning performed, at four weeks post intervention, $p=0.078$.

The primary reason for performing tracheal suctioning was documented by the one-to-one nurse as audible or visible secretions in the tracheostomy tube (Appendix M). Following the data collection the patient's tracheostomy tube was successfully closed for a full 24 to 48 hours, with routine peripheral tracheal suctioning performed once to twice a day to clear saliva from within the inner tube of the tracheostomy tube. One-week after data collection ceased the tracheostomy tube was successfully removed and the patient was breathing on room air, without the need for any further tracheal suctioning.

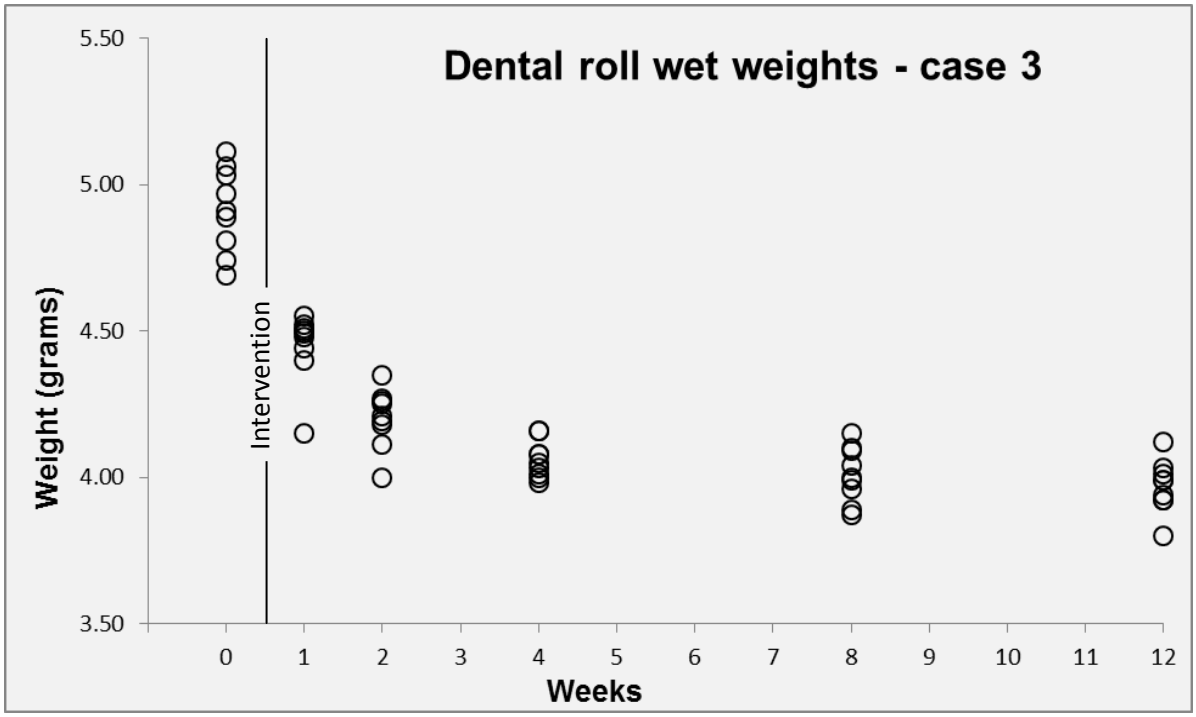

Figure 5 Dental rolls wet weights in grams, at pre and post intervention time-points (case 3)

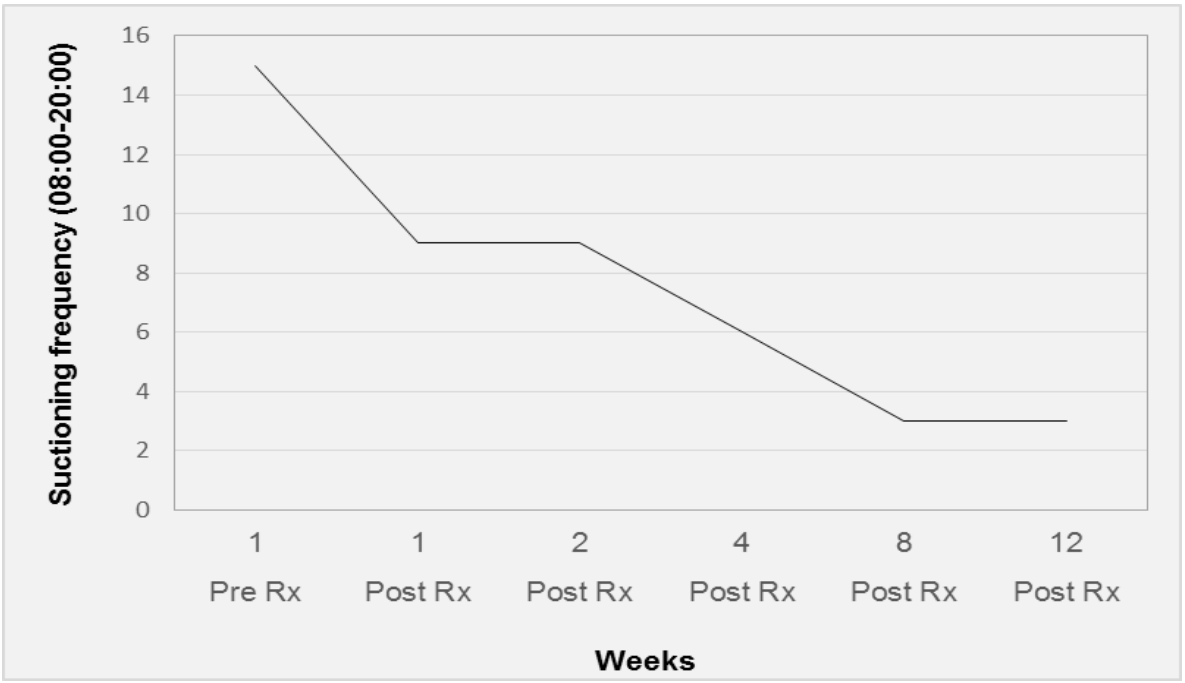

Figure 6 Average suctioning frequency (12-hour period) pre and post treatment (Rx) (case 3)

4.14 Cases 1 – 3

In all cases each primary caregiver rated that the tracheostomy tube caused them concern and that they were scared when tracheal suctioning was required, and rated these statements as being ‘very much true’ throughout (Appendices K, L and M). All caregivers also reported that their relative having the tracheostomy tube in place made them feel sad and discouraged and all reported ‘very much true’ a sense of feeling frustrated (Appendices K, L and M).

There was a significant reduction (P<0.001) in saliva, in all participants post one week treatment intervention. The primary caregivers reported a change in the amount of tracheal suctioning required, with two rating requiring regular suctioning as ‘very much true’ pre-treatment intervention to a ‘little true’ post 12-weeks intervention and the other rating it as ‘very much true’ pre-treatment intervention to ‘somewhat true’ post 12-weeks intervention (Appendices K, L and M).

The visual analogue scale (VAS) score for saliva ranged from 100 (copious amounts of saliva) to 0 (no difficulties with saliva). In all cases both the one-to-one nurse and the patient’s primary caregiver reported a reduction of saliva on the visual analogue scale, with all rating saliva pre-treatment at 100 (copious amounts of saliva). In two cases (cases 1 and 3) at 12-weeks post-intervention, the one-to-one nurse and caregiver rated the saliva at 10 (case 1) and 20 (case 3), suggestive of minimal amounts of saliva. In case 2 the one-to-one nurse rated saliva at 40 and caregiver at 50, suggestive of moderate amounts of saliva presence at 12-weeks post-intervention (Appendices K, L and M).

Table 4 Average number of tracheal suctioning performed for each participant (case) at each time-point

Participant	Pre intervention	1 week post intervention	2 weeks post intervention	4 weeks post intervention	8 weeks post intervention	12 weeks post intervention
Case 1	13	6	2	2	1	1
Case 2	10	10	12	15	8	6
Case 3	15	9	9	6	3	3

When analysing the frequency of tracheal suctioning using a Chi-Square test across all case participants there was a significant reduction in the frequency of tracheal suctioning performed post treatment intervention, Fisher's Exact Test p=0.094 and Cramer's V=0.253, suggesting an approximate variance of 25%.

