MENZIES SCHOOL OF HEALTH RESEARCH

Evaluation of a Comprehensive Case Management Support Program for the Prevention of Hearing Loss Associated with Otitis Media with Perforation in Indigenous Children

FINAL REPORT

for the

Office of Hearing Services
Department of Health and Ageing

JULY 2013

Evaluation of a Comprehensive Case Management Support Program for the Prevention of Hearing Loss Associated with Otitis Media with Perforation in Indigenous Children

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Project funded by the Office of Hearing Services, Australian Government Department of Health and Ageing, Australian Capital Territory

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PROJECT 1: IHEAR BETA Study: The Indigenous Healthy Ears- Betadine, Tissues and Antibiotics study. A randomised controlled clinical trial (NHMRC proposal).

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PROJECT 2: Text messaging to improve treatment and follow-up in chronic conditions: A Systematic Review of evidence applicable to disadvantaged populations (to be submitted as a paper for publication).

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PROJECT 3: Can mobile phone MMS and text messages improve clinic attendance for Aboriginal children with chronic otitis media?: a randomised controlled trial (to be submitted as a paper for publication).

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PROJECT 4: Prevalence study of children with otitis media living in regional and remote Northern Territory

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EXECUTIVE SUMMARY

Background

Aboriginal children in the Northern Territory have the highest reported rates of acute and chronic ear infections in the world, with severe otitis media being one of the most important health problems. Subsequently, 50-80% of Aboriginal children living in the remote Northern Territory are likely to have significant hearing loss; a condition which leads to learning difficulty and social problems in an already disadvantaged population. Chronic suppurative otitis media (CSOM) is present when the middle ear infection causes pus to drain from the ear for periods greater than 6 weeks (and often years). This severe infection causes progressive (and often permanent damage) to the tympanic membrane. It also has the greatest impact on hearing. For Aboriginal children in the NT, the early stage of onset (and the persistent nature of this infection) means that early intervention, ongoing effective medical management, and monitoring of the disease are critically important.
Commonwealth funding was provided to the Ear Health Unit of the Child Health Division of the Menzies School of Research to conduct 4 projects. All the projects are related to achieving more effective treatment, management and monitoring of chronic suppurative otitis media (CSOM) in Aboriginal children living in remote Northern Territory.

These projects include:

1. The design of a randomised controlled clinical trial with the primary aim of determining the beneficial effects of additional antiseptic syringing and oral antibiotic treatment in children with chronic suppurative otitis media (*NHMRC proposal*).
2. A Systematic Review of the literature surrounding mobile text messaging, and its effect on treatment and follow up in people with chronic conditions (*paper for publication*).
3. A randomised controlled trial exploring whether multi media phone messages/text messaging can improve clinical attendance for children with otitis media (*paper for publication*).
4. Gathering of prevalence data of children with otitis media living in regional and remote Northern Territory (*surveillance data to inform delivery of services and research priorities*).

Project 1: IHEAR BETA Study: The Indigenous Healthy Ears - Betadine, Tissues and Antibiotics study. A randomised controlled clinical trial (NHMRC proposal).

Background/Hypothesis:

Otitis media remains unacceptably common, as well as severe, in Aboriginal children. The World Health Organization recommends that rates of otitis media in excess of 4% should be regarded as a massive health problem. In some remote communities of the Northern Territory, more than 30% of children are affected.

Although there is a considerable amount of published research on the treatment of otitis media, most of the recommendations are still limited by a lack of relevant randomised controlled trial data.

Aim:

The major aim of this randomised controlled trial is to explore the effectiveness of:

a) Providing a new antiseptic treatment for otitis media in addition to the standard antibiotic treatment (compared to standard treatment alone)
b) Providing a twice daily antibiotic treatment in addition to the standard antibiotic treatment (compared to placebo)

Application:

Current treatment options are based on evidence from well designed studies and are described in the most recent Office of Aboriginal and Torres Strait Islander Health Clinical Practice Guidelines. During the update process, the need for better evidence on the impact of betadine ear washes and oral cotrimoxazole were identified as research priorities. In this proposed randomised controlled trial, effectiveness of treatment will be determined by detailed clinical and laboratory examination.

The study meets the goals of the 'Close the Gap' initiative in Indigenous health that identifies hearing health in the Northern Territory as a priority. Better evidence on the effectiveness of treatments for chronic suppurative otitis media is urgently needed. This proposed study would represent an important addition to the literature on medical management for this condition.

Project 2: Text messaging to improve treatment and follow-up in chronic conditions: A Systematic Review of evidence applicable to disadvantaged populations (paper for publication).

Background:
Aboriginal people living in remote Northern Territory communities experience extreme disadvantage. High levels of stress, household overcrowding, poor housing and a range of other factors related to poverty lead to young children within these communities experiencing a high burden of recurrent acute and chronic infection. The need to identify strategies that promote treatment adherence, within this context, is urgent.

Aim:
This systematic literature review investigates whether regular Short Message Service or Multi-Media Messaging service, sent via mobile telephone, leads to improved treatment adherence and attendance of follow-up review among carers of children with a chronic disease.

Findings:
Following a process developed by the National Health and Medical Research Council for Systematic Reviews, literature since 1999 was examined. Of the initial 890 titles extracted, 31 studies were considered eligible for review. Of these, 6 studies were considered in more detail. Only one eligible study included children, and none included Indigenous participants. The search identified no research concerning the use of Media Messaging Service to promote adherence to treatment.

Conclusion:
From the limited evidence available, it appears that Short Message Service messaging should be seen as only one component of a multifactorial intervention to promote adherence to treatment regimes and follow-up. The existing relationship with the health service provider, as well as patient and family preferences, also require consideration. Characteristics of the actual messaging must be taken into account and should be developed in partnership with community members.

Project 3	**Can mobile phone MMS and text messages improve clinic attendance for Aboriginal children with chronic otitis media?: a randomised controlled trial (paper for publication).**

Background:

Otitis media is a chronic condition largely affecting children. Poor adherence to treatment often results in associated hearing loss, which has a significant effect on a child's language, education and social outcomes.

Aim:

This study is the first randomised trial in remote Australian Indigenous settings to evaluate the use of mobile phone multimedia and text messaging intervention for carers of children with otitis media in order to promote ear health through increased clinic attendance and adherence to treatment.

Method:

The study took place over a 6 week period in two remote Indigenous communities in the Northern Territory. Both communities have a medical clinic with a full time doctor as well as nurse and/or Aboriginal health worker. After randomisation, the intervention group received multimedia messages in two Indigenous languages, reminding the carers about the importance of ear health. They also received short text messages, in English, recommending weekly clinic visits for ear check-ups and treatment reviews.

Conclusion:

There was no significant improvement in clinic attendance or ear health outcomes between those receiving messages and those not receiving messages. The media and text messaging were accepted by Health Workers and carers as a mode of communication. This study has demonstrated the potential of this medium as a tool in the management of chronic disease in remote and disadvantaged populations.

Project 4	**Prevalence data of children with otitis media living in regional and remote Northern Territory (surveillance data)**

Background:

The most recent report of extremely high rates of otitis media (90%) and tympanic membrane perforation (24%) in Aboriginal children in the Northern Territory was published in 2006. These data were collected in 2001 by the trained research nurses from the Menzies School of Health Research using accepted definitions and recommended diagnostic tests (pneumatic otoscopy, tympanometry and video-otoscopy).

In 2008, the Commonwealth's Emergency Response Child Health Check Initiative reported a lower rate of otitis media in children (30%, n=3463) aged 0-5 years. These data were collected by general practitioners employed on short term contracts. The definitions used for each of the diagnostic categories were not clear. Most assessments were by simple otoscopy. The use of more objective diagnostic tests was not recorded.

Aim:

To update the most recent prevalence data for otitis media in children living in remote Aboriginal communities.

Findings:

Between 2008-2010, the Menzies School of Health Research monitored otitis media in children 0-5 years. Following the introduction of conjugate pneumococcal vaccination, surveys of 29 communities found similar rates of otitis media (90%) to that of the 2001 findings. The data were very similar for children aged 0-30 months and 0-5 years. In some communities, tympanic membrane perforation rates were more than 30%. Over the three year period there was no significant change in rates for all types of otitis media. The rate of CSOM was documented to be less in 2010 although this change was not statistically significant. Further surveillance with larger numbers of children will be required to clarify this issue.

Conclusion:

Otitis media remains a significant health problem in children aged 0-5 years of age in the remote Northern Territory. While the overall rate of otitis media is not decreasing, there is possibly a modest decrease in CSOM over time. Further surveillance with larger numbers of children will be required to confirm this. The difference in the overall prevalence of otitis media between previous research studies and the Emergency Response Child Health Check Initiative is likely to reflect different assessment methods and inclusion of children from outside remote Aboriginal communities in the Child Health Check Initiative.

SUMMARY

The four projects have been conducted by the Menzies School of Health Research Ear Health Team as part of their broader research program. The focus on chronic suppurative otitis media (CSOM) is appropriate. CSOM remains the most disabling form of otitis media and it continues to present a major challenge to Australian Aboriginal families and their health care providers. Unfortunately, there is a lack of high quality research addressing this condition. Project 1 has resulted in a NHMRC funding submission for the largest randomised trial of treatment for CSOM in Aboriginal children. The treatments to be tested are both identified as research priorities by the experts contributing to the Technical Advisory Group of the updated Clinical Care Guidelines. The development of the funding application is a critical first step in linking high quality research studies to better clinical practice in remote Aboriginal communities.

Projects 2 and 3 have addressed the potential role of mobile phones in improving health outcomes for Aboriginal children with CSOM. The systematic review identified a small number of trials that were conducted in different populations and addressed different conditions. While the results were encouraging, further high quality research will be needed. Project 3 describes the first randomised controlled trial involving Australian Aboriginal families. The study demonstrated that text and MMS messages are acceptable to Aboriginal families from 2 remote Aboriginal communities. However, use of these messages did not substantially improve clinical practice.

Project 4 has provided the latest data on the burden of CSOM in a range of Aboriginal communities in the Northern Territory. Unfortunately, the very high rates of all forms of otitis media persists. The good news is that the data are consistent with a reduction in the overall rates of CSOM in young children. This information, along with current evidence-based treatment recommendations and training, is disseminated to remote community staff by the Menzies Ear Health team and the visiting Northern Territory Government Tele-Otology Outreach Team. Project 4 also highlights the importance of diagnostic accuracy in studies reporting the prevalence of all forms of otitis media. Large differences in estimates of burden of disease are possible if different methods of diagnosis are used. For high risk Aboriginal children, there is a need for a consistent diagnostic approach that utilises appropriate technology (tympanometry and video otoscopy) in order to ensure estimates of burden of disease are not misleading.

CSOM in remote Aboriginal communities is essentially a disease of poverty. While improvements in the social determinants of health are likely to be beneficial, better primary health care is needed to minimise the impact of this disease on children who have already been affected. These projects have contributed important new information about the current burden of disease and identified some important opportunities for better health in the future.

FINAL REPORT

Evaluation of a Comprehensive Case Management Support Program for the Prevention of Hearing Loss Associated with Otitis Media with Perforation in Indigenous Children

INTRODUCTION

Aboriginal children in the Northern Territory have the highest reported rates of acute and chronic ear infections in the world, with severe otitis media being one of the most important health problems.[1-4] Subsequently, 50-80% of Aboriginal children living in the remote Northern Territory are likely to have significant hearing loss;[5-6] a condition which leads to learning difficulty and social problems in an already disadvantaged population. Chronic suppurative otitis media (CSOM) is present when the middle ear infection causes pus to drain from the ear for periods greater than 6 weeks (and often years). This severe infection causes progressive (and often permanent damage) to the tympanic membrane. It also has the greatest impact on hearing.[6] For Aboriginal children in the NT, the early stage of onset (and the persistent nature of this infection) means that early intervention, ongoing effective medical management, and monitoring of the disease are critically important.[7]

Chronic suppurative otitis media (CSOM) is the most disabling ear disease affecting Aboriginal Australians.[8] Children with pus draining from their ears are common in rural and remote communities. The early age of onset, the severity of the hearing loss, and the persistence of this infection, mean that improving medical management for this condition is a priority. Once CSOM has become established, it is extremely difficult to treat. While topical antibiotics have been shown to be more effective than oral antibiotics and topical antiseptics, it is unclear whether there are any benefits of combining these treatments.[9,10] Other treatment options, such as prolonged antibiotic intravenous treatment in hospital[11,12] or partial mastoidectomy have not been used (or accepted) in the management of children from remote Aboriginal communities.

Commonwealth funding was provided to the Ear Health Unit of the Child Health Division of the Menzies School of Health Research to conduct 4 projects. All the projects are related to achieving more effective treatment, management and monitoring of chronic suppurative otitis media (CSOM) in Aboriginal children living in remote Northern Territory.

The projects were informed by previous studies and surveillance data collected by the Menzies School of Health Research and the development of the updated Office of Aboriginal and Torres Strait Islander Clinical Practice Guidelines on the Management of Otitis Media.[13] The projects covered the design of a new randomised controlled trial testing the impact of 2 additional treatments of chronic suppurative otitis media, the evidence for health benefits from use of mobile phones, text messaging and SMS messaging in disadvantaged settings, the impact of text messaging and SMS messaging on the management of chronic suppurative otitis media in 2 remote Aboriginal communities, and updated surveillance data on all forms of otitis media in remote communities of the NT.

The projects represent an important part of the Menzies Ear Health Research Program over the past 4 years. The projects are also likely to have major impact on future research activities through funding of intervention studies for CSOM and provision of high quality evidence on the use of text and SMS messaging in health care. As mobile phones become an even more important part of life in remote Aboriginal communities, the significance of these projects is likely to increase.

PROJECT REPORTS

Project 1 IHEAR BETA Study: The Indigenous Healthy Ears - Betadine, Tissues and Antibiotics study. A randomised controlled clinical trial (NHMRC proposal).

SUMMARY

Background/Hypothesis:

Otitis media remains unacceptably common, as well as severe, in Aboriginal children. The World Health Organization recommends that rates of otitis media in excess of 4% should be regarded as a massive health problem. In some remote communities of the Northern Territory, more than 30% of children are affected.

Although there is a considerable amount of published research on the treatment of otitis media, most of the recommendations are still limited by a lack of relevant randomised controlled trial data.

Aim:

The major aim of this randomised controlled trial is to explore the effectiveness of:

1. Providing a new antiseptic treatment for otitis media in addition to the standard antibiotic treatment (compared to standard treatment alone).
2. Providing a twice daily antibiotic treatment in addition to the standard antibiotic treatment (compared to placebo).

Application:

Current treatment options are based on evidence from well-designed studies and are described in the most recent Office of Aboriginal and Torres Strait Islander Health Clinical Practice Guidelines. During the update process, the need for better evidence on the impact of betadine ear washes and oral cotrimoxazole were identified as research priorities. In this proposed randomised controlled trial, effectiveness of treatment will be determined by detailed clinical and laboratory examination.

The study meets the goals of the 'Close the Gap' initiative in Indigenous health that identifies hearing health in the Northern Territory as a priority. Better evidence on the effectiveness of treatments for chronic suppurative otitis media is urgently needed. This proposed study would represent an important addition to the literature on this issue.

The study meets the goals of the 'Close the Gap' initiative in Indigenous health that identifies hearing health in the Northern Territory as a priority.

Project Grant Application

AIMS

The primary research questions are:

Among Aboriginal children with chronic suppurative otitis media (CSOM), does either of the following strategies reduce the proportion of children with discharging perforations after 16 weeks of treatment?

(i) Twice daily antiseptic ear wash (>= 20mls povidine-iodine 0.5% solution syringed into the ear canal) prior to standard topical antibiotic treatment (compared to standard topical antibiotic treatment alone),

(ii) Twice daily oral antibiotic treatment (cotrimoxazole 4mg/kg per dose of trimethoprim component) given in addition to standard topical antibiotic treatment (compared to placebo).

Secondary aims:

Prevalence of CSOM: To describe the prevalence of severe otitis media (chronic suppurative otitis media- CSOM and dry perforation) in large Aboriginal communities in the Northern Territory.

Microbiology of CSOM: To describe the prevalence and antibiotic susceptibility of bacteria cultured from nasopharyngeal and ear discharge swabs in children with CSOM.

Clinical course of CSOM: Using clinical databases with video-otoscope images, tympanometry and audiology data, we will document the clinical course of CSOM over a 12 month period.

BACKGROUND

Aboriginal children in the Northern Territory (NT) have the highest reported rates of acute and chronic ear infections in the world.[1, 2] Severe otitis media is one of the most important health problems affecting young Aboriginal children in Australia today.[3, 4] The impact of the illness is compounded by its effects on hearing. Overall, 50-80% of young Aboriginal children living in remote NT communities are likely to have significant hearing loss.[5, 6] Of all forms of ear disease, children diagnosed with CSOM had the highest levels of hearing loss at 83%. Over 60% of these children have bilateral hearing loss.[6] While effective timely treatment of acute otitis media with perforation (AOMwiP) aims to prevent CSOM, the challenges involved in delivering appropriate treatment in remote settings mean that a large group of children develop chronic severe ear disease.[7]

Chronic suppurative otitis media (CSOM) is the most disabling ear disease affecting Aboriginal Australians.[8] Children with pus draining from their ears are common in rural and remote communities. The early age of onset, the severity of the hearing loss, and the persistence of this infection, mean that improving medical management for this condition is a priority. Once CSOM has become established, it is extremely difficult to treat. While topical antibiotics have been shown to be more effective than oral antibiotics and topical antiseptics, it is unclear whether there are any benefits of combining these treatments.[9, 10] Other treatment options, such as prolonged antibiotic intravenous treatment in hospital[11, 12] or partial mastoidectomy have not been used (or accepted) in the management of children from remote Aboriginal communities.

The recent clinical care guidelines for the management of otitis media, distributed by the Office of Aboriginal and Torres Strait Islander Health, (the 'OATSIH Guidelines') used a transparent and comprehensive search strategy to identify all high quality treatment studies.[13] An expert writing group (Darwin Otitis Guidelines Group) and advisory group (Technical Advisory Group) used this evidence to inform all recommendations. Although there is a considerable amount of published high quality research on otitis media, most of the treatment recommendations were still limited by the lack

of relevant randomised controlled trials (RCTs). Importantly, the guidelines emphasised the need for more effective strategies for managing CSOM where the lack of appropriately designed RCTs was most evident.[13] This research project will address the 2 medical treatment options with most significant variation in current clinical practice.

Summary of important background information

- Otitis media (OM) remains unacceptably common and severe in Aboriginal children. In April 2009, the Federal Government committed another $58 million over 4 years to help address the very high rates of chronic ear and eye disease affecting Indigenous Australians. This is in addition to the many millions spent on ear surgery for children identified through the NT Emergency Response. A substantial amount of this funding has been spent on interventions of unknown effectiveness.

- In NT communities, AOMwiP frequently leads to CSOM. In some communities more than 50% of young children are affected. The last reliable CSOM prevalence data were collected in 2001-3.[14]

- The World Health Organization recommends that rates of CSOM in excess of 4% be regarded as a massive public health problem.[15]

- While quinolone antibiotics (e.g. ciprofloxacin) are theoretically more active against the bacteria commonly associated with CSOM (*Pseudomonas aeruginosa*), they have failed to eradicate all pathogens involved (particularly *Staphylococcus aureus*) . There are no large studies describing the microbiology of CSOM in Aboriginal children.

- The only Randomised Controlled Trial (RCT) in Aboriginal children to describe a treatment that was effective in the majority of children with CSOM used the combination of povidine-iodine ear washes followed by ciprofloxacin ear drops.[16] There were important differences in the severity of disease in these children compared to those currently living in remote communities of the NT.

- Children with CSOM in the NT are often treated with oral antibiotics. In our most recent CSOM study, 75% of children who sought clinical care were prescribed amoxicillin.[17] It is unclear whether this is ever indicated.

Antiseptic Ear Washes:

The OATSIH Guidelines define CSOM as present when discharge has persisted for at least 2 weeks.[13] The progression from AOMwiP to CSOM is associated with secondary infection with a range of bacteria that are much less susceptible to commonly used antibiotics (*Pseudomonas*, *Staphylococcus*, *Proteus*, and *Klebsiella* species) than those present in acute otitis media (AOM).[18] Previously the OATSIH Guidelines recommended that topical antibiotics alone (after cleaning by dry mopping) be first line therapy. The revised guidelines have acknowledged that there is a lack of evidence for the effectiveness of combining antiseptic ear washes and topical antibiotics. The guidelines now state "Clean the ear canal by using twisted tissue paper (dry mopping) or syringing with dilute betadine (1:20)….-Level IV evidence".[13, p21] While the expert writing group reached consensus on this recommendation, we did not identify any controlled studies assessing the impact of antiseptic ear washes.

In support of this treatment option, recent studies have documented the presence of aggregates of microorganisms (biofilm) in the middle ear of Aboriginal children with CSOM.[19-21] In Western Australia (where antiseptic ear washes prior to insertion of antibiotic drops is standard treatment) it is proposed that the ear washes disrupt the biofilm. As a consequence, the mucosal infection may

become more receptive to topical antibiotic treatment. While this approach has been used and reported in one clinical trial, there is little other supporting evidence available.[16] Couzos et al reported using gentle syringing with dilute povidine-iodine (0.5%) and dry mopping until the tympanic membrane (TM) was clear of pus before applying antibiotic ear drops in their RCT. Both the comparison groups (ciprofloxin versus Sofradex®) received the antiseptic ear washes, so its impact could not be assessed. However, this trial described very high cure rates: 76% of children in the ciprofloxacin group compared to 54% in the Sofradex group had dry ears after 9 days of treatment.[16] In comparison, a study conducted in remote NT community schools (comparing the same two topical antibiotic drops but without any ear wash) found only 14% in the ciprofloxacin group with dry ears at the 12-28 week follow up.[22] The only other randomised trial to assess povidone iodine solution compared a more concentrated solution (5%) (given as topical ear drops) with ciprofloxacin drops. This study of 40 patients with CSOM did not find any difference between these 2 approaches (with 90% of both groups achieving dry ears by the 4 week follow up).[23]

Currently, there is very little information on how often antiseptic ear washes are used even when they have been recommended. In the NT, the impression to date has been that ear washes increase Health Worker involvement, require more effort on the part of families, are technically difficult, and are messy. All of these factors may affect adherence. However, if this approach increased the proportion of children with dry ears by 20%, it would be supported by primary health care staff. We will be using aqueous povidine-iodine, which does not carry the ototoxicity risk that comes with alcohol-based povidine-iodine formulations.

Oral antibiotic treatment:

The revised OATSIH Guidelines now state "Treatment with oral antibiotics (eg. quinolones) is not recommended routinely for CSOM. Oral antibiotics are usually less effective than topical treatment- Level 1 Evidence".[13] While the expert writing group reached consensus on this recommendation, we did not make a specific recommendation on the addition of oral antibiotics to topical antibiotic treatment. A small study in adults found no benefit from the addition of oral ciprofloxacin to topical ciprofloxacin treatment.[24] Another small study found that oral amoxicillin plus topical chloramphenical was not as effective as topical ciprofloxacin treatment.[25] However, the only placebo-controlled trial found the addition of cotrimoxazole to topical aminoglycoside treatment reduced persistent discharge from ~50% to ~30% after 6 and 12 weeks of treatment.[26]

Our previous randomised trial comparing topical treatments for CSOM found that *Staphylococcus* species were the commonly isolated pathogens in ear discharge after treatment (present in 75% of specimens).[22] In the Top End of the NT, around 20% of community acquired staphylococcal infections are resistant to methicillin (MRSA) and 20-30% of the remote community population is colonised. Cotrimoxazole is recommended oral therapy for children with suspected community acquired MRSA infection. Our microbiological work has also documented the importance of ongoing non-typable *Haemophilus influenzae* (NTHi) infection of the middle ear discharge. In our most recent CSOM study, the following pathogens were isolated from ear discharge: NTHi 68%, pneumococcus 3%, *S.aureus* 24%, and *Pseudomonas* 37%.[17] Dense nasopharyngeal colonisation may contribute to recurrent exacerbations of CSOM, and suggests a potential role for oral antibiotics. The Dutch trial found that cotrimoxazole reduced the isolation of *Haemophilus* (and pneumococcus and *Moraxella*) in ear discharge.[26] Isolation of *Pseudomonas* was not affected.

Oral cotrimoxazole is a cheap, safe, and widely used antibiotic that is effective in the treatment and prevention of acute otitis media.[27] It provides good theoretical coverage of the range of organisms associated with CSOM in children. It also has the advantage that it comes in ready-made suspension and does not require refrigeration (a major challenge in settings where many families do not own a fridge).

We have chosen a treatment period of 16 weeks for several reasons. The largest RCT of CSOM treatment in African children found the greatest beneficial effect at this time point. This study

reported persistent discharge in 50% of children receiving cleaning plus topical antibiotics versus 80% in those receiving cleaning alone (or no treatment).[28] In the NT, referral for Ear, Nose and Throat (ENT) review is recommended after treatment failure is confirmed at 16 weeks.[13] We have previously shown that 6 months of amoxycillin (25mg/kg BD) will reduce the risk of discharging ears in infants.[29] The Dutch study found 12 weeks of cotrimoxazole was effective.[26] Finally, 16 weeks is also a reasonable time frame for preparation for tympanoplasty. Currently, there is a preference for surgical repair of the tympanic membrane in older children with chronic perforations that are dry at time of surgery.[30]

Feasibility of proposed research project

The intervention to Close the Gap in Indigenous health has identified hearing health in remote Aboriginal communities of the NT as a priority. As a result, the NT Department of Health is currently implementing training for community workers in hearing health in Regional Development Sites. Sound-proof hearing booths, tympanometers and video-otoscopes have also been provided. The Department of Health Hearing Health Program Leader (Sandra Nelson) is a Chief Investigator (CI) on this study. She has been overseeing the ear health program delivered to the participating communities for many years. The senior ENT surgeon on the program is also a CI (Harvey Coates). The Menzies ear health team have previously collaborated on randomised trials with over 30 remote Aboriginal communities in the NT.[31, 32] Fifteen communities participated in our most recent antibiotic randomised trial (Azithromycin for Asymptomatic Acute Otitis Media, AAAOM, NHMRC 436023).

RESEARCH PLAN

Setting:

The study will be conducted in 10-20 Aboriginal community health centres or Aboriginal Medical Services in Regional Development Sites of the Northern Territory. In these Regional Development/Health e-Town Sites training of Aboriginal Community Workers - Hearing (CWH) is under way and expected to be complete in 2014, and each has a sound-proof hearing booth, video-otoscopes, tympanometers and audiometry equipment.

Participants:

All Aboriginal children aged >6 months and <17 years of age who are resident in participating communities will be eligible to be screened for CSOM. Children most at risk of CSOM will be identified through electronic health record review of the Patient Care Information System (PCIS) and the Hearing Health Information Management System (HHIMS). We will target examination in around 2,000 children (Figure 1) (from a population of around 4,000 children). Since we are targeting children who are known to be at high risk for CSOM, we anticipate identifying the condition in around 1/3 of these children. We estimate that 2/3 of children with perforations will have active discharge. Only children with a tympanic membrane (TM) perforation and a diagnosis of CSOM in at least 1 ear will be eligible for randomisation. The following children will be excluded: i) previously been randomised; ii) ciprofloxacin, cotrimoxazole or iodine allergy; iii) mastoid surgery in the preceding 12 months; iv) ear surgery scheduled in the next 4 months; v) congenital ear or hearing problems; vi) known immunodeficiency; or vii) pregnancy.