In all three cases there was a reduction in the frequency to perform tracheal suctioning, as measured across a 12-hour period (08:00-20:00), in case 1 the average frequency of tracheal suctioning pre-intervention was 13, which was reduced to an average of 1, at 12-weeks post-intervention. In case 2 tracheal suctioning was performed on average10 times pre-intervention and scored at an average of 6 times at 12-weeks post-intervention. In case 3 tracheal suctioning was performed on average15 times pre-intervention and scored at an average of 3 times at 12-weeks post-intervention. In all cases the primary reason for performing tracheal suctioning was cited as being 'secretions audible', followed by 'secretions visible' and then listed as 'other', describing the need to perform tracheal suctioning due to the patient coughing (Appendices K, L and M).

In all cases pre-treatment intervention all one-to-one (the same) nurse rated the statement 'the patient constantly requires tracheal suctioning' on the nurse survey as 'very much true' and at 12-weeks post-intervention at 'not at all true' (case 1) (Appendix K); 'somewhat true' (case 2) (Appendix L) and 'a little true' (case 3) (Appendix M).

Throughout the study the patients primary caregivers rated that having a tracheostomy tube in-situ made them feel frustrated and sad as 'true' (Appendices K, L and M). Caregivers also all rated that they were scared when tracheal suctioning was required, rating this as 'very much true' (cases 2 and case 3) (Appendices L and M) or in case 1 as 'quite true' (Appendix K).

Chapter 5

5 Discussion of results

Saliva is a valuable oral fluid that is often taken for granted. Saliva is produced in and secreted by the salivary glands and is crucial to the preservation and maintenance of oral health. However, it is not until a change in the quantity or quality that it becomes an area of concern. When saliva is diminished, this may lead to a dry mouth, resulting in feelings of discomfort and difficulties in swallowing. Conversely too much saliva or inability to control saliva may have more serious consequences, affecting quality of life and health status. Drooling is rarely due to excessive production of saliva, but is a problem in the coordinated control of the muscles of the oral cavity, face, tongue and palate, usually due to impaired neurological control. This impaired control results in a dysfunctional swallow and may lead to excessive accumulation of saliva in the oral cavity and the unintentional loss of saliva from the mouth or into the pharynx. Furthermore, the inability to swallow adequately also increases the risk of developing aspiration pneumonia, which can be life-threatening and in some cases fatal. Patients with copious amounts of saliva, who are unable to clear material effectively from the airway may require assistance in manually removing the saliva, using suctioning, via a tracheostomy tube, to prevent saliva obstructing the airway, making it difficult for the lungs to get the oxygen they need. Tracheal suctioning involves the removal of secretions, including saliva from the trachea or bronchi, by inserting a catheter through the tracheostomy tube.

There are no licensed products that are available to assist in reducing saliva in patients who may require a tracheostomy tube for the purpose of providing tracheal suctioning, but often unlicensed medications are prescribed ‘off-label’ to assist in this regard. This study showed that ‘Scopoderm TTS®’ transdermal patches were effective in reducing saliva in all three patients and thereby resulted in a reduction in the frequency of tracheal suctioning required.

In this study saliva was collected using the swab method (White 2007) and dental rolls were placed intra-orally, but placement had to be modified in each case. Two participants who presented with head injury and in a low-awareness state (cases 2-3) and who had a bite reflex, therefore placement of dental rolls on the tongue or sublingually were not possible, as it would've been difficult to place and / or retrieve the rolls after placement. There was also a risk that the dental rolls may fall into the airway if placement onto the tongue was possible and then non-retrievable following a bite-reflex response. Therefore all data collection of saliva involved placement of three dental rolls; one in the anterior sulcus and one-each in the lateral sulci, which was the same in each case series. As data was compared within participants this did not affect the overall outcome of data collected.

All participants were non-mobile and therefore dependent on being positioned as close to 90 degree sitting, by the one-to-one nurse, with placement of the dental rolls made by the primary investigator in each case. Using the swab method of saliva collection (White 2007) would have been more challenging with participants who were more mobile or presented with cognitive deficits, as they may not have co-operated in holding the dental rolls orally for the duration of five-minutes and spat-out the rolls, making it difficult to gain accurate readings of saliva collection.

Concurrent speech and language therapy intervention, which involved a sensory stimulation programme, including swallowing stimulation was offered alongside the pharmacological treatment in each of the participants. It is difficult to dissociate the effects of therapy intervention from that of the pharmacological intervention and how this may have influenced the amount of intra-oral saliva collected, however it was not possible to withhold therapy intervention as doing so would have been unethical. Data collection of saliva made by the primary investigator for each participant occurred at three fixed time-points (10:00am, 1:00pm and 4:00pm) and were recorded at these set time intervals pre and post treatment and did not coincide with any speech and language therapy sessions, or other interventions, so thereby limiting any immediate effects of therapy intervention on saliva data collection.

With an increasing demand for intensive care beds more nurses in acute and high dependency wards are expected to care competently for patients who have a tracheostomy tube in-situ (Haines and Coad 2001). Tracheal suctioning is an essential part of effective airway management in these patients. However, tracheal suctioning has many associated risks and complications, ranging from trauma and hypoxaemia to, in extreme cases, cardiac arrest and death (Santus, Gramegna et al. 2014).

In a study by Day (Day, Farnell et al. 2002), looking at nursing knowledge of tracheal suctioning, Day concluded that there was a poor level of knowledge for many nurses and this was also reflected in practice, as suctioning was performed against many of the recommended guidelines. Many practitioners were unaware of recommended practice and a number demonstrated potentially unsafe practice. In addition, there was no significant relationship between knowledge and practice (Day, Farnell et al. 2002). In their study they concluded that in practice only 2 out of the 28 nurses provided pre-oxygenation prior to suctioning, although 10 indicated knowledge to do so. Also despite a large number (n=19) indicating that suctioning should be performed after auscultation, in actual practice only 2 did so. Furthermore they found that there were errors associated to infection control prior to tracheal suctioning with only 2 nurses carrying-out correct hand-washing procedures (Day, Farnell et al. 2002). This study did not investigate the competencies of the nursing staff, but all nurses who were providing the one-to-one care for the patients were deemed to be competent in caring for patients who required tracheostomy tube care and tracheal suctioning.

If the frequency and the need to perform tracheal suctioning are reduced, by diminishing saliva flow, this may reduce the amount of saliva that potentially falls into the airway, thereby reducing the need and known associated risks with performing tracheal suctioning (Fiorentini 1992; Kapadia, Bajan et al. 2000). Furthermore reducing the need for performing tracheal suctioning may assist in successful removal of the tracheostomy tube and thus no longer necessitates a one-to-one nurse to provide care, which may assist in reducing costs. In all case series (cases 1-3), the primary reason for a one-to-one 24-hour nurse,

was to provide regular tracheal suctioning in order to clear saliva that had fallen into the airway, as these participants were unable to independently clear their saliva. All other care could be provided as routine care, such as regular positioning, set-up and deliverance of PEG tube feeding and washing and dressing, not necessitating one-to-one nursing care.

In each case the saliva flow rate pre-treatment for each case was at 0.38ml/min (case 1), 0.76ml/min (case 2) and at 0.53ml/min (case 3). This flow rate corresponds to a normal rate in an unstimulated state (Tenovuo and Lagerlof 1994). So each participant had a normal salivary flow rate, but associated swallowing dysfunction which led to an accumulation of saliva in the oral cavity and subsequent posterior overspill into the airway (Reddihough, Erasmus et al. 2010). However one week post treatment there was a reduction in the saliva flow rate for each patient which was at 0.19ml/min (case 1), 0.36ml/min (case 2) and at 0.45ml/min (case 3), which can be classified as low rate in the unstimulated state in case 1 and within the normal range in the unstimulated state for cases 2 and 3 (Tenovuo and Lagerlof 1994). The greatest change in saliva flow rate occurred in the case of the patient who had a primary diagnosis of cerebral vascular accident (case 1) and although there was a significant reduction in the two other patients whose primary diagnosis was head injury, the change was not as great, but it did lead to a reduction in the need to perform tracheal suctioning in each case.