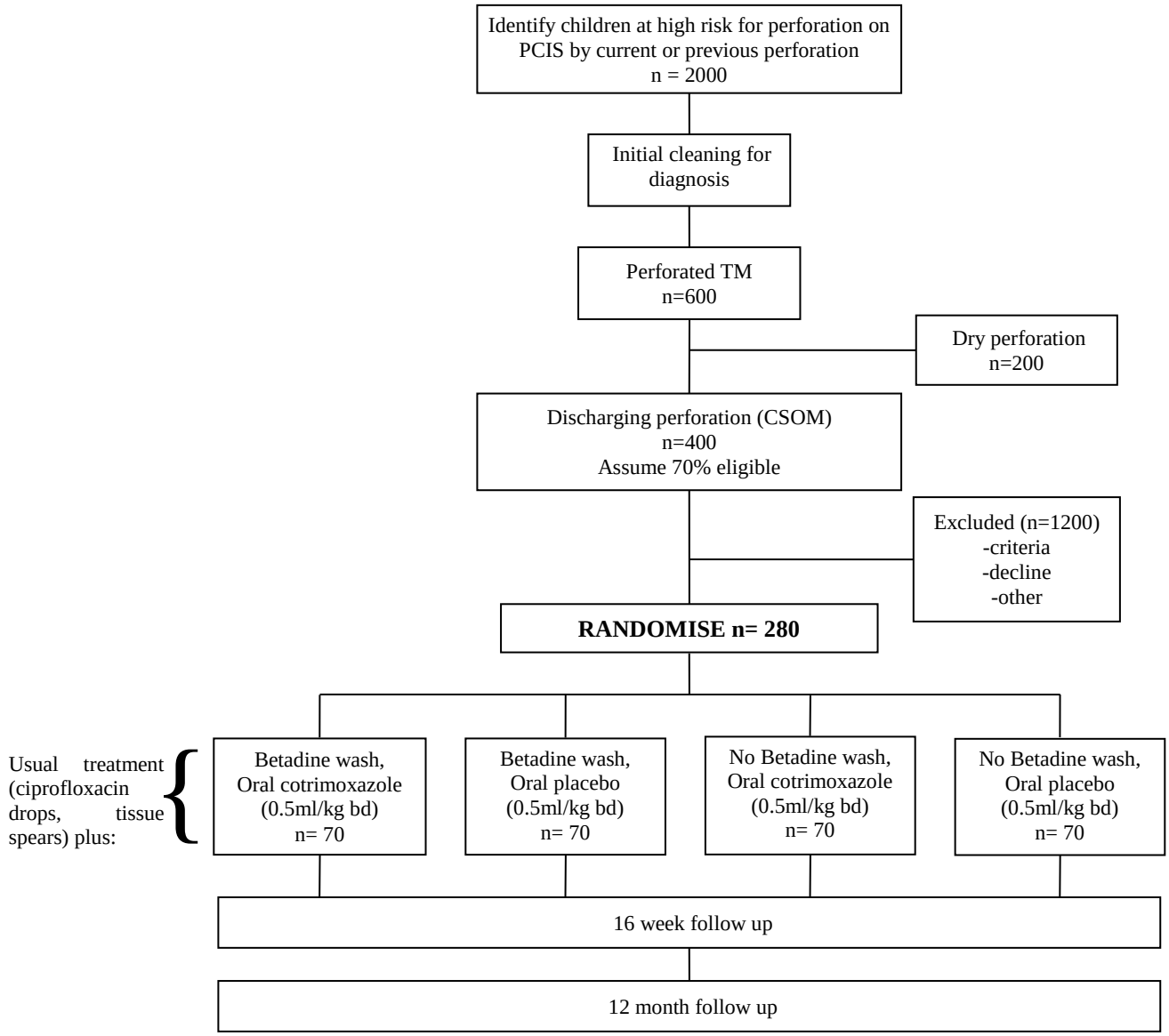
Consent:

Consent to participate in the prevalence survey and the randomised trial will be sought from the parents/guardians of children before examination. Assent will be required of young people >10 years old. Participating communities should have sufficient resources provided on the approach for the study in first language. Materials used for informed consent will be provided by the Darwin based staff utilising flip charts designed by Ms Katrina Hodson (Aboriginal Health Worker) that have been customised for all our recent OM studies. These flip charts visually describe the study and explain the important features of a randomised controlled clinical trial.

Randomisation:

Each enrolled child with CSOM will be randomly allocated to receive one of four treatment regimens. Each regimen consist of one of two topical treatments and one of two oral medication treatments). Children will be stratified according to: i) community; and ii) age (<3y; 3-10y; over 10y. On consent of an eligible participant, the research team will open a double sealed sequentially numbered opaque envelope from the appropriate stratification group. This will contain the topical treatment code and the oral medication treatment code. These will be documented in their clinic records. The allocation sequence will be concealed from all of the investigators throughout the study. The treatment codes used in the study will be used by the study statistician (CI) to present outcomes by coded treatment group if requested by the Data Safety Monitoring Committee.

Figure 1: Flow diagram of study design for IHEAR BETA



Blinding:

The research assistants collecting the primary outcome data will be unaware of the treatments assigned to each child (i.e. outcome assessor blinded). Families and staff will be aware of which

topical treatment is allocated. Previously, awareness of allocation status by families has not resulted in significant performance bias. Families will not know whether their child is receiving oral antibiotic or placebo medication.

Clinical Assessment:

At the screening assessment, we will conduct a parental questionnaire, a review of clinical health records and a clinical assessment. The following information will be recorded from clinical records, school records, and interview: date of birth, history of past ear infections, pneumococcal immunisation status, recent antibiotic use, and any health problems at the time of examination. Data on all previous ENT and audiology reviews (including all hearing assessment and teleotology reviews) and current referrals will be documented. We will record any side effects of treatment or preferences for specific management options. Attendance at child care, pre-school or school (and treatment provided at these locations) will also be documented.

Baseline, 16 weeks and end of study (12 month) clinical assessments will be made by the trained ear health research team. Assessments will be made using a tympanometer (Grason Stadler GSI 139), a voroscope (Welch Allyn LumiView) with Siegel's speculum for pneumatic otoscopy, and a video-otoscope with macro view (Welch Allyn macroview or MedRx video-otoscopes). Ear canals will be cleaned under direct vision. Data will be recorded using standardised forms. Video-otoscope images will be stored on a digital video recorder. All video-otoscope images and tympanograms will be reviewed by a second trained observer. Any disagreements in the assessments will be resolved by discussion with the study paediatrician.

Middle ear states will be categorised as follows: (1) normal; (2) otitis media with effusion (OME); (3) acute otitis media without perforation (AOMwoP); (4) AOM with perforation (AOMwiP); (5) dry perforation; and (6) chronic suppurative otitis media (CSOM). The following definitions will be applied to children diagnosed with a TM perforation: CSOM- Perforation size >2% and discharge for more than 2 weeks; Dry perforation- perforation with no discharge; AOMwiP- bulging TM and discharge < 2 weeks and/or with perforation <2% pars tensa. The final middle ear diagnosis will reflect the child's more severely affected ear. The hierarchy for clinical severity is pre-specified: Perforation and discharge > Perforation and no discharge > No discharge and at least moderate bulging > No discharge and mild bulging > No discharge and neutral or retracted.

Children who are found to have other forms of otitis media at the screening assessment will receive recommended standard treatment. They will be referred to health centre clinical staff for appropriate ongoing care. We have developed training videos illustrating the appearance of TMs and showing how perforation first occurs in young Aboriginal children. These will be used for professional development of health practitioners and in discussions with parents. Children participating in the study will also continue to receive additional medical and surgical treatment as indicated.

Records of the most recent hearing assessment will be documented at baseline and at the end of the study. The current OATSIH Guidelines recommend that hearing is tested within 3 months of the diagnosis of CSOM and to monitor the outcomes of interventions. Similarly, the Department of Health recommends testing of hearing in all children with dry perforations so suitability for surgery can be determined. As a minimum, all the children in this study would be expected to have hearing assessed at baseline and again at follow-up. Since the collaborating communities are Regional Development Sites, they have access to a sound proof booth and a visiting audiology service.

Microbiology:

Ear discharge and nasopharyngeal swabs will be collected at each examination. These will be frozen and flown to Darwin in a liquid nitrogen shipper. All nasal and ear discharge swabs will be cultured for respiratory bacteria (*Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella*

catarrhalis) and the most important pathogens associated with CSOM (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Proteus mirabilis*, and *Klebsiella pneumoniae*). Quantitative PCR (qPCR) will also be used because of the low culture isolation rates in ear discharge. Molecular typing will be used to compare concurrent nasopharyngeal (NP) and ear discharge strains and to distinguish new infection from persistence. Levels of antibiotic resistance will be monitored using the disk method and the E-test. We will also monitor the impact of long-term oral and topical antibiotics on the common bacterial respiratory pathogens that are carried in the nose. Our laboratory has extensive experience in the use of these methods. Specimens will be stored at -70^{o}C and available for further culture, serotyping and molecular typing as required. If *Staphylococcus* is confirmed to be a major pathogen, we have the technological capacity to look at sequence typing.[33]

Treatments

A) Topical treatment

Either i) Ear wash (Povidine-iodine (Betadine®)) 0.5% given twice daily (>=20mls per discharging ear)) plus usual topical treatment (dry mopping with tissue spears and ciprofloxacin drops 5 drops twice a day) followed by tragal pumping; or ii) usual topical treatment alone. Families will be shown how to do the ear washes and given treatment packs (aimed at minimising technical difficulties) with 1L of prepared povidine-iodine solution, 10ml syringes, a soft, specifically designed nozzle, plastic cups, and a kidney dish. Each discharging ear should be washed with 10mls of solution at a time. This is repeated until no more pus is removed (ie. at least 20mls used). Families will be informed that they can get replacement packs from the ear health worker of the local clinic. All packs also contain tissues and ciprofloxacin ear drops. Both treatment regimes should continue until the ear has been dry for 3 days (confirmed on two clinical examinations at least 3 days apart). Children who respond to treatment and then develop a recurrence of ear discharge will receive their original allocated topical treatment regime. The ear wash protocol is based on Western Australian studies and their standard treatment guidelines.[34] Clear instructions are included in the WA Ear Health Manual available though the Ear InfoNet (3rd edition "Aboriginal and Torres Strait Islander Ear Health Manual" in press).

B) Oral medication treatment

Either: i) twice daily oral antibiotic treatment (cotrimoxazole 4mg/kg per dose of trimethoprim component); or ii) a placebo medication that is identical in appearance, smell and taste. IDT Australia (formerly Institute of Drug Technology) will prepare the placebo suspension and repackage the cotrimoxazole (a 100ml bottle containing trimethoprim 40mg/5 mls and sulphamethoxazole 200mg/5mls). IDT have prepared the medications for our previous placebo-controlled trials.

Outcome assessment

The primary outcome of the study will be clinical failure after 16 weeks of treatment. This will be determined by the presence of ear discharge at the end of study clinical examination. This clinical assessment will be done by an experienced assessor who is unaware of allocation status (or treatment received) by each of the children. The blinded assessor will determine the presence or absence of ear discharge on review of the video-otoscopy images of the middle ear and ear swab combined with results of ear discharge microscopy and culture. A second blinded assessor will also review the video image and tympanometry results without knowledge of the original clinical diagnosis or the allocation status. Any disagreement will be resolved by consensus.

Secondary outcome measures will include i) hearing level (determined by audiometry and summarised as the pure tone 4 frequency average hearing level at 500, 1000, 2000 and 4000 Hz in the better hearing and worse hearing ears); ii) failure to improve (determined by perforation size and amount of discharge); iii) change in perforation size and amount of discharge (determined by

comparison of standardised assessment at baseline with end of study); iv) time to cessation of discharge (determined by review of health records); v) adherence to recommended management including attendance for specialist review (determined by review of health records); vi) presence of recognised bacterial pathogens in nose and ear discharge (determined by standard microbiological culture and sensitivity methods); vii) complications (defined as development of a related illness requiring additional medical treatment); and vii) side effects (defined as development of illness requiring cessation of prescribed antibiotics). We will review clinic record and ask parents about recurrences of ear discharge in the intervals between visits. We will also describe any contact with family and/or staff, the feasibility of monitoring progress via PCIS, all relevant investigations and treatment, and the distribution and use of the antiseptic ear wash packs and study medication.

Statistical analysis plan

A full detailed statistical analysis plan will be developed and approved by the CIs before any outcome data are analysed.

Primary outcome:

As the efficacy of the topical treatment intervention is expected to *in no way* depend on which of the two oral medication treatments was given, the primary analysis will report the absolute risk difference and 95% confidence interval for:

(i) the difference in failure rates between children allocated to receive the ear wash plus usual topical treatment, and children allocated to receive usual topical treatment alone;

(ii) the difference in failure rates between children allocated to receive twice daily oral antibiotic treatment and children allocated to receive placebo.

The number of children in each of the 4 treatment regimens with missing primary outcome data will be reported. However, this number is expected to be small. Such children will not contribute to the above-mentioned primary analysis.

Secondary outcomes:

Rates of clinical failure after 12 months will be analysed in the same manner as above. The primary outcome analysis will be repeated using a "treatment received" approach. Any differences in effect compared with the primary analysis will be described. Differences in the proportions of children who experienced the following outcomes will also be measured using the final outcome data: failure to improve (determined by perforation size and amount of discharge); complications (defined as development of a related illness requiring additional medical treatment); and side effects (defined as development of illness requiring cessation of prescribed antibiotics). Differences in hearing level (a continuous outcome) will be assessed using analysis of covariance (ANCOVA). A comparison of the time to recorded cessation of ear discharge in the two treatment groups will be made using survival analysis. The impact on other illnesses and rates of antibiotic resistance will be described. Differences in the secondary efficacy outcomes not supported by a difference in the primary outcome will be regarded as "hypothesis generating". We will also describe the prevalence of CSOM and dry perforation and the associated bacterial pathogens (see secondary aims). This will be the first systematic prevalence study since 2001-3 and the first large CSOM microbiology study in this population.

Sample size

We estimate that at least 70% of children receiving current standard therapy for CSOM will (unfortunately) not be cured after 16 weeks of treatment. This is consistent with the medium term outcomes (after 8 weeks of supervised treatment) in the ciprofloxacin group of our previous trial.[22] With a total of 280 children randomised, this study will have ~88% power to detect an improved outcome in an additional 20% of children for each intervention (at the 5% significance level), assuming 10% loss to follow up. Treatment effects of less than 20% would require further consideration of the potential benefits and harms (due to concerns about the resource implications). Since recent surveys have identified that over 20% of NT Aboriginal children have TM perforations (and most have CSOM), we should identify sufficient children for the study. Our aim is to enrol at least 20 children from between 10-20 communities (to a maximum of 300 children).

Data and Safety Monitoring

An independent Data Safety Monitoring Committee (DSMC) will be formed before the start of the study. The DSMC will include an independent clinician familiar with Aboriginal child health problems, an independent statistician, and a representative of the Child Health Indigenous Reference Group. The DSMC will meet before the study starts and at its conclusion. Progress reports documenting all serious adverse events will be provided to the DSMC every 4 months. Any life threatening or disabling event will be reported immediately to the study safety monitor and DSMC. Although we have not planned an interim analysis, the DSMC will be able to request a confidential review of the available data if there is evidence that participation in the trial may be harmful.

Follow up

Our previous otitis media studies have achieved a follow-up rate of 90%. Participants with CSOM at the end of study assessment will be advised to continue treatment with dry mopping and ciprofloxacin drops for one further week followed by review at the local clinic. Where there is evidence that the discharge has been present for a prolonged period, the child will be prioritised for ENT, audiology and paediatric review (if this has not occurred recently). All children who have other ear diagnoses will be referred to the community clinic for appropriate management. The research team will support better adherence with treatment recommendations in the OATSIH Guidelines and Central Australian Rural Practitioners Association (CARPA) Manual. Contact with families, Community Workers - Hearing, and clinic staff will occur as required. The needs of individual children will be identified through mobile phone interviews and electronic health record monitoring. In addition to access to the Patient Care Information System (PCIS), from 2014 the NT Hearing Health Information Management System (HHIMS) will automatically collate field data (including tympanometry and digital video-otoscopy) and integrate ear and hearing health clinical data into a shared care plan framework.

Research Plan for 2014-2017

Jan - June 2014	Planning. Finalisation of study protocol. Employ and train study coordinator. Community consultation visits. Ethical approval. Formation of Indigenous Reference Group. Formation of Independent DSMC.
July - Dec 2014	Employment and training of staff. Preparation of intervention materials. Scheduling of community visits with Northern Territory Department of Health.
Jan - June 2015	Intervention period begins. Review of electronic health records (PCIS and HHIMS) and community screening of all eligible Aboriginal children aged 6 months to 17 years (~50 per day). Randomisation target to proceed at a rate of 20-40 children per screening visit in larger communities. Allowing for inclusion of smaller communities and communities with lower rates of CSOM, we plan 16 weeks of field work.
July - Dec 2015	Intervention period continues. Target 180 children randomised by Dec.

Jan - June 2016	Intervention period continues. 12 month follow up assessments begin for 2015 participants. Repeat of screening assessments and randomisation of eligible children. Target 100 children (total 280 children) randomised by middle of year.
July - Dec 2016	Continue 12 month follow-up assessments for 2015 participants.
Jan - June 2017	Completion of 12 month follow up assessments.
June - Dec 2017	Community feedback, reports, educational materials, and publications.

Feedback, publication and ongoing health education

This is an extremely important part of any research involving Aboriginal communities. The senior investigators will collaborate with both Aboriginal research assistants and the Child Health Indigenous Reference Group of the Menzies School of Health Research. This approach is used to ensure that the study findings are translated into culturally appropriate health messages and effective health policy. This will be made considerably easier through the involvement of senior policy officers from the health and education departments. One Aboriginal research assistant will be employed for the full 4 years of the study. This person will promote: i) culturally appropriate research practice; and ii) practical feedback to communities that is able to improve current standards of primary care. Training will be provided by the senior investigators and the project officers and after the study support will be given by a consultant hired to assist with the feedback process. We aim to provide the level of skills required to coordinate (or contribute to) a similar research project in the future.

OUTCOMES AND SIGNIFICANCE

The proposed study is an important development for the assessment of interventions in Aboriginal health. It combines the recent experience of intensive studies involving small numbers of children with a practical approach to more effective medical treatments for an important and common health problem. The results of the trial will become the best available evidence to guide the medical management of CSOM in high-risk children. It will be an important contribution to the medical literature and the results will have implications for all disadvantaged populations where adverse outcomes are common. This project will also provide improved training and education materials for a large number of NT health staff. Ongoing education and support is essential in the transition toward more effective prevention and management of chronic otitis media in Aboriginal children.

Project 2 Text messaging to improve treatment and follow-up in chronic conditions: A Systematic Review of evidence applicable to disadvantaged populations (paper for publication).

Summary

Background:

Aboriginal people living in remote Northern Territory communities experience extreme disadvantage. High levels of stress, household overcrowding, poor housing and a range of other factors related to poverty lead to young children within these communities experiencing a high burden of recurrent acute and chronic infection. The need to identify strategies that promote treatment adherence, within this context, is urgent.

Aim:

This systematic literature review investigates whether regular Short Message Service or Multi-Media Messaging service, sent via mobile telephone, leads to improved treatment adherence and attendance of follow-up review among carers of children with a chronic disease.

Findings:

Following a process developed by the National Health and Medical Research Council for Systematic Reviews, literature since 1999 was examined. Of the initial 890 titles extracted, 31 studies were considered eligible for review. Of these, 6 studies were considered in more detail. Only one eligible study included children, and none included Indigenous participants. The search identified no research concerning the use of Media Messaging Service to promote adherence of treatment.

Conclusion:

From the limited evidence available, it appears that Short Message Service messaging should be seen as only one component of a multifactorial intervention to promote adherence to treatment regimes and follow-up. The existing relationship with the health service provider, as well as patient characteristics require consideration. Characteristics of the actual messaging must be taken into account and should be developed in partnership with community members.

BACKGROUND

Many childhood chronic conditions involve complex regimens and require regular attendance at health facilities. The need to adhere to children's treatment regimens and attend for regular appointments can be stressful for the primary carer and / or the child [1-3]. The extent of the delivery of health care to children in the home is dependent on the ability, willingness, motivation and socio-economic circumstances of primary carers (and other family members). No matter how effective treatments are, the health of children is compromised if parents are unable, unmotivated, or unwilling to adhere to treatment regimens and attend review appointments [4-6].

Aboriginal people living in remote Northern Territory (NT) communities experience extreme disadvantage. The key underlying causes for this disadvantage are considered social inequality and powerlessness. These factors impact negatively on health and well being [4]. Aboriginal families experience high levels of stress related to poverty, household overcrowding and poor housing. Household membership consists of extended family members, and frequently includes one or more individuals with special needs (for example - frail older people, or people with psychiatric disorders and/or in poor health from chronic diseases). Misuse of alcohol, drugs, or problem gambling, may also increase the stress experienced by some families [5]. Parenting practices more suited to the hunter-gatherer lifestyle than permanent settlement, high rates of teenage pregnancy, and a high proportion of single parent households all present as risks to children's health and wellbeing in remote communities. These factors contribute to young children living in these communities experiencing a high burden of recurrent acute and chronic infection. This results in children experiencing chronic health conditions not commonly found among their non-Indigenous counterparts, for example chronic suppurative otitis media (CSOM) with fluctuating or permanent hearing loss and chronic lung disease [6-9]. The need to identify strategies that promote treatment adherence for Aboriginal children with chronic conditions is urgent. The underlying reason for completing this review was to investigate the strength of the evidence available to support the use of Short Message Service (SMS) to promote improved treatment adherence for CSOM for this population group. Aboriginal children with CSOM require complex and co-ordinated care [10]. Treatment delivered in the home, and the presentation of children for regular medical and audiological review, are important elements to successful resolution of CSOM.

Globally, communicating by means of SMS is popular. Messages sent by SMS are reported to be a well accepted by recipients [11]. It is generally considered that SMS communication provides a cost-effective and efficient way to send reminder, educational and motivational communications to improve adherence to treatment and attendance for follow-up review [11]. Ownership of mobile telephones among Aboriginal people living in the remote NT communities (that have mobile communication coverage) is high [12,13]. Mobile communication coverage in remote areas of Australia is growing, by June 2013 the Australian Government plans that two thirds of remote Australia will have mobile communication coverage.

In this systematic literature review, we investigate the evidence to support that regular SMS or MMS sent via mobile telephone will improve treatment adherence and attendance for follow-up review among carers of children with chronic conditions. The findings of this review will contribute to a body of knowledge to inform future policy and practice in relation to the implementation of evidence-based interventions in remote Aboriginal community contexts [14].

Review Objectives

The primary objective of this review was to determine whether:

a) Regular text or multimedia messages sent via mobile telephone (to persons who have conditions that require daily therapy and ongoing medical follow-up) are effective at improving

   i) Adherence to therapy regimens; and/or
   ii) Attendance rates for follow-up care.

METHODS

This review is reported here informed by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement guidelines [10]. A protocol was developed to inform all review criteria and processes.

Types of Studies

The study designs considered eligible for inclusion in this review are randomised controlled trials (RCTs) and meta-analysis.

Types of Participants

Studies involving participants of any age who were receiving managed medical care that included daily monitoring and therapy for chronic conditions (for example - requiring taking medication or completing a daily activity) and attendance for regular review (appointments at therapists, doctors, dentists or outpatient departments).

Within the broader category described above we planned to group participants into sub-groups.

Subgroup 1. This group included Indigenous and non-Indigenous persons who are identified as socially and economically disadvantaged.

Subgroup 2. This group to include children aged between 0-18 years.

Types of Interventions

We considered RCTs of the following interventions eligible for inclusion:

a) Regular (weekly or more frequent) SMS or MMS sent via mobile phone to promote:

   i) Adherence (for example, taking medication and/or completion of an activity like monitoring, therapy or treatment); and
   ii) Regular attendance for medical appointments.

We excluded interventions with these characteristics:

- Reminder or motivational text promoting: i) the adoption of healthy lifestyle behaviours, for example, smoking cessation, weight loss, safe sex, increasing physical activity, and use of sun screen; ii) uptake of universal public health programs, for example, immunization and mammography screening; and iii) attendance for a single appointment; and

- Text messaging that required a response from participants. This was excluded on the grounds of reducing tasks that might be perceived as onerous by carers, cause cost to carers, and to take account of variable levels of English literacy.

Types of Outcome Measures

The primary outcome measures of interest included the proportion of participants with improved rates of:

i) Treatment adherence; and
ii) Attendance for follow-up medical appointments.

The secondary outcome measure of interest was:

(i) Any marker (including more sensitive continuous variables) that indicates an improvement in health status, for example –blood sugar level.

We considered satisfactory adherence to be:

i) The delivery of 80% of the prescribed treatment (for example - medication, physical therapy, wound care) on 80% of the occasions for which the treatment is prescribed; and ii) attendance for follow-up of appointments is 80% or more.

Search methods for identification of studies

Studies published from 1 January 1999 to 11 November 2012 were eligible for inclusion.

The electronic data base search included Medline via Pubmed, Embase, PsychINFO, ERIS, Web of Science, Cinahl, and the Cochrane Library and Trials Register.

The following search terms and fields were used to search Medline via Pubmed. These terms were adapted to search the other electronic databases.

("Cellular Phone"[Majr] OR "Text Messaging"[Majr] OR ("multimedia"[MeSH Terms] OR "multimedia"[All Fields]) OR ("text messaging"[MeSH Terms] OR ("Cellular Phone"[Majr] OR "Text Messaging"[Majr] OR ("multimedia"[MeSH Terms] OR "multimedia"[All Fields]) OR ("text messaging"[MeSH Terms] OR ("text"[All Fields] AND "messaging"[All Fields]) OR "text messaging"[All Fields]) OR "Short Message Service"[All Fields]) AND ("Reminder Systems"[Mesh] OR "social support"[MeSH Terms] OR "Health Promotion"[Mesh] OR ((("health education"[MeSH Terms] OR ("health"[All Fields] AND "education"[All Fields]) OR "health education"[All Fields]) AND ("medical subject headings"[MeSH Terms] OR ("medical"[All Fields] AND "subject"[All Fields] AND "headings"[All Fields]) OR "medical subject headings"[All Fields] OR "mesh"[All Fields])) AND "patient compliance"[MeSH Terms])) ("text"[All Fields] AND "messaging"[All Fields]) OR "text messaging"[All Fields]) OR "Short Message Service"[All Fields]) AND ("Reminder Systems"[Mesh] OR "social support"[MeSH Terms] OR "Health Promotion"[Mesh] OR ((("health education"[MeSH Terms] OR ("health"[All Fields] AND "education"[All Fields]) OR "health education"[All Fields]) AND ("medical subject headings"[MeSH Terms] OR ("medical"[All Fields] AND "subject"[All Fields] AND "headings"[All Fields]) OR "medical subject headings"[All Fields] OR "mesh"[All Fields])) AND "patient compliance"[MeSH Terms]))

Hand searching included screening the reference lists of studies identified eligible for inclusion and more general searching of the grey literature.