Where individuals were identified as requiring tracheal suctioning to assist in the clearance of saliva from within the trachea, the medical teams seemed to have a preference to use off-labelling prescription of Scopoderm TTS® transdermal patches over the use of other pharmacological options such as the off-label prescribing of botulinum toxin, despite not being coerced by the primary treating speech and language therapist, tracheostomy team or nursing staff as to which treatment approach to prescribe. Despite the average frequency of tracheal suctioning identified pre-treatment in each case (13 in case 1, 10 in case 2 and 15 in case 3), there was no discussion between the team, consultant or participants and/or carers to agree an acceptable treatment intervention. As botulinum toxin or any other pharmacological treatment was not prescribed in any of these cases, it is difficult to speculate whether the treatment affect would

have been more instantaneous and resulted in a quicker reduction in the amount of saliva. Jongerius et al (Jongerius, Rotteveel et al. 2004) concluded in their study that there was a greater effect, when comparing single-dose botulinum toxin injections into the salivary glands with scopolamine treatment, in children with Cerebral Palsy.

It is difficult to say whether the treatment intervention led to a reduction in saliva or whether this was related to an increase in the number of reflexive swallows to clear saliva or a combination of both, although data recordings were collected at times of non-stimulation. Throughout the course of normal therapy intervention the tracheostomy tube may be capped-off (closed-off), where appropriate, or a one-way valve applied to the end of the tracheostomy tube. This valve allows air to enter via the tracheostomy tube and closes upon exhalation to direct air through the mouth and nose, normalising airflow across the larynx and facilitating an oral airstream (Hess 2005). Normalising airflow and promoting an oral airstream, causing greater airflow across the larynx increases sensitivity and may assist in increasing the number of reflexive swallows to clear saliva (Windhorst, Harth et al. 2009). However in each case series, the tracheostomy tube was not closed-off until the later-part of post-intervention treatment, after 10-12 weeks post intervention in case 1 and intermittently for a couple of hours during the day post eight-weeks intervention in case 2 and at post 12-weeks intervention in case 3. All participants were assessed by the speech and language therapist within 24-hours of admission and therapy intervention commenced thereafter, which continued until they were discharged from the hospital.

In the stimulated state, saliva flow rates drastically change the percentage contributions from each gland, with the parotid gland contributing more than 50% of total salivary secretions (Edgar 1990), producing large volumes of serous saliva, in response to a stimulant. The Wellington Hospital has an established oral hygiene protocol and policy for all non-ventilated patients, which comprehensively details how and when to perform oral hygiene care. Providing this care and physically placing the dental rolls might have stimulated an increase in saliva, but in order to minimise this occurrence oral hygiene was

not performed in any of the participants within an hour of the data collection times (10:00am, 1:00pm and 4:00pm). Care was also taken when placing the dental rolls, so as to minimise the level of intra-oral stimulation and external stimuli given, which was performed by the primary investigator who collected all data recordings.

All patients routinely received saline nebulisers, every 4-6 hours pre and post treatment intervention to avoid any possible complications of 'plugging-off' of the tracheostomy tube, which is caused by thick saliva blocking the inside of the tracheostomy tube. Saline nebulisers are sodium chloride water solutions that convert liquids into aerosol droplets, which assist in breaking down thick saliva (AARC 2003). In each case series nebulisation was not administered at times around data collection (10:00am, 1:00pm and 4:00pm).

All patients in this case series were non-verbal, unable to follow verbal commands or swallow to command, and unable to report any adverse side-effects to the treatment. They were therefore dependent on their primary care-giver, nursing reports and chart observations to indicate any adverse reactions to the treatment. Despite the fact that the patients were unable to report any adverse side effects, such as dizziness, blurred vision or dry-mouth, it was deemed in their best interest that the treatment benefits of reduced oral saliva and reduction in the potential need for tracheal suctioning would outweigh the potential adverse side-effects of Scopoderm TTS® transdermal patches. None of the patients within this study were on any known medications that would induce or inhibit saliva flow (Nahri 1994). All patients continued to receive therapy with no observed adverse reactions that were reported by the therapy team or the one-to-one nurse special or primary care-giver.

In each case series, saliva as measured using the swab method (White 2007) did not show an increase from baseline (pre-treatment) and at each recorded time-point remained at a stable level or showed a reduction. As it would be unethical to remove the treatment once instigated, we could not show that it was largely the Scopoderm TTS® transdermal patch that had a causal relationship in reducing the saliva. Removing the treatment may have shown an

increase in saliva weights, which may then be directly attributed to the Scopoderm TTS® intervention.

In this case series a single Scopoderm TTS® transdermal patch (1.5mg) was administered and replaced every three days, which on average allows the absorption of 1mg across three days (Novartis Consumer Health UK Ltd 2016). In every-day practice following periods of prescribed Scopoderm TTS® patches (1.5mg), where there is no perceived changes in the amount of pooled saliva, prescribers often use greater dosages, prescribing one and a half patches (2.25mg) instead of one patch, particularly in cases where there are copious amounts of saliva. It is therefore questionable whether an increased dosage may have resulted in a greater reduction in oral saliva. However in this study each participant received a single patch of Scopolamine TTS® throughout the study, therefore not affecting the data collection.

The patient's tracheostomy tube chart (Appendix I) recorded the number of tracheal suctions performed and the reasoning for this was also noted (appendix A), indicating that the one-to-one nurse was systematically thinking and documenting why and when tracheal suctioning was required and performed. However the nurse did not document if and when oral suctioning was performed to remove pooled saliva from within the oral cavity, which may have influenced the subsequent need to then perform tracheal suctioning. Oral suctioning reduces the amount of orally pooled saliva, which may have led to a reduction in the amount of saliva overspill into the airway and therefore reduced the need to perform tracheal suctioning. This would then result in altered recordings of tracheal suctioning; however this was controlled by avoiding any therapeutic or nursing interventions at or around times of data collection. Also an average of tracheal suctioning was taken across three consecutive days at one-week prior treatment, one-week, two-weeks, four-weeks, eight-weeks and at 12-weeks post treatment and an average obtained across the three days of readings.

Participants and care-givers in this study were not 'blinded' to the treatment and intervention could not be withheld or a placebo could not be administered instead, as we were observing the clinical management of saliva in these

participants. Knowing that treatment was prescribed may have caused bias from the one-to-one nurse and also from the primary caregiver, which may have influenced the scores they rated on the saliva visual analogue scale. Although the carer and nursing staff were unaware of the weights of the intra-oral dental rolls at each time-point, being aware that saliva was being monitored may have influenced their decisions on the need and frequency to perform tracheal or oral suctioning; however this was regulated by providing guidelines and recording charts, to document clearly as to why tracheal suctioning was being undertaken. There was also a reduction recorded at each time-point (one-week, two-weeks, four weeks, eight weeks and at 12-weeks) post intervention in the weight of the dental rolls, and also a reduction in the mean frequency of tracheal suctioning performed at each of the time-points, so suctioning should not have influenced, the dental roll weights.

Post one week treatment there was a reduction in the saliva flow rate for each patient of 0.19ml/min (case 1), 0.36ml/min (case 2) and at 0.45ml/min (case 3), which can be classified as a low rate in the unstimulated rate in the first case and within the normal range in the unstimulated state for the subsequent two cases (Tenovuo and Lagerlof 1994). In the case of low rate in the unstimulated condition (case 1), the primary diagnosis was cerebral vascular accident and different to that of the two other cases, which were diagnoses of head injury (case 2 and 3). In future studies it may be useful to compare between diagnoses, in order to compare outcomes in patients who have a focal injury versus that of diffuse brain injury. It is difficult to make a definitive conclusion between the saliva flow rates in the patient with a cerebral vascular accident versus the other patients with head injuries, as the sample size was small.