Selection of studies

One reviewer completed the study selection process guided by rules set down in the protocol. Eligible studies were identified according to the following steps.

Step 1. Scanning of titles

Lists are available of the papers considered not eligible for Step 2 review.

Step 2. Review of abstracts

The abstracts of the titles were reviewed in accordance with the review's eligibility criteria. A record of papers considered not eligible for full text review is available.

Step 3. Review of full text

Data was extracted using a standardised data collection form. A record is available of all studies considered not eligible with the reasons for exclusion clearly stated (Appendix 1- Table 1).

Quality assessment rating

Eight criteria were used to assess and score the risk of bias of individual studies including: randomisation; concealment of allocation; use of appropriate controls; intention-to-treat analysis; blinded assessment of primary outcome; baseline measurement; reliable primary outcome measure; protection against contamination. These indicators were rated as not done, done, or unclear. Next, the studies were categorised according to their quality assessment rating (Table 1).

Table 1. Level of evidence and associated risk of bias rating score

Risk of Bias Rating	**Evidence Category**
Five of the six criteria rated as low risk of bias.	Clear evidence of benefit.
Three or four criteria rated as low risk of bias.	Some evidence of benefit.
A study showing a positive outcome or no effect with less than three criteria rated as low risk of bias.	This rating includes two categories: 1. No evidence of benefit (or harm) and methodological concerns. (A study shows no or negative effect and the study design is weak.) 2. No clear evidence of benefit (or harm) due to methodological concerns. (A study reports some effect but the study design is weak.)
A study with a minimum of five of the six criteria rated as low risk of bias.	This rating includes two categories: 1. Evidence of no benefit or harm. (A strong study that shows no difference and the confidence intervals around the estimated effect are narrow.) 2. No evidence of benefit or harm. Further studies required. (A strong study where no statistically significant difference is shown but the confidence intervals around the estimated effect is wide.)

We adapted a method/process developed by the National Health and Medical Research Council (NHMRC) [15] to formulate recommendations concerning the relevance of the intervention in the remote Indigenous context. The factors considered to assess the body of evidence were:

- Volume of evidence;
- Consistency of the study results;
- Potential clinical impact of the proposed recommendation;
- Generalisability of the body of evidence to the target population; and
- Applicability of the body of evidence to the Australian healthcare context.

Other measures of relevance

Data were extracted to gain information about intervention development, design, implementation process and issues concerning health system or health service delivery. The approach used to ascertain if study interventions and methodologies reflect current best practice thinking around achieving sustainable health improvements. Such factors included physical and social context in which studies took place; characteristics of participants; underlying theory supporting the intervention; the use of single or multifaceted interventions; implementation issues (workforce, feasibility, sustainability); consumer acceptability (to message sent); health service capabilities; and cost. These factors were considered also to test if interventions might be suitable to use, and feasible to implement, in remote Indigenous communities.

Data analysis

We planned a two phased approach to analyse the data.

Phase 1. Knowledge support – aggregative phase

Single studies to be reviewed in relation to intervention effectiveness. Results of individual studies to be examined to determine if analysis was based on the 'intention to treat'. The risk difference between the SMS group compared with the control group was to be abstracted or calculated where suitable information was available and studies were considered to be sufficiently powered. Anticipating heterogeneity between studies, a random effects model of analysis was planned. Meta-analysis was to be completed only if combining the studies was thought not to be misleading.

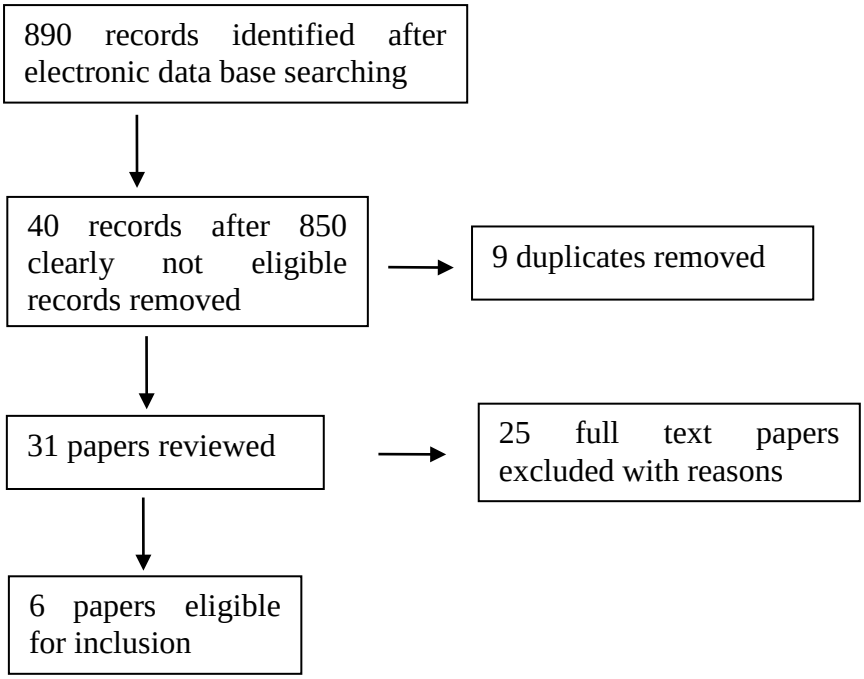
Phase 2. Decision support phase and relevance testing

In this phase, factors regarding the relevance of studies to the question asked, problem addressed and context were to be considered.

RESULTS and DISCUSSION

Search Findings

Figure 1 describes the search process and outcomes.



Description of studies

Electronic data base searching identified 890 studies. Forty studies that clearly did not meet eligibility criteria and nine duplicate studies were removed. After reviewing titles of remaining studies (with abstracts where available), 31 studies were considered eligible for review. A further 25 full text papers were excluded with reasons reported (Appendix 1- Table 1). Six studies (5 studies [16-20] and 1 review and meta-analysis [21]) were considered eligible for inclusion once the full text was reviewed against the eligibility criteria (Appendix 2- Table 1).

Our search identified no research or evaluations concerning the use of MMS messaging to promote adherence.

Characteristics of study participants and contexts

Three of the eligible studies were completed in resource poor counties (Brazil [16], Kenya [17] and India [18]) and two in resource rich countries (the United States of America [20] and Denmark [19]).

In four studies [16-20] participation was based on individuals experiencing a health condition. In one study [18] the participants were mothers of children who all attended the same preschool. In this study, the intervention targeted children's carers with the view to improve a child health outcome (reducing the Visible Plaque Index on children's teeth). Participants in the other studies were all aged over 18 years.

Study design

Study designs included were one meta-analysis [21] and five RCTs [16-20]. Three of the five RCTs were very small (<50 participants).

Intervention Effectiveness/Outcomes

Sub-group categorisation was not possible due to the small number of eligible studies. Only one eligible study included children, and none included Indigenous participants.

Meta-analysis was not completed due to the clinical heterogeneity between intervention characteristics (in design or intention) and the variable quality of the studies. In this section, the eligible studies are present according to the type of health condition, that is - human immunodeficiency virus (HIV), oral health, asthma, systemic lupus erythematosus (SLE).

Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV Infection

One systematic review [21] (consisting of 2 studies – for one study the intervention design did not meet the eligibility criteria for this review, i.e. a SMS response was required from the study participant) and two studies [16-17] are included in this category (one study [17], included in the aforementioned review). The studies were completed in Kenya and Brazil.

Table 1. Mobile phone text messaging - HIV

	Study ROB Rating[1]			**Findings**
	Low[2]	**Medium[3]**	**High[4]**	
Review[24]	1			Seven out of 8 criteria were met by the strong study. Analysis for the study was conducted both for 'intention to treat' and 'per-protocol'. Five criteria were demonstrated to be met by the moderate study. The sample size in this study was very small (C: n = 15, I: n = 14). Five participants in the intervention group did not receive the intervention and were excluded from the analysis. The strong review and strong study showed clear evidence of benefit that weekly SMS of any length was associated with a lower risk of non-adherence compared with standard care. The moderate study showed no evidence of benefit or harm. Meta-analysis showed i) the effect of short SMS was also significant compared with standard care; and ii) patients receiving weekly SMS were at lower risk of non-adherence at 48 weeks than were patients receiving daily messages of any length. Health outcome measures were not measured in the strong or moderate studies.
2 Studies	1	1		
Study Quality Score		Study[40]	Study[16]	
randomisation		yes	yes	
concealment of allocation		yes	unclear	
used appropriate controls		yes	yes	
analysis by intention to treat		yes	no	
blinded assessment of primary outcome		yes	yes	
baseline measurement		yes	yes	
reliable primary outcome measure		yes	yes	
protection against contamination		unclear	unclear	

[1]Risk of Bias. [2]Low ROB ≥5/6 criteria. [3]Medium ROB 3-4/6 criteria. [4]High ROB < 3 criteria.

In both studies, the SMS message content was developed after consulting with clinic staff and others. This was to ensure message appropriateness and a good level of acceptability by recipients. Adherence was measured at the 90% level for one medication in the Kenyan study [22] and as the percentage of participants with adherence >95% in the Brazilian study [16]. The Brazilian study measured adherence by three means: self-reporting, pill counting, and via a monitoring device built into the lid of the medication bottle.

The Kenyan study also used the latter method to measure adherence. The theory underlying intervention design included:

- Four text message intervention types (short, long/daily, weekly) were used to address perceived different barriers to adherence, for example - forgetfulness and lack of social support.

- The short messages served as simple reminders and long messages provided some additional social support. Daily messages were sent close to the time of medication usage.

- Weekly messages were meant to avoid the possibility of patients developing a dependence on the reminder system.

- HIV and antiretroviral therapy (ART) were not included in messages to ensure participant privacy.

Participants in the Kenyan study were provided with mobile phones at no cost. All participants received 15-minute lessons to ensure they could work the phone and read messages. The study provided practical and financial assistance to participants, for example - financial assistance to charge phones (some homes were without electricity), financial support to pay for travel to appointments. Across the four intervention groups, 69 participants (24%) lost their phones and these were not replaced. Fifty-one participants (18%) changed phone numbers. On several occasions, the mobile phone wireless system was interrupted so participants did not receive messages. The authors of this study hypothesised that habituation, or the diminishing of a response to a frequently repeated stimulus might explain why weekly reminders improved adherence when daily reminders did not. They also considered that participants might have felt daily reminders to be intrusive.

In the Brazilian study, patients were excluded from the study if they did not already own a mobile phone or if they were illiterate. All participants (intervention and control) were judged experienced SMS users at the commencement of the intervention. A single identical SMS message was automatically sent 30 minutes before the required time of the last required medication dose on each occasion. The message read "*The UNIFESP informs: take good care of your health*" (p. 259). The intervention was delivered for three months. The schedule for sending was every Saturday and Sunday and on alternate days throughout the working week. No response was required from participants. The message was not sent daily because the researchers felt this could aggravate participants or lead them to trivialise the messages.

The authors of the review concluded that policy-makers should consider funding programs proposing to provide weekly SMS as a means for promoting adherence to antiretroviral therapy. They suggest there is a need for large RCTs of this intervention in adolescent populations and resource rich countries.

Mobile-phone text messaging (SMS) to mothers of preschool children promoting improved oral hygiene behaviour to reduce dental caries

One study [24] is included in this category. The study was implemented in an urban setting in India. Study participants were the mothers of young children attending a pre-school.

Table 2: Mobile-phone text messaging - oral health education

	Study ROB[1] Rating			Findings
	Low[2]	Medium[3]	High[4]	
Study[18]		1		This study met 3 out of 8 criteria. No clear evidence of benefit due to methodological concerns. It is reported that both SMS messages and the provision of pamphlets showed benefit in reducing the Visible Plaque Index on children's teeth. Significant improvements in mothers' knowledge (*p* 0.001), attitudes (*p* 0.001) and practices (*p* 0.001) are reported in both groups.
Study Quality Score				
randomisation			yes	
concealment of allocation			unclear	
used appropriate controls			no	
analysis by intention to treat			no	
blinded assessment of primary outcome			unclear	
baseline measurement			yes	
reliable primary outcome measure			yes	
protection against contamination			unclear	

[1]Risk of Bias. [2]Low ROB ≥5/6 criteria. [3]Medium ROB 3-4/6 criteria. [4]High ROB < 3 criteria.

This Indian study involved sending 21 SMS messages (three each day for 7 days). The intervention was delivered over four weeks and messages were repeated weekly. A measure of adherence was not provided. The health outcome, the Visible Plaque Index (VPI), was measured. The length of the messages varied from short, for example - "*Brush your child's tongue gently*" to very long, for example - "*You should consume sweets only at the main meals. Don't eat sweets between meals. During meals the saliva production is increased neutralizing most of the acids. That's why a sweet during the meal is less hazardous than one taken between meals*" (p 433). The authors state that SMS was the preferred communication method because SMS has the advantage of instant transmission, a smaller chance of being lost (compared with postal reminders) and are less intrusive in the daily lives of people compared with telephone calls. Proficiency in English was a prerequisite for inclusion in the study. The main purpose for the researchers providing dental health education to mothers was to influence the child's carer who exerts the strongest influence on a young child's life. The researchers identified that the reduction in the level of plaque in the children included in the study was small and that the carers need more than just simple information, cajoling or simple encouragement to change their everyday behaviour. The researchers reported that overall the messages sent were well received by carers. Among the 71 participants in the SMS group, four participants dropped out. Two carers reported they did not receive the messages and two asked for the messages not to be sent because they found them "*irritating*" (p 434). The authors of this study concluded that in their country (India) where literacy levels are not high, SMS is not the best means of communicating with people whose health is most at risk.

Daily SMS reminder to increase adherence to asthma treatment.

One study [19] is included in this category. This study was completed in an urban setting in Denmark.

Table 3. Mobile phone text messaging – asthma

	Study ROB[1] Rating			Findings
	Low[2]	Medium[3]	High[4]	
Study[19]		1		This study met 3 out of 8 criteria. Some evidence of benefit was shown with methodological concerns. However, the number of study participants at commencement was small (n=26) and not all participants completed the study (n=22). Analysis was not by intention-to-treat.
Study Quality Score				
randomisation			unclear	
concealment of allocation			unclear	
used appropriate controls			yes	
analysis by intention to treat			no	
blinded assessment of primary outcome			unclear	
baseline measurement			yes	
reliable primary outcome measure			yes	
protection against contamination			unclear	

[1]Risk of Bias. [2]Low ROB ≥5/6 criteria. [3]Medium ROB 3-4/6 criteria. [4]High ROB < 3 criteria.

In the Danish study, adherence was defined at the 80% level. The intervention was delivered over 12 weeks. Participants self selected by responding to an advertisement. Those who volunteered to participate received a medical screening to determine eligibility. Those deemed eligible were randomised to intervention or control groups. The researchers considered that a daily SMS message would create a higher awareness of asthma control and treatment and this would lead to improved adherent behaviour. The daily message was intended to counter the reported problem of forgetfulness. The non-personalised message sent was "*Remember to take your asthma medication morning and evening. From the Respiratory Unit"* (p 168). The researchers reported that participants' perceived receiving an SMS as positive. A non-personalised SMS message was sent at 10am each day. Participants did later report that this time was inconvenient. Most of the participants in the intervention group reported that although they noticed the SMS daily they stopped reading it after some weeks. The researchers report that the SMS appeared to serve as a simple alarm clock on a cell phone after a number of weeks.

Mobile Phone text messaging for improving adherence among adolescents and young adults with SLE

One study [20] is included in this category. The study was completed in an urban USA context and all participants in the adherence component of this study were aged over 18 years.

Table 4. Mobile phone text messaging – Systemic Lupus Erythematosus

	Study ROB[1] Rating			**Findings**
	Low[2]	**Medium[3]**	**High[4]**	
Study			1	This study met 2 out of 8 criteria. No clear evidence of benefit due to methodological concerns.
Study Quality Score				
randomisation			unclear	
concealment of allocation			unclear	
used appropriate controls			unclear	
analysis by intention to treat			no	
blinded assessment of primary outcome			unclear	
baseline measurement			yes	
reliable primary outcome measure			yes	
protection against contamination			unclear	

[1]Risk of Bias. [2]Low ROB ≥5/6 criteria. [3]Medium ROB 3-4/6 criteria. [4]High ROB < 3 criteria.

Adherence to medications or clinic visits was measured at the 80% level. The authors noted some improvement in "visit" adherence in a sub-group of "non-adherent participants". The intervention was delivered for 14 months. SMS were considered the ideal means of communication with adolescent and young adults based on high usage rates. SMS were sent seven, three and one day/s prior to each scheduled follow-up clinic appointment for the "visit" adherence component of the study. Non-attendance was followed-up with a further SMS. These messages were personalised by including the scheduled time of the upcoming clinic appointment. For the medication sub-group component of the study, the SMSs were individualised to match self-reported medication consumption times. SMS messages were worded using SMS vernacular, for example, the message "*It's time 4ur meds*" was used for twice daily regimens and for daily regiments "*Take ur HCQ now*" (p 176). There was no difference between patients who received once daily versus twice-daily SMSs. The researchers hypothesised that young patients did not take their SLE medication because the benefits were not instantaneous. Not personalising SMS reminders was perceived by the researchers to be a likely a barrier to achieving better adherence. Furthermore, they considered that the novelty of receiving the SMS wore off and constant reminders became repetitive and likely ignored by recipients over time. The researchers considered that the relatively small number of participants in their study, short follow-up period and lack of power might have contributed to the lack of observed changes in both visit adherence and medication adherence components of the study.

Overall assessment of the evidence

The overall assessment of the evidence was completed based on a recognised grading scale [15].

The quality and findings of one strong review [21], one strong study [17], three moderate studies [16, 18,19] and one weak study [20] were considered in this assessment of the evidence. There was variability in the risk of bias associated with the methods used, study contexts, implementation processes, and characteristics of study participants. Despite this, the body of evidence does provide some support that regular SMS messaging (sent via mobile phones to persons who have conditions that require daily therapy and ongoing medical follow-up to improve adherence) is effective. However, care should be taken in its application.

The potential for mobile phone technology to make an impact on health has been popularised in the literature and lay press. A large number of studies have been conducted utilizing some form of mobile phone technology as an intervention to promote adherence. Few met the eligibility criteria for this review. It is clear from the research evidence (and other literature) that other factors need to be considered in assessing the evidence. Factors that can modify the impact of a SMS intervention include:

- Strength of the existing relationship with the health service provider;
- Recipient characteristics, for example - socio-economic status, level of literacy, age, gender, diagnosis, parent of child with chronic illness. It is important to know what barriers individuals or populations are facing in trying to adhere to treatment and to attend for follow-up.
- Characteristics of the message including:
  - Acceptability and relevance of message content
  - Message length (short verses long)
  - Frequency of broadcast and time of receipt;
- Messages being personalised or generic;
  - Duration of program and development of tolerance (SMS ignored) or habituation creating dependence;
- A two-way communication system that allows patients to contact health services between appointments;
- Purpose of message (for example – message is intended to remind, educate, motivate, raise awareness);
- Level of reliability of supporting technology.

SMS messaging to promote adherence or attendance for follow-up represents one component of a multifaceted medical management plan. Therefore, it is important that message recipients value and trust the health system of which they are a part, also that they believe their own or their child's welfare is the prime reason for receiving the messages. High levels of non-adherence and non-attendance are likely to prevail if patients find health workers or the health system not to be empathetic and supportive [3].

It is widely reported that individuals find it acceptable to receive SMSs that carry a health message [11]. This appears to apply across age ranges and gender and in both resource poor and resource rich countries. Adolescents and younger adults are generally considered to be most accepting of this technology [11]. However, for adults and children with chronic diseases, the high acceptance levels of SMS messages does not necessarily translate into improved adherence or attendance [20,22]. One-off messages intended to remind individuals of medical or dental appointments are reported to have had some success in improving appointment attendance rates [23]. However, the strength of the evidence to support this finding is not strong [24]. The apparently same intervention may not work in changed contexts or for persons with different health profiles.

It is advised that messages be developed after consultation with members of the local population for whom the messages are intended. Recipient characteristics and their routines of daily living influence what is the acceptable content, the length of messages and broadcast time [25,26].

Several studies report that personalising messages increases adherence rates [25-27]. For example, in the case of simple reminder SMS to an individual to remind them to attend an appointment including details such as the actual date and the time of the appointment can improve attendance rates.

Persons receiving SMSs can ignore messages (develop a tolerance to the messages) and be non–adherent after receiving messages at a predictable time over days or weeks [17]. Non-adherence in some cases partly believed to be due to individuals receiving no immediate benefit or change in their health status from the prescribed treatment [20]. Messages sent at the same time/s daily for an extended time are considered by some to take on the function of an alarm clock reminder system. Some individuals may become reliant on an SMS to prompt them taking treatment and it is possible that habituation will result [19].

A two-way SMS communication system that provides for patients being able to respond to or initiate messages is considered to promote better adherence and attendance [28]. Interactive messaging is considered to provide a cost effective and practical alternative for communication between health providers and patients in between appointments [28,29]. In some cases it is considered to provide an additional means of social support [29].

The technology that supports mobile communications is not always reliable [16,17,22]. High rates of loss of mobile phones, or changes in phone number can impact on the effectiveness of SMS messaging to promote adherence or attendance for follow-up [17]. It is important, especially if persons come to rely on SMS messages, that programs have mechanisms to ensure that messages are sent and received by those for whom they are intended.

In many of the studies, the underlying theory supporting the use of SMS messages to promote the adherence to treatment regimens is not clear. Some studies provided rationales for the content, length or timing of messages but no theory of how messages are likely to influence behaviour [26]. Although not explicitly expressed, the use of SMS in many studies is primarily to counteract patient forgetfulness or provide “push” support [30]. Theoretical explanations for how and why SMS is likely to be effective has been most developed for the conditions of diabetes and psychosocial and health behaviour treatments [22,30].

Limitations

The search strategy used to identify studies and reports potentially relevant for this review appears to have been successful. However, it is possible that some unpublished evaluations or reports on projects and programs were not identified, and therefore the potential for publication bias should be considered.

Some studies were reviewed that might otherwise have been excluded on the grounds of high risk of bias. These were assessed in an attempt to gain more information on intervention design and implementation issues that may be useful in considering options for future policy and program development.

Implications for policy and practice

No studies were identified that included the use of SMS messaging interventions and Indigenous populations. None were identified that involved using SMS messages targeting carers of infants or young children with chronic medical conditions to promote adherence to treatment regimens and improve follow-up. Hence, recommendations for policy development, improved practice and potential inclusion of SMS interventions as discussed here are drawn from the experiences of population groups and contexts other than that of the Australian Indigenous peoples.
Important implications for policy and practice taken from the general literature include:

- There is a need to understand the multi-factorial nature of non-adherence to treatment regimens for chronic illness in Indigenous children living in remote communities.
- Interventions to promote better adherence, or other health behaviour change, need to be identified and developed in parallel with more supportive and responsive health service delivery system development.
- Interventions to promote better adherence to treatment regimens for chronic illness in children need to take account and promote improving the quality of family life and strengthening mother (carer) and child relationships.
- Good communication is needed to ensure there is alignment, common understanding of the goals for children's health aspired to by clinicians and those aspired to by carers.
- Interventions to promote adherence should aim to support carers of children with chronic illness and not cause them additional stress.

The implications for policy and practice from the research evidence included in this review (especially as this applies to young children with chronic conditions living in remote Northern Territory communities) are:

- SMS messaging sent via mobile phone to persons who have conditions that require daily therapy needs and ongoing medical follow-up should be seen as only one component of a multi-factorial intervention to promote adherence to treatment regimens and improved follow-up.
- To promote acceptability and effectiveness all elements of SMS message interventions should be developed in partnership with community members.
- The use of SMS messaging over extended times has the potential to lead to tolerance and messages being ignored, feelings of intrusiveness, or dependence.
- Interactive SMS messaging communication interventions have the potential to offer social support and promote self-efficacy.

Conclusion

There is an urgent need to identify strategies to improve treatment and follow-up review adherence rates for Aboriginal children living in remote communities with chronic conditions. There is some evidence to support that SMS sent by mobile telephone can play a supporting role in achieving improved adherence. Important individual, family, treatment and health service characteristics can affect the effectiveness of SMS leading to improved adherence. These factors represent real or perceived barriers to adherence.

Attachments

Appendix 1 - Table 1. A list of excluded studies and reason for exclusion
Appendix 1 - Table 2. A list of the six studies eligible for inclusion

List of abbreviations

GPP – good practice point
HIV - human immunodeficiency virus
MMS - multi-media messaging service
NT - Northern Territory
SLE - systemic lupus erythematosus
SMS - short message service
RCT - randomised controlled trial
ROB – risk of bias

Project 3	**Can mobile phone MMS and text messages improve clinic attendance for Aboriginal children with chronic otitis media?: a randomised controlled trial (paper for publication).**

Summary

Background:

Otitis media is a chronic condition largely affecting children. Poor adherence to treatment often results in associated hearing loss, which has a significant effect on a child's language, education and social outcomes.

Aim:

This study is the first randomised trial in remote Australian Indigenous settings to evaluate the use of mobile phone multimedia and text messaging intervention for carers of children with otitis media in order to promote ear health through increased clinic attendance and adherence to treatment.

Method:

The study took place over a 6 week period in two remote Indigenous communities in the Northern Territory. Both communities have a medical clinic with a full time doctor as well as nurse and/or Aboriginal health worker. After randomisation, the intervention group received multimedia messages in two Indigenous languages, reminding the carers about the importance of ear health. They also received short text messages, in English, recommending weekly clinic visits for ear check-ups and treatment reviews.

Conclusion:

There was no significant improvement in clinic attendance or ear health outcomes between those receiving messages and those not receiving messages. The media and text messaging were accepted by Health Workers and carers as a mode of communication. This study has demonstrated the potential of this medium as a tool in the management of chronic disease in remote and disadvantaged populations.

INTRODUCTION

Aboriginal children living in remote areas of the Northern Territory (NT), Australia have the world's highest reported rates of eardrum perforation, with the problem continuing into adulthood.[1–3] The associated hearing loss may have significant effects on language, education and social outcomes.[1,4–7] Acute otitis media with perforation (AOMwiP) frequently progresses to chronic suppurative otitis media (CSOM), which is persistent disease and large perforation size. Treatment recommendations for AOMwiP include long oral courses of antibiotics; recommendations for CSOM include weekly clinic reviews to monitor progress, frequent daily ear cleaning and topical antibiotic drops for many months.[7,8]

In 2002, the prevalence of tympanic membrane perforations among children of six to thirty months of age in two remote communities was 23% and 38%.[9] In non-Aboriginal children the prevalence is 0.1%.[10] Furthermore, GP presentations in Australia for severe otitis media were 8% in Indigenous populations and 2% in non Indigenous populations and presentations for discharging ears were 40 times greater (4% versus 0.1%).[10] In an Australia wide survey, ear problems were the fourth most common problem managed overall, with otitis media seen more commonly in Indigenous than non Indigenous children (10% versus 7% of consultations).[10]

Indigenous families living in remote communities struggle to provide the level of care needed for the effective resolution of otitis media in their children, particularly CSOM. Attendance rates at Aboriginal health services in the Australian Capital Territory for any form of otitis media have typically been low.[11] In the NT in the first year of life in five separate communities, ear problems were a frequent reason for clinic attendance.[12] However, considering the high burden of disease, attendance rates are far lower than they should be.