When analysing the frequency of suctioning there appears to have been a significant reduction in amount of tracheal suctioning performed two-weeks post intervention in case 1 ($p=0.007$), and at four-weeks post intervention in case 3 ($p=0.078$), but no significant differences found in case 2. This finding may be related to the primary medical diagnoses of each of the participants in that cases 2 and 3 were diagnosed with a hypoxic brain injury and Head Injury, resulting in a Glasgow Coma Scale (GCS) (Teasdale and Jennett 1976) of 8 out of 15 and 5 out of 15 respectively, whereas in comparison, case 1 had a

diagnosis of cerebral vascular accident with a GCS of 11 out of 15. A GCS of 8 or less indicates severe injury, one of 9-12 a moderate injury, and a GCS score of 13-15 is obtained when the injury is minor (Teasdale and Jennett 1974). Taking the these differences in GCS into account the participants in case 2 and 3 had more severe diffuse brain injury, whereas the participant in case 1 had a moderate injury, which was a focal brain injury, which may have influenced the outcome. McPherson and Stephens reported that patients with a reduced conscious level are unable to clear their own secretions and cannot protect their own airway (McPherson and Stephens 2012). They suggested that a Glasgow Coma Scale of 8/15 or below is often considered the threshold at which intubation is necessary (McPherson and Stephens 2012) and that patients with reduced conscious level are at risk of aspiration (McPherson and Stephens 2012).

Both participants in cases 2 and 3, were dependent on tube feeding with no oral intake and scored at level 1, as rated on the functional oral intake scale (FOIS) (Crary, Mann et al. 2005), whereas the participant in case 1 was tube dependent for feeding, but receiving inconsistent oral trials with their speech and language therapist and scored at level 2 on the FOIS (Crary, Mann et al. 2005).This difference may explain the improvement in case 1 with an earlier significant reduction in saliva, as measured by dental roll weights, and also a reduction in the frequency of tracheal suctioning, in that this individual was starting to receive inconsistent oral trails, thus showing an improvement in their swallowing status and therefore beginning to swallow their secretions.

Drooling occurs in about one in two patients affected with Motor Neurone Disease and one in five needs continuous saliva elimination (Giess 2000), its prevalence is about 70% in patients with Parkinson Disease (Jongerius 2004), and between 10 to 80% in patients with Cerebral Palsy (Boothwell 2002). Despite this high rate of prevalence and the need to eliminate saliva in these patient populations there are no recognised national, government-led guidelines, policies or procedures to manage saliva in these patient populations, as well as in patients who have a tracheostomy tube in-situ.

The National Institute for Health and Care Excellence (NICE) Guideline for the use of non-invasive ventilation in the management of Motor Neurone Disease (National Institute for Health and Care Excellence 2010), states that before starting non-invasive ventilation, the multidisciplinary team should prepare a comprehensive care plan, after discussion with the patient and their family. This should include 'secretion management and respiratory physiotherapy assessment, including cough assist', and how the team should assist in saliva management. It does not however make any other reference to the management options of saliva in the event of difficulties in managing excessive saliva and difficulties due to neuromuscular weakness.

In the NICE full Clinical Guideline on the management of Parkinson's Disease, injection of salivary glands with botulinum toxin A is one option suggested for the treatment of hypersalivation (The National Collaborating Centre for Chronic Conditions 2006), but no mention of other treatments for drooling. However there are no recommendations for the treatment or management of saliva in the case of drooling in the NICE guideline for spasticity in children and young people with non-progressive brain disorders (National Institute for Health and Care Excellence 2012). The guideline advises on the use of botulinum toxin type A for focal spasticity and advises children, young people and their parents or carers that one of the serious side effects and complications of its use is swallowing difficulties. The guideline makes no reference to the management of drooling or management options for excessive saliva. Systematic reviews of botulinum toxin in the management of hypersalivation have been published (Lim 2006; Stone 2009) and overall suggest that botulinum toxin treatment is a safe, minimally invasive. It is accepted that the use of botulinum toxin is a useful tool in the treatment of hypersalivation in Parkinson's disease, despite not being licensed for this purpose. There are also a number of studies that have investigated the management of drooling in children with Cerebral Palsy (Walshe, Smith et al. 2012). In their study Jongerius et al.(Jongerius, Rotteveel et al. 2004), carried-out a controlled clinical trial on the treatment of drooling in children with Cerebral Palsy, in which botulinum toxin injections to the submandibular glands were compared with scopolamine treatment and

botulinum toxin injections were found to significantly reduce drooling from baseline measures, when compared to the effects of scopolamine treatment. Despite the use of botulinum toxin injections in these studies with these patient populations there seems to be a reluctance to consider the use of botulinum toxin injections into the salivary glands with patients who have a tracheostomy tube in-situ. The primary treatment prescribed by the consultant to manage saliva in this patient population, was the use of Scopolamine TTS® transdermal patches. One possible reason for using transdermal patches as a primary treatment method is that it is a non-invasive treatment option and is preferred over the more invasive technique of injecting botulinum toxin into the salivary glands.

Since the administration of botulinum toxin is invasive and requires expertise to perform the intervention, patient access to treatment is restricted (Hyson 2002) and this may further have restricted the referral to this treatment modality over the use of Scopoderm TTS® transdermal patches. Furthermore the effects of repeated injections of botulinum toxin over time, or the risk of developing antibodies, are not known (Meningaud 2006). Jongerius et al. (Jongerius 2004), showed that both treatments of scopolamine and botulinum toxin injections into the salivary glands significantly reduced drooling compared with baseline. In their study the outcomes of both treatment modalities were in the same range and no significant differences were found between Drooling Quotient measurements. However a disadvantage in the treatment using scopolamine was the high percentage of observed adverse reactions, which were xerostomia, restlessness, drowsiness, blurred vision and confusion, whereas botulinum toxin injections only required a general anaesthesia and had minimal reported temporary adverse reactions (Jongerius 2004). Given that the patients within this study were in a low-arousal condition, they were unable to provide details of any possible perceived adverse reactions they may have experienced during therapy sessions, although none were reported by the same one-to-one nurse or the primary care-giver.

Another reason for choosing Scopoderm TTS® transdermal patches over injections of botulinum toxin into the salivary glands is that the cost of botulinum toxin and procedure is much higher than that of prescribing and applying

transdermal patches. A local cost analysis estimated that the costs associated with intra-glandular botulinum toxin injections would be seven times more costly than an equivalent three-month supply of Scopoderm TTS® transdermal patches.

The known risk factors and possible adverse side-effects of each of the treatment interventions are well documented in the summary of product characteristics for each medication (Allergan 2015). The main side effects of injecting botulinum toxin into the salivary glands are dysphagia, due to diffusion into nearby bulbar muscles, weak mastication, parotid gland infection, damage to the facial nerve/artery and dental caries (Allergan 2015). In comparison the use of Scopolamine TTS® transdermal patches may cause drowsiness, dizziness, confusion, visual hallucinations and possible urinary retention issues, albeit rarely (Novartis Consumer Health UK Ltd 2016). In conjunction with these possible adverse side-effects, the clinical effect of botulinum toxin injections lasts for approximately 2 - 6 months (Allergan 2015) and then resolves once new axon terminals form. In comparison the Scopolamine TTS® transdermal patches can be removed immediately upon any report of clinical adverse side-effects (Novartis Consumer Health UK Ltd 2016). The length of reversal of the botulinum treatment would take much longer in the event of any identified adverse side-effects, and again would be a contributing factor when deciding upon which treatment modality to prescribe. The main side effects of Scopolamine TTS® transdermal patches are it may cause drowsiness, dizziness, confusion or visual disturbances in certain individuals, which may affect the ability of the patients to participate and engage within a therapeutic programme; however two patients (cases 2 and 3) were in a low-awareness state with a Glasgow Coma Scale (GCS) (Teasdale and Jennett 1974) of 8/15 and 5/15 respectively and case 1 did not appear to present with any of these side-effects, who had a GCS of 11/15.

The initial treatment of preference offered by the primary consultant was the use of Scopoderm TTS® transdermal patches. Given that there was an overall reduction in salivary flow, as measured using the saliva swab collection method (White 2007) and no reported adverse side-effects in these three cases an alternative treatment intervention was not sought.