Improving clinic attendance rates and adherence to treatment is likely to improve ear health outcomes for these children. Mobile phone ownership in remote Indigenous communities has increased exponentially with nearly every household owning a mobile phone.[13,14] Previous studies have shown that mobile phone based interventions in low socio economic populations can have significant benefits in terms of clinic attendance, long-term adherence to treatment plans and medication compliance.[13–18] Personalised text messages were more effective than generic messages.

The impact of sending text and MMS health messages to remote Australian Indigenous populations has not previously been evaluated. This 2010 pilot randomised controlled trial, conducted over six weeks in two remote NT communities, investigated the possible attendance and health benefits of sending regular MMS to families of children with CSOM.

METHODS

1.1 Study design

This was a multi-centre, parallel group randomised controlled trial conducted in two remote communities in the Northern Territory (NT), Australia.

1.2 Ethics approval

Informed consent was obtained from parents or guardians. This study was approved by the Human Research Ethics Committee of the Northern Territory Department of Health and the Menzies School of Health Research (HREC – EC00153) and conformed to the provisions of the Declaration of Helsinki in 1995 (as revised in Tokyo 2004).

1.3 Study settings

The study took place over a six week period in two remote NT Indigenous communities between October and December 2010. Both communities have a medical clinic with a full-time doctor on site. Children are able to visit the doctor, nurse or Aboriginal health worker on any working day, without an appointment. In these communities, English is generally a seldom used second language.

1.4 Participants

To be eligible for inclusion in the study, participants had to have all of the following: (i) be an Indigenous child aged 13 years or under; (ii) have a tympanic membrane perforation (acute or chronic); (iii) live in one of the two remote communities long term; and (iv) have a parent/carer or other family member living in the same household with a working mobile phone who was willing to provide its number to us.

1.5 Intervention

Eligible participants were randomised into two groups: intervention and control. The parent or primary carer (or someone else in the household with a mobile phone) of those in the intervention group were sent seven multimedia ear health related messages (MMS) in the locally dominant Indigenous language, every four days, with a window of ± 24 hours. The MMS were accompanied by personalised ear health text messages in English that included a prompt to visit the clinic for the children's health check ups.

The control group received no MMS and accompanying text messages. However, both groups received two stand alone text messages in English, one at the start acknowledging their participation in the study and one at the end asking them to attend the clinic for the final assessment. Both the intervention and control groups also received an information sheet giving details about treatment and stating that the child should attend the clinic each week for care as recommended by local clinical practice guidelines.

The messages were sent using the Telstra Online Text Buddy system. The videos were short caricature animations of well-respected Indigenous people, such as elders, grandparents, Aboriginal health workers or football players. The emphasis of each video was to remind families of the importance of hearing in an Aboriginal context. For example, "to be a good hunter, you need good hearing" or "to be a good footballer, you need to be able to hear well – remember to go to the clinic this week to get your ears checked."

Ear assessments

An initial detailed ear examination was performed on each child and standardised data forms were used to record the findings and document baseline demographic and medical information. Using recommended clinical criteria for diagnosis in this population,[7] we categorised middle ear states as follows: [0] normal; [1] normal mobility but abnormal appearance; [2] retracted mobile drum; [3] otitis media with effusion; [4] acute otitis media without perforation (AOMwoP); [5] acute otitis media with perforation (AOMwiP); [6] dry perforation (DP); and [7] chronic suppurative otitis media (CSOM). Children with a diagnosis of 5, 6 or 7 for one or both ears were eligible to participate. The overall diagnosis reflected the state of the child's more severely affected ear. After this initial assessment, eligible children were randomised and assessors were blinded to the intervention allocations. Another ear examination was conducted at the end of the six week trial period for comparison.

Upon completion of the study, a second blinded ear health research officer made an independent diagnosis of all the cases that were accompanied by sufficiently clear video footage. Where the

second blinded assessor's diagnosis disagreed with the original clinical diagnosis, a consensus diagnosis was made in consultation with a third blinded assessor.

Sample size

In order to have 80% power to detect a difference of two clinic visits during the six week study period (from an estimate of one visit in the control group to three visits in the intervention group) with a two-sided alpha value of 5%, the estimated required sample size was 70. We aimed for a sample size of 90 to allow for attrition. Our final sample size was 53.

1.6 Randomisation: sequence generation and allocation

We used Stata Version 11.1 for participant randomisation.[19] The randomisation sequence was stratified by age and community, with a 1:1 allocation.

Outcome measures

The primary outcome of this study was measured as the number of clinic appointments attended, for any reason, during the six week intervention period by each child. Attendance was determined by accessing the community clinic's electronic patient information system.

The secondary outcomes were: (i) ear health state (less ear discharge, reduced perforation size or healed tympanic membrane) assessed by trained ear research nurses using standardised data collection forms; and (ii) participant satisfaction with text messages and MMS, assessed by face to face structured interviews using standardised questionnaires.

The questionnaire at six weeks included a mixture of dichotomous, open ended and multiple choice questions such as: "Did you see any phone messages from the Menzies Ear Health team?"; "Do you think our messages helped you remember to take (child's name) to the clinic for ear checks?"; "Which messages did you like?"; "Which messages did you not like?"; and "Would you be happy to receive other health related videos in the future?"

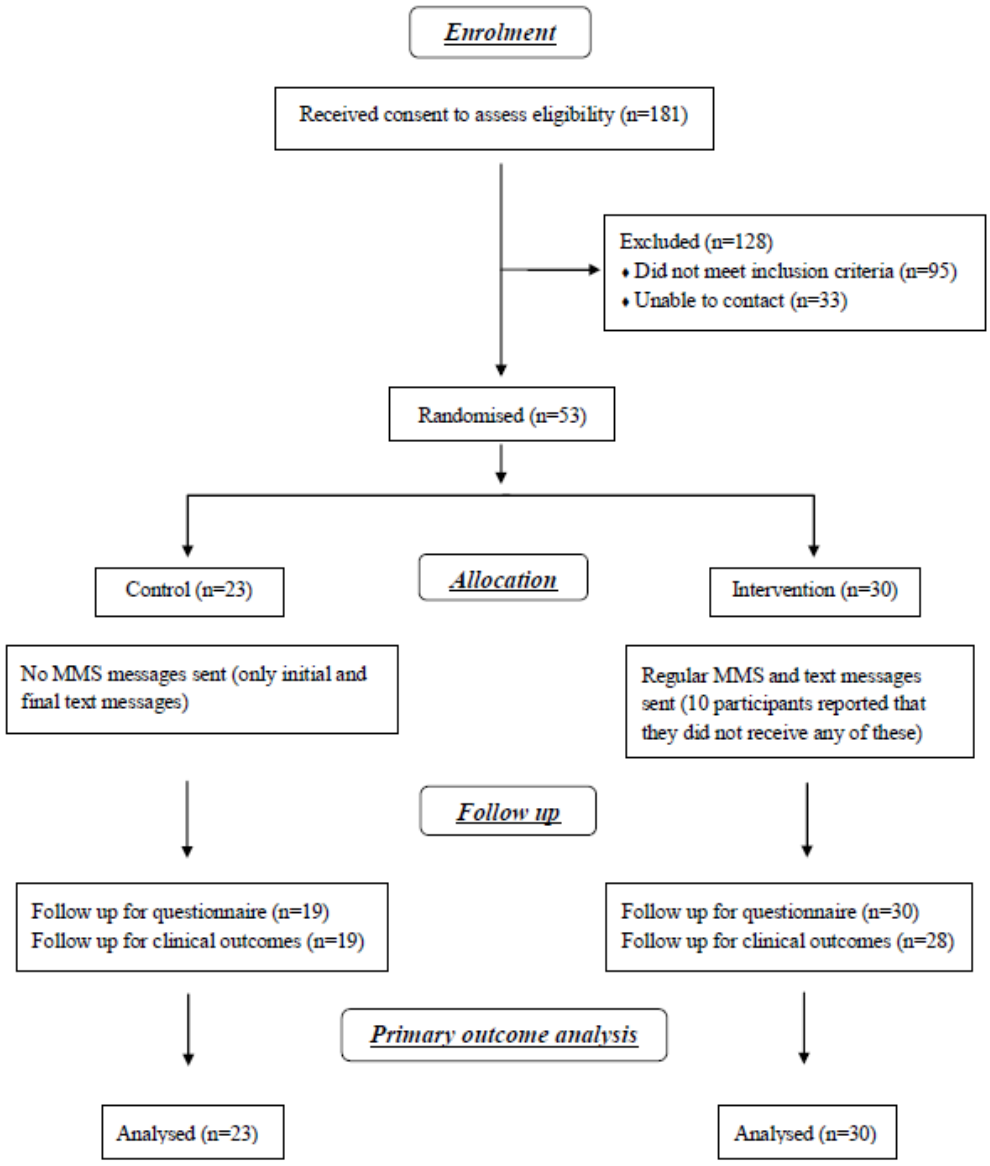
1.7 Statistical methods

We used Stata Version 11.1 for data analysis.[19] The differences in attendance rates were estimated with 95% confidence intervals (CIs) using the Student's t test. Differences in categorical outcomes were analysed using Fisher's exact test. Where the 95% CI did not include an estimate of no effect, we assumed a statistically significant difference. We analysed our data using an intention to treat approach (i.e. we included all the participants, irrespective of whether they attended the final assessment). We also conducted a per protocol analysis.

2. RESULTS

We received signed informed consent for 181 children. Of these, 53 (30%) were eligible to be randomised (Figure 1).

Figure 1. Flow diagram detailing the structure of the research project, from enrolment to allocation, follow up and primary outcome analysis.



The control group had 23 participants and the intervention group had 30. Clinic attendance was determined for all 53 children; 47 (89%) children had a follow up examination and questionnaire. At the start of the six week study, participants were categorised according to their more severely affected ear (Table 1).

In the intervention group, 10 out of 30 respondents (33%) at the end of the study reported not seeing any of the messages. Of these, two had a phone that was broken, one phone number had been incorrectly transcribed, four did not see the messages because a relative had the phone, and one participant reported that the messages did not work. We received no explanation from the remaining two participants.

Table 1. Baseline diagnoses by worse ear for all children enrolled in the study (n=53).

	Control group		Intervention group		Totals	
	No.	%	No.	%	No.	%
AOMwiP[4]	1	4	1	3	2	4
Dry perforation	2	9	7	24	9	17
CSOM[5]	20	87	22	73	42	79
Totals	23	100	30	100	53	100

Of the 28 primary carer respondents who owned the phone (mostly the child's mother or grandmother), 8 (29%) reported that they did not see any of the messages. Of the 11 primary carer respondents who did not own the phone (the phone belonged to the child's father, aunt or older sibling), six (55%) reported that they did not see any of the messages.

A. Primary outcome – clinic attendance

i) Intention to treat analysis

There was no significant difference in clinic attendance rates between the two groups (Table 2). Clinic attendance rates were 1.3 visits per child in both the control and intervention groups.

Table 2. Clinic attendance rates over the six week period for all children enrolled in the study (n = 53). Figures in parentheses represent 95% confidence intervals.

	Control group	Intervention group	Mean Difference
No. clinic attendances	31	38	
Clinic attendances per child	1.3 (0.6, 2.1)	1.3 (0.6, 1.9)	-0.1 (-1.1, 0.9)
Clinic attendances per child (for ear problem)	0.4 (0.0, 0.9)	0.2 (0.0, 0.3)	-0.3 (-0.8, 0.2)

Thirty three children (62%) attended the clinic at least once and nine (17%) attended at least once where the primary reason was for an ear problem.

ii) Per protocol analysis

In this analysis, we excluded 10 families who reported not having seen any messages. There were no significant differences in the results.

[4] Acute otitis media with perforation.
[5] Chronic suppurative otitis media.

B. Secondary outcomes

1. Ear health outcomes

We were able to perform follow up clinical examinations on 47 (89%) children (Table 3). Three children in the intervention group and one child in the control group had resolved ear perforation states at the six week assessment. Around 70% in both groups still had CSOM and 20-25% of children had a DP. There were no statistically significant changes in the diagnoses between the two groups (Tables 1 and 3).

Table 3. Follow-up diagnoses, by worse ear, for all children at week 6 (n=47).

	Control group		**Intervention group**		**Totals**	
	No.	%	No.	%	No.	%
No perforation	1	5	3	11	4	9
AOMwiP[6]	0	0	0	0	0	0
DP[7]	5	26	6	21	11	23
CSOM[8]	13	69	19	68	32	68
Totals	19	100	28	100	47	100

The average perforation size in the intervention group had increased from 20% (95% CI 15, 25) of the total eardrum at baseline to 25% (95% CI 15, 35). In the control group, the average baseline perforation size was 20% (95% CI 10, 30). At follow up it was unchanged at 20% (95% CI 11, 30). This was not a significant difference in the change in perforation size between the two groups.

Table 4. Proportion of parents who reported being happy to receive messages in the future (n=49).