Although there was a positive outcome in the reduction of saliva flow in these three case series, further studies using more participants with multiple diagnoses and using a range of treatment modalities need to be undertaken. Considering the social burden to the affected patients and known associated complications of tracheal suctioning (Fiorentini 1992; Kapadia, Bajan et al. 2000), it is relevant to develop national clinical guidelines to distinguish the types of treatment that are available to manage saliva in patients who have a tracheostomy tube in-situ and to optimise the treatment that are specifically effective.

In conclusion, during treatment intervention using Scopoderm TTS® transdermal patches there was a clinically relevant reduction of saliva in these case series, in adults who had a tracheostomy tube in-situ, with the maximum effect occurring between 1 to 2 weeks post intervention. There was also a reduction in the frequency and need to perform tracheal suctioning in each case and all one-to-one nurses and patients' primary caregivers reported a reduction in saliva as reported on a visual analogue scale (Appendices K, L and M). Additional research is required with a larger sample size and range of treatment modalities to optimise the therapeutic effect of each treatment.

Chapter 6

6 Conclusions

The result of this pilot study indicates that excessive saliva can be successfully managed in tracheostomised patients with the use of Scopoderm TTS® Transdermal patches. This is the first study which has investigated the medical management of saliva in this patient population. Other studies have reported the successful use of botulinum toxin injections into the salivary glands to manage drooling in other patient populations(Jongerius, Rotteveel et al. 2004; Lagalla, Millevolte et al. 2006); however in this study the medical teams did not prescribe the use of botulinum toxin injections as a treatment intervention for these tracheostomised patients.

During Scopolamine TTS® transdermal patches application, a clinically relevant reduction in saliva was achieved in the three patients in this study, demonstrating maximum effect 1- 2 weeks after application. In these three cases there were no reported side-effects and all participants were successfully decannulated from their tracheostomy tube: one-week post data collection in cases 1 and 3 and three-weeks post data collection in case 2. In this pilot study the sample size was very small and all three participants were treated solely with Scopolamine TTS® transdermal patches, as prescribed by their primary consultant. It is recommended that future research implements a multi-site centred study, thus promoting a larger sample size and comparing the use of different interventions at reducing saliva. Furthermore it is important to provide education to the medical teams of the benefits and potential side-effects of each of the intervention options in order to allow informed decision making.

A recent report produced by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD), reviewing the care received by patients who underwent insertion of a tracheostomy tube (Wilkinson, Martin et al. 2014),

explored factors surrounding the insertion and subsequent management of tracheostomy tubes in both the critical care and ward environments by:

• ‘Exploring (percutaneous and surgical) tracheostomy-related complications following insertion in the operating theatre or the critical care unit’

• ‘Exploring remediable factors in the care of adult patients (aged 16 and over) undergoing the insertion of a surgical or percutaneous tracheostomy tube’

• ‘Assessing the number and variability of percutaneous tracheostomies performed annually in the critical care unit’

• ‘Making recommendations to improve future practice’ (Wilkinson, Martin et al. 2014)

However the document does not address or highlight issues related to patients who have a tracheostomy tube in-situ, who present with difficulties in managing excessive pooled saliva or discuss any management options that can be considered in order to aid in the reduction of saliva and reduce the need for tracheal suctioning. This report was undertaken to help identify the difficulties in the pathway of care for patients with a tracheostomy and in various hospital settings and subsequent NCEPOD report produced (Wilkinson, Martin et al. 2014).

There are no national government supported policies or documents that provide guidelines or procedures in the management of excessive saliva and no officially licensed medications to assist in reducing the amount of saliva produced in any patient populations. A larger scale study to investigate the management of saliva in this patient population would assist in developing best practice guidelines and inform healthcare professionals, patients and their families in making informed decisions when addressed with difficulties in the clinical management of saliva.

A Clinical Trial Authorisation (CTA) is required for any clinical trial of an investigational medicinal product (CTIMP) to be conducted in the UK that fall within the scope of the EU Clinical Trials Directive and the Medicines for Human

Use (Clinical Trials) Regulations 2004 (MHRA 2013). The application for a CTA is made to MHRA who are responsible for advising on the Regulations and the requirements for CTA. There are 4 phases of a clinical trial, and a product can only go to the next phase if it has passed the safety and effectiveness tests of the previous one (MHRA 2013). When making an ethics application for a clinical trial the application must specify the phase in which your study lies.

In order to make such an application to ethics for consideration of a clinical trial of an investigational medicinal product an application must be made to the MHRA for an EudraCT number and then this must be included within ethics application form stating in which phase (I-IV) your clinical trial will be (MHRA 2013). The four phases of a clinical trial are listed below and a product can only go to the next phase if it has passed the safety and effectiveness tests of the previous one (MHRA 2013).

Phase I trials, sometimes called first-in-human trials, test a small number of subjects to find out how the treatment works in the body. This type of trial aims to find the lowest dose at which the treatment is effective (the minimum therapeutic dose) and the highest dose at which it can be taken without causing harm.

Phase II trials test the treatment in several hundred people with a given disease or condition. They aim to find out how well the treatment works in larger numbers, identify common side effects, and refine the dose and length of treatment.

Phase III trials typically compare the treatment across several thousand patients to gather more detailed information on how well it works in groups of patients and its safety. The results influence the prescribing and patient information of a medicine once it is marketed.

Phase VI Trials are carried out after a medicine has been licensed and put on the market. These trials are designed to find out more about the long term harms and benefits of a medicine and to discover new uses for it.

Robey (Robey 2004) suggested an adaptation of a five-phase model of clinical-outcome research as a means for structuring forms of clinical research throughout audiology and speech-language pathology. He suggests that the sequence of research tasks are; Phase I for identifying treatment protocols, justifying the enormous expense of extensive clinical testing; Phase II for making all of the preliminary tests and preparations necessary for testing the protocol in a clinical trial; Phase III for conducting a clinical trial to test efficacy; and Phase IV for testing the effectiveness of efficacious treatments. For treatment protocols proving effective, an additional phase of research is required: Phase V for testing the worth of a treatment (i.e., does the obtained value justify the cost of achieving that value?). This interrupted times-series evaluation falls within the domains of a Phase II study (Robey 2004), whereby the research is exploring the dimensions of the therapeutic effect and making the necessary preparations for conducting a clinical trial. Further Phase II studies (Robey 2004) are required with a larger sample size, with patients with varying primary diagnoses, to determine the presence and magnitude of efficacy.

In a report by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD) (Wilkinson, Martin et al. 2014), NCEPOD states in its report that one of its important roles is to ‘provide an amplifier for the professional voices who need to insist to management that training is not an optional extra or a one-off episode. It has to be part of the day to day work of a unit managing these patients’ (Wilkinson, Martin et al. 2014). However it omits an important part of the daily care in managing patients who have a tracheostomy tube in-situ, in providing care and treatment for pooled saliva and potential complications associated with knowledge and practice in clearing aspirated saliva via tracheal suctioning. The report acknowledges that an assessment of the upper airway by a speech and language and the patient’s ability to deal with saliva and therefore

more accurately quantify the risk of aspiration is valuable (Wilkinson, Martin et al. 2014), but does not advise on saliva management options.

The Royal College of Speech and Language Therapists (RCSLT) produced the 'Tracheostomy Competency Framework' (Royal College of Speech and Language Therapists 2014), although the core competencies makes reference to having theoretical knowledge of being aware of use and timing of different instrumental tools (e.g. Fibreoptic Endoscopic Evaluation of Swallowing (FEES), Videofluoroscopy (VFS) to assess laryngeal integrity for phonation, secretion (saliva) management and swallow function, it does not make reference to intervention options in order to manage excessive saliva. Instead the document relates to how able the individual is to swallow their own saliva and the ability of the speech and language therapist (SLT) to identify food / fluid stained secretions in the tracheostomy tube or at the stoma site.

In section 2 of the RCSLT competency document under the core tracheostomy skills it states the importance of training others, which includes members of the multidisciplinary team, the family and the patient. It recommends that training should include the impact of a tracheostomy tube on communication and swallowing, use of one-way / speaking valves and the use of heat moisture exchange (HME) devices. Many of these individuals who have a tracheostomy tube in-situ will be dependent on tracheal suctioning to clear saliva that has fallen into the airway but the report states that 'SLT suctioning is not covered within the scope of this document' (Royal College of Speech and Language Therapists 2014). Without having the knowledge and skills on saliva management options, which have implications for communication and swallowing and will impact on the ability to use one-way / speaking valves and HME devices, the therapist cannot be fully informed and fully achieve these core skills.

6.1 Clinical Implications

Speech and language therapists are asked to assess, diagnose and treat patients who have a tracheostomy tube in-situ and present with associated swallowing difficulties post neurological insult. They are often the professionals who comment on the ability of the patient to safely swallow their saliva and in collaboration with the medical and other allied health professionals if the tracheostomy tube can therefore be closed-off and eventually removed, as it is no longer required for tracheal suctioning to clear aspirated saliva from within the airway. However to date there are no recognised guidelines or policies that directs the medical management of saliva in this patient population or in any other patient populations. Furthermore there are no licensed medications that assist in the medical management of excessive saliva. Most prescribed medications are done so 'off-label' (Blum 2002; Kelly, Gazarian et al. 2005).

There have been several reported studies in the treatment of drooling in people with Parkinson's Disease and in patients with Amyotrophic Lateral Sclerosis by using injections of botulinum toxin into the salivary glands (Bushara 1997; Moller, Karlsborg et al. 2011). These injections have successfully been administered by land-marking the injection site, without the need to use ultra-sound guidance or electromyography and have led to a successful reduction in drooling (Pal, Calne et al. 2000; Ondo, Hunter et al. 2004).

In everyday practice there are regular clinics for patients with Parkinson's disease and associated drooling difficulties, where injections of botulinum toxin are administered to the parotid salivary glands through land-marking, which have proved to be beneficial in reducing drooling. Speaking to a Consultant Maxillofacial Surgeon, who leads one of these clinics in London, she stated that there was high demand for this service and a clinic which was ceased had to be re-instated at the request of patients and their carers.

Although botulinum toxin injections into the salivary glands cannot be considered non-invasive, it is less invasive than surgery and has none to minimal side effects, as do most pharmacologic treatments. As mentioned

above, significant education regarding the benefits versus the potential side-effects needs to occur. The impact on the patient of having the tracheostomy tube ultimately removed, given the known evidence regarding the lack of knowledge and skills in tracheostomy care (Day, Farnell et al. 2002), outweighs the potential side-effects in the majority of cases. It would therefore be beneficial if the multidisciplinary team consider and discuss all treatment options including the potential use of botulinum toxin, especially in this patient population, who already have a tracheostomy tube in-situ, for the main purpose of providing tracheal suctioning to clear saliva that has fallen into their airway, so any transitory, minimal side-effects of dysphagia would not cause further detriment. McGowan et al. (McGowan, Ward et al. 2014) recognised that there appears to be a lack of consistency or guidance and that decision making is not provided in an optimal team environment, despite emerging evidence that tracheostomy teams may enhance patient outcomes (McGowan, Ward et al. 2014). The majority of these patients are also 'nil-by-mouth', not eating and drinking orally, but dependent on tube feeding at level three or below on the functional oral intake scale (FOIS) (Crary, Mann et al. 2005), therefore any transitory, minimal side-effects of dysphagia should not cause further detriment.

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The US Food and Drug Administration (FDA) had received concerning systemic adverse reactions (Food and Drug Administration 2008), including 'respiratory compromise and death', following the use of botulinum toxin. The warning section of the labelling for botulinum toxin products note that important systemic adverse effects, including severe difficulty swallowing and difficulty breathing have occurred in patients with neuromuscular disorders after local injection of typical doses of botulinum toxin. The use of botulinum toxin has increased tremendously in the United Kingdom, not only for use in neurological conditions but predominantly for a variety of cosmetic uses. Concern has been expressed as to who was injecting botulinum toxin, citing Dentists, General Practitioners, and Physiotherapists (The Dystonia Society 2012).

It is recommended that botulinum toxin should only be administered by qualified medical personnel (The Dystonia Society 2012), who have experience in making-up the correct dosages and ability to inject through land-marking into the salivary gland. I believe that while it is essential for speech and language therapists to be knowledgeable regarding botulinum toxin and its uses, allowing them to be able to offer sound advice to patients / primary caregivers and the medical teams, they are not qualified to administer the toxin.

It is hoped that the information contained in this study provides speech and language therapists with information and guidelines regarding treatment options in the medical management of excessive saliva in this patient group.

The aetiology of excessive saliva needs to be carefully considered by the speech and language therapist before a recommendation as to which treatment to consider is made. Primary drooling is caused by an increase in saliva production, which may be associated with inflammation, enlarged adenoids and tonsils, dental caries, mouth infections, specific medications, and oesophageal reflux. Often drooling of this nature can be improved by attending to the primary cause of the drooling. Secondary drooling is due to impaired neuromuscular control and / or sensory dysfunction, which can lead to an accumulation of excessive saliva within the oral cavity. Whether drooling is anterior or posterior (Reddihough, Erasmus et al. 2010) also warrants close examination, as posterior drooling can lead to congested breathing, coughing, gagging, vomiting and occasionally aspiration of saliva into the trachea leading to possible pneumonia (Smith 2008). This may then warrant the insertion of a tracheostomy tube to manage this aspirated saliva.

Factors that can exacerbate drooling, such as poor body and head positioning, poor oral-motor control, and a constantly open mouth need to be considered. Treatment should focus on these areas first before considering any other invasive treatment interventions.

Presently there are no formalised assessment tools or models to determine eligibility and for determining the use of one treatment intervention against

another, for managing excessive saliva or drooling in any patient population. When making an informed decision as to which treatment intervention to prescribe in the management of saliva, information from the case history, provided by numerous professionals, as well as the primary caregivers, needs to be collated before a decision can be made as to which treatment intervention to prescribe (Figure 1).

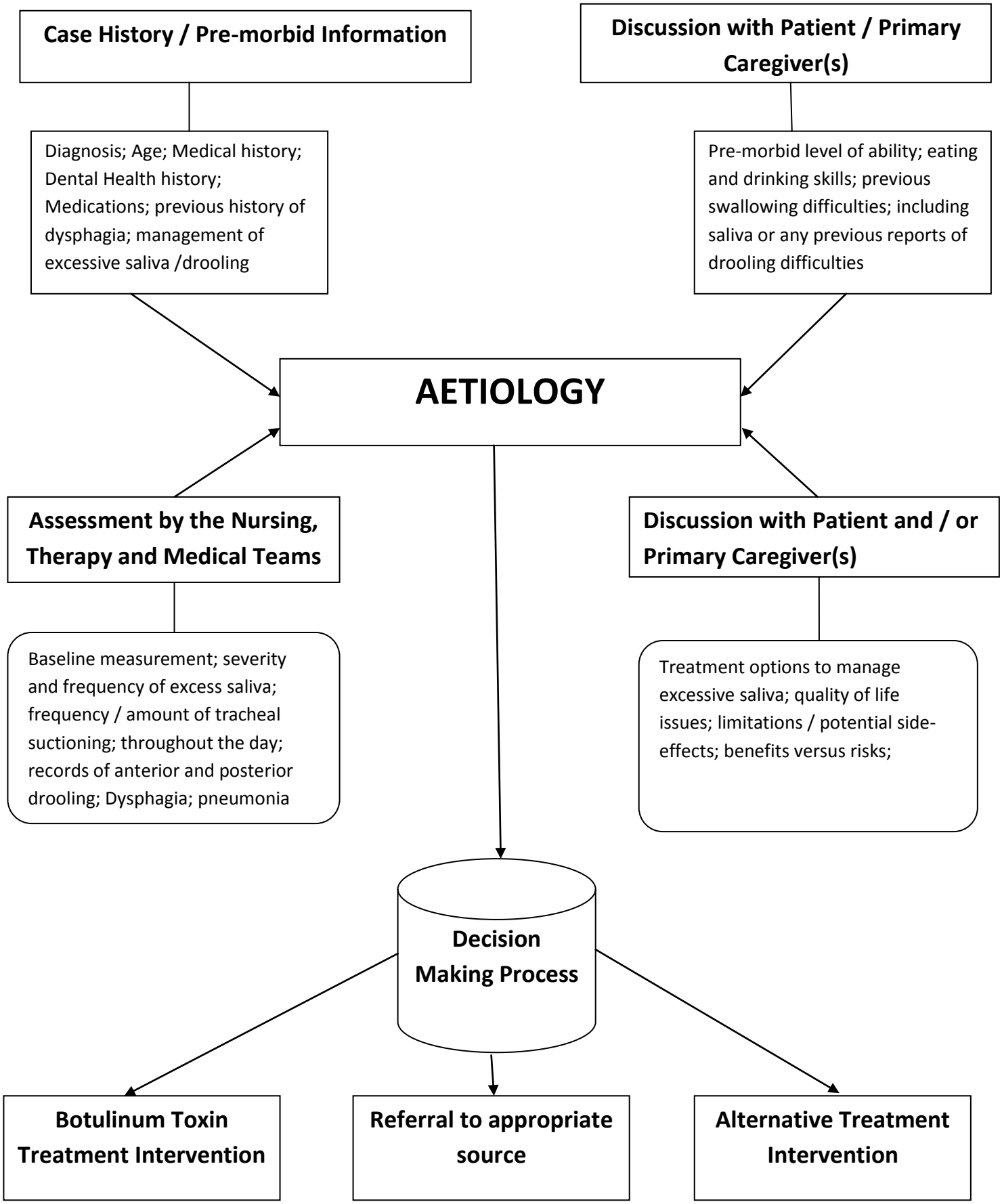

Figure 1 A proposed suggestion for the decision making process in determining treatment intervention for the management of saliva and subsequent drooling

At present no pharmacological interventions (including the use of botulinum toxin or Scopolamine TTS® transdermal patches) are licensed for the management of anterior or posterior drooling (Reddihough, Erasmus et al. 2010). In this study it can be seen that the medical teams preferred the prescription of Scopolamine TTS® transdermal patches over that of prescribing botulinum toxin intra-glandular injections. Several studies have investigated the cost effectiveness of using botulinum toxin for dystonia or spasticity (Jankovic 2004; Esquenazi 2006). The conclusions are that the financial expense involved with botulinum toxin is more than justified when compared to the cost of drugs, physiotherapy or surgery (Jankovic 2004; Esquenazi 2006). Cost effectiveness studies related to the use of botulinum toxin for the management of excessive saliva need to be performed. As can be seen from this study, there was a significant reduction in saliva with treatment intervention using Scopolamine TTS® transdermal patches, which was most effective one to two weeks post intervention; however if treatment using botulinum toxin injections into the salivary glands was administered, the effect may have been more instantaneous and the requirement for the tracheostomy tube for the purpose of tracheal suctioning made redundant, thus leading to quicker removal of the tracheostomy tube and negating the need and associated costs for one-to-one nursing care. So ultimately the use of botulinum toxin could possibly provide numerous benefits, one of which could be reduced overall costs through the removal of one-to-one specialist nursing and, improved quality-of-life, post removal of the tracheostomy tube (Gilony, Gilboa et al. 2005).

6.2 Quality of Life / Patient Well-Being

One of the aims of reducing saliva in this patient population is to reduce the need to perform tracheal suctioning, which is known to be associated with varying levels of bad practice (Day, Farnell et al. 2002). Although at this stage there are few studies and little known about the relationship between having a tracheostomy tube in-situ and tracheal suctioning and patients / carers perceptions, it is known that patients who have a tracheostomy tube have

significantly reduced life-satisfaction and body-image perceptions (Gilony, Gilboa et al. 2005). Thus by assisting in the successful closure and ultimate removal of the tracheostomy tube, patients may show improvements in their body-image perceptions, life-satisfaction and reduce any secondary complications associated with mal-practice related to tracheal suctioning (Figure 2).

In all three case reports all primary caregivers reported that the “tracheostomy tube causes me concern”, and the statement “I get scared when I require suctioning via the tracheostomy tube”, and rated these statements in the tracheostomy tube self-perception survey as being ‘very much true’ throughout the study from pre-intervention until the end of data collection at 12-weeks post-intervention (Appendices K, L and M). All caregivers rated in the self-perception survey that “having a tracheostomy tube in-place makes me feel sad” and the statement, “I’ve been discouraged by having a tracheostomy tube” as either ‘very much true’ (cases 2 and 3) (Appendices L and M) or ‘quite a bit true’ (case 1) (Appendix K). In cases 2 and 3 it was indicated ‘very much true’ a sense of “feeling frustrated” throughout the study (Appendices L and M), whereas in case 1, this was recorded as ‘somewhat true’ throughout the study (Appendix K). The difference may have been related to the fact that the participant in case 1 was far less dependent than in cases 2 and 3, with a higher Glasgow Coma Scale (Teasdale and Jennett 1974) and was more awake, with his eyes open. All three participants had their tracheostomy tube successfully removed once data collection had ceased at post 12-weeks intervention. In cases 1 and 3 this was after one-week post data collection and three-weeks post data collection in case 2. In each case participants required routine tracheal suctioning to clear any coughed sputum from within the tracheostomy tube and needed to be able to have their tube closed for a full 24-72 hours, before considering removal, this did not occur until the end of data collection in cases 1 and 3 and two-three weeks after data collection in case 2. They were not asked to complete a questionnaire post removal of the tracheostomy tube, which would have been a useful comparator, to see if there had been changes in their responses.

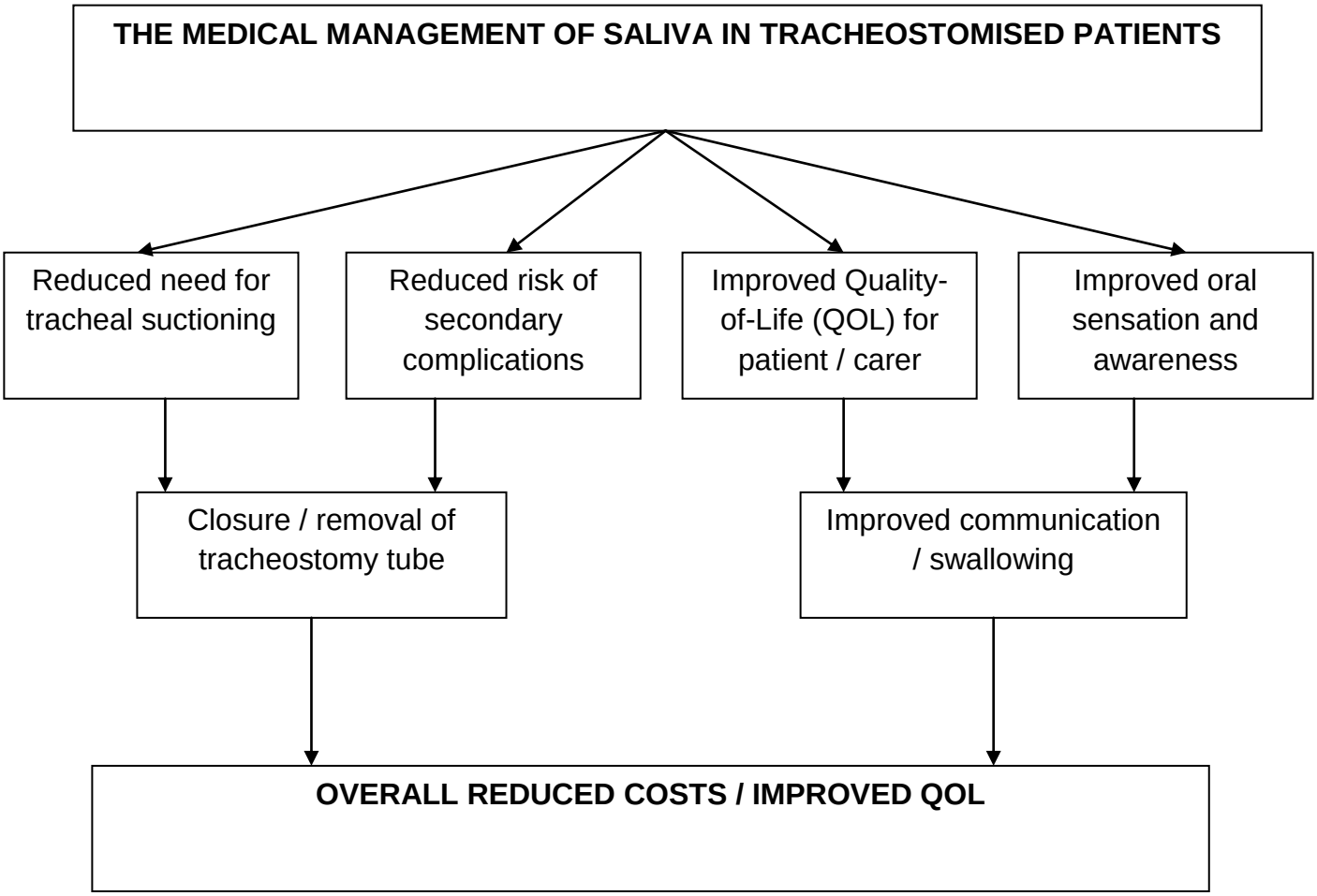

Figure 2, possible benefits as a result of effectively managing excessive saliva in tracheostomised patients

6.3 Research Implications

The results of this study have highlighted several areas for further research, which includes further Phase II type studies (Robey 2004) with larger numbers of participants, determining the presence and magnitude of efficacy of the intervention and any associated side-effects. Likewise a replication of the study with larger numbers of participants categorised with a number of different primary diagnoses and severity of injury as indicated by their GCS score (Teasdale and Jennett 1974), age, sex and baseline ratings of saliva would be beneficial and help determine if there is a relationship between efficiency of

response to either of the treatment interventions. Furthermore trends relating to diagnoses, age and severity of injury can be grouped and effectiveness of one treatment intervention against that of another can be compared.

6.4 Limitations of the Study

In this study the 'swab' method (White 2007) for collecting saliva was utilised, but due to the presentation of the participants the swabs could not be safely placed within the intra-oral cavity, because of the risk of either having the swab falling into their airway, or being unable to retrieve the swab, as a result of the participant having a bite-reflex response to items being placed onto their tongue. Future studies may wish to use alternative methods of saliva collection, which allows collection of saliva from within the intra-oral cavity. This might include collecting drooled saliva through the use of collection cups and/or measuring the 'wetness' of bibs as a result of drooling.

During this study all patients continued to receive speech and language therapy intervention, in conjunction with the prescribed Scopolamine TTS® transdermal patches treatment. During this study none of the interventions were withdrawn and participants continued to receive therapy alongside the medical treatment, but in order to be sure it was solely the prescribed Scopoderm TTS® transdermal patches intervention that related to a reduction in saliva, future research may want to consider a control group, that receives neither of the treatment interventions, or a placebo intervention, which then compares outcomes, with and without therapy intervention. Alternatively a study that adopts a within-subject design, where each participant receives one treatment and then the next treatment, with a washout period between each treatment could be used.

The primary swab readings were collected and made by the primary investigator and future research may wish to use independent individuals who collect and record the weight of the saliva collected, who are 'blinded' to the intervention treatment, thus avoiding any possible bias. In this study 'swab' recordings were taken at three specified time-points across a 12-hour period, a

larger number of readings across a 24-hour period may have resulted in differing trends of saliva throughout the day and throughout the night-time (Dawes 1974) and future studies may wish to take this into consideration.

In this study the same one-to-one nurse who provided tracheal suctioning was asked to record the reason for administering tracheal suctioning each time it was performed, but no official training was given, other than a list of most-common reasons to provide tracheal suctioning. This might have biased the nurse into recording why they provided suctioning, whereas not being as prescriptive and withdrawing a list of reasons, allowing the nurse to cite why it was performed may have been a better indicator as to why tracheal suctioning was administered.

All patients within this study were in a low-awareness state, with varying degrees of consciousness (Teasdale and Jennett 1974), it is suggested that future research, uses a wider cohort of patients with differing primary diagnoses and presentation, so that this would enable not only the primary care-givers to respond to questions relating to the tracheostomy tube, but also allow those patients who are not in a low-awareness state to also respond.

There is no universal scale to clinically measure the amount of excessive saliva, or classification of what constitutes mild, moderate or severe anterior or posterior drooling of saliva (Reddihough, Erasmus et al. 2010), but this is just an objective clinical judgement, which clinicians refer to as copious amounts or large amounts of saliva in this patient population. It would be advantageous to have a scale that clinicians and medical teams can use with inter-rater reliability to classify and grade amounts of excessive saliva. In this study the use of a small sample prevents generalisation to the wider population.

When statistically analysing the data, linear regression was used with the assumption that there was a linear relationship between the two variables, which were a reduction in saliva over time, post intervention, which in all three case reports there was; however in a larger study there may be other confounding variables, such as medications that may increase or decrease

saliva flow (Allergan 2015; Novartis Consumer Health UK Ltd 2016), which may result in a non-linear relationship, in which case linear regression analysis cannot be utilised. In these three case reports participants were not on any known prescribed medications that are known to induce saliva flow or cause hypersalivation. Due to small numbers in this study, the participants could not be grouped to analyse across diagnoses or compare against ages and outcomes. A larger multicentre study with greater numbers of participants, presenting with a range of differing variables, such as age and diagnoses, in which participants can be grouped, would allow for wider analysis and generalisation of findings to be applied.

6.5 Concluding Remarks

There is every indication to suggest that there is more research required investigating the medical management of saliva in patients who have a tracheostomy tube in-situ. The current medical management options for the treatment of excessive saliva in everyday practice have been shown to be very limited. Although the use of botulinum toxin injections into the salivary glands to reduce drooling in neurologically impaired patients has been shown to be effective (Porta, Gamba et al. 2001), there appears to be some reluctance in its application in this patient population. It is important that medical teams and allied health professionals are fully aware of all treatment options available in the medical management of saliva in patients who have a tracheostomy tube in-situ, thus enabling the patient, their carers and the treating team to make an informed decision as to which intervention to prescribe.

Given the known secondary complications associated with having a tracheostomy tube in-situ (Beards and Nightingale 1994) and evidence that supports the lack of knowledge and skills in providing tracheal suctioning (Day, Farnell et al. 2002), it would make clinical sense to assist in successfully aiding in its removal as soon as is possible, by effectively managing the excessive saliva and making the need for tracheal suctioning redundant thus allowing the tube to be closed-off and ultimately removed. This would not only be cost-

effective, but improve the quality of life, not only for the participants, but also for their primary caregivers.

If the judicious use of prescribed drugs are to be extended to treat excessive saliva and be licensed for this use, all stakeholders, from pharmaceutical companies, hospitals, medical aids and government need to work collaboratively to issue policies, procedures and national guidelines in its use in this patient and wider patient population.

Whilst I am aware of the expense and the tremendous hurdles needed to make this happen, the use off-label drugs (Blum 2002; Kelly, Gazarian et al. 2005) in managing excessive saliva in patients who have tracheostomy tube in-situ may help in minimising the event of any secondary complications (Beards and Nightingale 1994) associated to mal-practice in tracheal suctioning in caring for patients who have a tracheostomy tube and in-turn reduce the need for one-to-one care in a specialised setting, thus in the longer-term driving down overall costs.

In this study pharmacological intervention was administered with the use of Scopoderm TTS® transdermal patches in the medical management of saliva in tracheostomised patients and was shown to significantly reduce saliva in all participants. There was also a significant reduction in the need to perform tracheal suctioning in all cases and a reported reduction in the amount of saliva, as reported by both the same one-to-one nurse special and the patient's same caregiver on a visual analogue scale. Further research needs to be conducted comparing the using a range of differing interventions in the medical management of saliva in tracheostomised patients. These interventions might include the use of other anticholinergic medications and the use of botulinum toxin to reduce saliva flow in this patient population and determining the most effective treatment, monitoring for the presence and severity of any potential side-effects of each intervention, in the immediate and longer-term, ensuring that follow-up is provided, even after successful decannulation (removal) of the tracheostomy tube.

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8 Appendices Contents Page[2]

[2] All appendices found within attached compact disc (CD).