	Control group		**Intervention group**		**Totals**	
	No.	%	No.	%	No.	%
Yes	16	84	21	70	37	76
No	2	11	3	10	5	10
Not sure	1	5	6	20	7	14
Totals	19	100	30	100	49	100

2. Participant views on mobile phone messaging in healthcare

We had follow up interviews with 49 (92%) participants, of which 19 were in the control group (83% of original participants) and 30 (100% of original participants) were in the intervention group. Thirty-seven (76%) of all participants said they were happy to receive health messages in the future (Table 4). This did not vary significantly between the control and intervention groups (84% versus 70%). On the morning of the follow-up interviews, we sent a plain text message in English to all participants

[6] Acute otitis media with perforation.
[7] Dry perforation.
[8] Chronic suppurative otitis media.

stating that we were in the community clinic for the follow up interviews and would attempt to make contact with them over the next few days. Nine participants (17%) presented to the clinic on the day they received this text message. Feedback provided from three participants was that they would prefer simple text messages with a specific appointment time.

DISCUSSION

This pilot randomised controlled trial did not identify significant differences in the attendance rates or ear health outcomes resulting from regular MMS and text messages. However, we were able to confirm the acceptability of mobile phone based interventions to promote health outcomes in these settings.

Strengths

The style, design and interpretation of messages were determined in consultation with local Indigenous teachers and interpreters. The decision to use MMS rather than text alone was based on local advice that MMS were a more interesting, novel and potentially a more appealing method of communication than texts, and that the videos could be shared amongst families.

Overall, feedback received from participants indicated that the information provided by the messages was interesting and appreciated and many did share the videos with others. In general, they did not object to future messages being sent. Some participants reported that they would prefer simple text messages with a specific appointment time and date. It was interesting to note that some presented spontaneously for the follow up examination after receiving a simple text message. Our video messages may have been unclear or confusing and simple text messages may be more effective.

Weaknesses

This pilot study was not able to recruit the desired sample size of 90 participants. One factor that contributed to this was unrest and fighting in one of the communities before and during the study, which restricted our time to contact and enrol families. In addition, although some surveys have reported that nearly every household in remote Indigenous communities owns a mobile phone,[13,14] in the two communities that participated in this study, phone ownership was lower than anticipated. These issues could be resolved in a similar trial conducted over a longer period of time and involving a greater number of remote communities. We were also not able to assess if participants did present to the clinic but did not wait to be seen. Lastly, we showed that messages are more likely to be seen if it is the primary carer who owns the phone.

Recommendations for research

We were not able to design our pilot study to address all the questions around the benefits or harms of mobile phones in improving health. Previous studies investigating the impact of mobile phones on behavioural change have shown significant benefits from an intervention period of between 26 and 52 weeks in low socio economic populations.[12–16, 20] It is possible that short, simple text message with appointment times or treatment at home reminders would be more effective in encouraging short term behaviour change. Alternatively, a study conducted over a longer time period would potentially be more effective.

Recommendations for clinical practice

This pilot randomised controlled trial was the first of its kind in a remote Indigenous setting to determine the acceptability and efficacy of using MMS to promote behavioural change in an Australian Indigenous population. In this small study, we were not able to document any beneficial effects. While MMS offers health care providers and health promoters an accessible, acceptable and novel approach for engaging families in remote Aboriginal communities, further research is needed to determine if it promotes clinic attendance and/or improves health outcomes.

Project 4 Prevalence data of children with otitis media living in regional and remote Northern Territory (surveillance data)

Summary

Background: The most recent report of extremely high rates of otitis media (90%) and tympanic membrane perforation (24%) in Aboriginal children in the Northern Territory was published in 2006. These data were collected in 2001 by the trained research nurses from the Menzies School of Health Research using accepted definitions and recommended diagnostic tests (pneumatic otoscopy, tympanometry and video-otoscopy).

In 2008, the Commonwealth's Emergency Response Child Health Check Initiative reported a lower rate of otitis media in children (30%, n=3463) aged 0-5 years. These data were collected by general practitioners employed on short term contracts. The definitions used for each of the diagnostic categories were not clear. Most assessments were by simple otoscopy. The use of more objective diagnostic tests was not recorded.

Aim:

To update the most recent prevalence data for otitis media in children living in remote Aboriginal communities.

Findings:

Between 2008-2010, the Menzies School of Health Research monitored otitis media in children 0-5years. Following the introduction of conjugate pneumococcal vaccination, surveys of 29 communities found similar rates of otitis media (90%) to that of the 2001 findings. The data were very similar for children aged 0-30 months and 0-5 years. In some communities, tympanic membrane perforation rates were more than 30%. Over the three year period there was no significant change in rates for all types of otitis media. The rate of CSOM was documented to be less in 2010 although this change was not statistically significant. Further surveillance with larger numbers of children will be required to clarify this issue.

Conclusion:

Otitis media remains a significant health problem in children aged 0-5 years of age in the remote Northern Territory. While the overall rate of otitis media is not decreasing, there is possibly a modest decrease in CSOM over time. Further surveillance with larger numbers of children will be required to confirm this. The difference in the overall prevalence of otitis media between previous research studies and the Emergency Response Child Health Check Initiative is likely to reflect different assessment methods and inclusion of children from outside remote Aboriginal communities in the Child Health Check Initiative.

Background

Otitis media is a significant health problem affecting Aboriginal children in remote Northern Territory. In 2006, Li (et al)[1] reported high rates of otitis media (90%) and tympanic membrane perforation (24%) in Aboriginal children in the Northern Territory. These data were collected in 2001 by the trained research nurses from the Menzies School of Health research using accepted definitions and recommended diagnostic tests (pneumatic otoscopy, tympanometry and video-otoscopy).

Two years later, the Commonwealth's Emergency Response Child Health Check Initiative,[2] the largest survey of ear health in Aboriginal children since the 1980 National Trachoma and Eye Health Program, found otitis media rates of around 30% in children aged 0-5 years (n=3,463). These data were collected by general practitioners employed on short term contracts. The definitions used for each of the diagnostic categories were not clear. Most assessments were by simple otoscopy. The use of more objective diagnostic tests was not recorded.

Despite the differing rates reported of otitis media, both reports have found rates that are unacceptable. Otitis media has profound adverse consequences on a child's hearing, often leading to periods of hearing loss. Periods of conductive hearing loss from otitis media may have a detrimental effect on speech development in children[3] and recent studies have also linked otitis media to educational problems, attention disorders and problems with social adaptation.[4]

This project aimed to survey the rates of otitis media in children aged 0-5 years in the remote communities of the Northern Territory. Comparisons would be made with the previous research data and the data from the Emergency Response Child Health Checks. This recent surveillance data will be used to inform service delivery and research priorities. While both the Menzies data and the Emergency Response data were consistent with high rates of otitis media, different management strategies would be appropriate if there had been a dramatic decrease in rates of disease.

Methods

Following a change in the conjugate pneumococcal vaccination schedule between 2008-2010, the Menzies School of Health Research monitored otitis media in children 0-5 years. In some of the 29 remote communities of the Northern Territory, it was possible to make comparisons with data that had been collected between 2001. The communities covered in this most recent period of surveillance included Victoria River (130 children), the Tiwi Islands (110 children), Roper Gulf Region (67 children), East Arnhem Land (88 children), West Arnhem Land (51 children), Kununurra (Western Australia- 76 children) and Coomalie (4 children).

Ear examinations were conducted by clinical research staff (registered nurses) who had received training in the diagnosis of middle ear disease. Each examination required a standardized ear assessment using a tympanometer (Grason Stadler GSI 38), a voroscope (WelchAllyn LumiView) with Siegel's speculum for pneumatic otoscopy, and a video-otoscope (WelchAllyn). All findings were recorded on standardized data collection forms. Video-otoscopy recordings were reviewed by a second independent observer. Any discrepancy in diagnosis was discussed with the data collecting clinicians to reach a final diagnosis that was used for analysis.

An initial detailed ear examination was performed on each child and standardised data forms were used to record the findings and document baseline demographic and medical information. Using recommended clinical criteria for diagnosis in this population,[5] we categorised middle ear states as follows: [0] normal; [1] normal mobility but abnormal appearance; [2] retracted mobile drum; [3] otitis media with effusion; [4] acute otitis media without perforation (AOMwoP); [5] acute otitis media with perforation (AOMwiP); [6] dry perforation (DP); and [7] chronic suppurative otitis media

(CSOM). Children with a diagnosis of 5, 6 or 7 for one or both ears were considered to have the most severe middle ear disease. The overall diagnosis reflected the state of the child's more severely affected ear.

Upon completion of the study, a second blinded ear health research officer made an independent diagnosis of all the cases that were accompanied by sufficiently clear video footage. Where the second blinded assessor's diagnosis disagreed with the original clinical diagnosis, a consensus diagnosis was made in consultation with a third blinded assessor.

Definitions

Six categories of middle ear conditions were defined based on criteria for diagnosis derived from specific clinical guidelines issued for this population by the Australian Office of Aboriginal and Torres Strait Islander Health (OATSIH).[5] A summary of the categories and criteria for diagnosis appears in table 1.

TABLE 1. Categories of middle ear conditions and diagnosis criteria derived from the Australian Office of Aboriginal and Torres Strait Islander Health (OATSIH) guidelines

Categories	Criteria for diagnosis
1. Normal	
2. Otitis media with effusion (OME)	Intact and non-bulging tympanic membrane (TM) and Type B tympanogram
3. Acute otitis media without perforation (AOMwoP)	Any bulging of the TM plus Type B tympanogram
4. Acute otitis media with perforation (AOMwiP)	Middle ear discharge observed and perforation recently healed or present for less than six weeks or covering less than 2% of the pars tensa of the TM
5. Dry perforation	Presence of a TM perforation without any discharge observed
6. Chronic Suppurative Otitis Media (CSOM)	Discharge observed and TM perforation present for more than six weeks and covering at least 2% of the pars tensa of the TM

Demographic and Risk Factor Questionnaire

A standardised questionnaire was also completed at the time of the surveys. This included age, gender, birth factors, antibiotic intake/type and cold symptoms. Other social risk factors were also recorded such as number of people per house, number of children in the household, percentage of houses with more than 7 people, whether the child was in childcare, maternal smoking and education, and whether the child is routinely near a campfire routinely, and whether the child was breastfed and/or uses a pacifier.

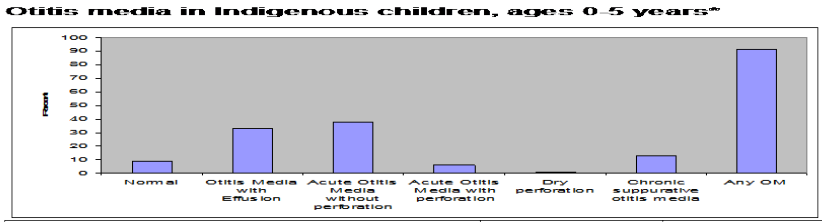
Results

Overall, 526 children and their families were seen in 24 communities as part of this surveillance project. Most children were seen (and most communities were visited) in 2009 and 2010 (see Table 2). There were 353 children aged 0-30 months seen and their results could be compared with the previous Menzies research data from 2001 (reported in 2006- see Figure 1 and Table 3).

Table 2. Number of children seen in each community, by year.

Community	Year 2008	2009	2010	Total
1	66	53	8	127
2	0	54	14	68
3	0	3	1	4
4	0	15	10	25
5	0	12	5	17
6	0	22	5	27
7	0	20	3	23
8	0	2	0	2
9	0	1	0	1
12	1	22	28	51
15	0	0	76	76
16	0	0	13	13
17	0	0	15	15
18	0	0	11	11
19	0	0	7	7
20	0	0	4	4
21	0	0	3	3
22	0	0	2	2
23	0	0	1	1
24	0	0	2	2
25	0	0	20	20
28	0	0	5	5
29	0	0	22	22
Total	67	204	255	526

Figure 1. Otitis Media in 353 Aboriginal children 0-30 months years living in remote communities of the Northern Territory examined 2008-2010



Diagnosis	Number	Percent (95% CI)
Normal	33	9 (6–12)
Otitis media with effusion	116	33 (28–37)
Acute otitis media without perforation	136	38 (33–43)
Acute otitis media with perforation	22	6 (4–9)
Dry perforation	4	1 (1–2)
Chronic suppurative otitis media	42	13 (9–16)
Any otitis media	323	91 (88–94)

Source: Menzies School of Health Research, unpublished data, 2008-2010.
*children vaccinated with Pneumococcal conjugate vaccine 7 (PCV 7).

- The previous report documented high rates of any type of otitis media (OM) (90%) and any tympanic membrane perforation (24%) in Aboriginal children up to 30 months of age living in rural and remote communities of the Northern Territory[1].
- Surveys following the introduction of conjugate pneumococcal vaccination documented similar rates of disease[2] (see figure above).
- The Northern Territory Emergency Response was the largest survey of ear health in Aboriginal children since the 1980 National Trachoma and Eye Health program. Around 30% of 3,463 children aged 0-5 years were identified with otitis media[3].
- Children seen by audiology and ENT services had higher rates of otitis media. Around 76% of 1,441 children aged 0-5 years had any type of OM and 24% were diagnosed with tympanic membrane perforation[4].

(1) Li SQ, Gubhaju SL, Turpin d'Espaignet E, Paterson BA. Ear health in infancy to young adulthood: health status in the Northern Territory 2006. Department of Health and Community Services, Darwin, 2007.
(2) Menzies School of Health Research, unpublished data, 2008-2010.
(3) Australian Government Department of Health and Ageing. Progress of the Northern Territory Emergency Response Child Health Check Initiative: Health Conditions and Referrals. 2008.
(4) Australian Institute of Health and Welfare. Ear and hearing health of Indigenous children in the Northern Territory, 2011. Cat. no. IHW 60.

Table 3. Otitis Media in 353 Aboriginal children 0-30 months years living in remote communities of the Northern Territory examined 2008-2010

Diagnosis	Number	Percent (95% CI)
Normal	33	9 (6-12)
Otitis media with effusion	116	33 (28-37)
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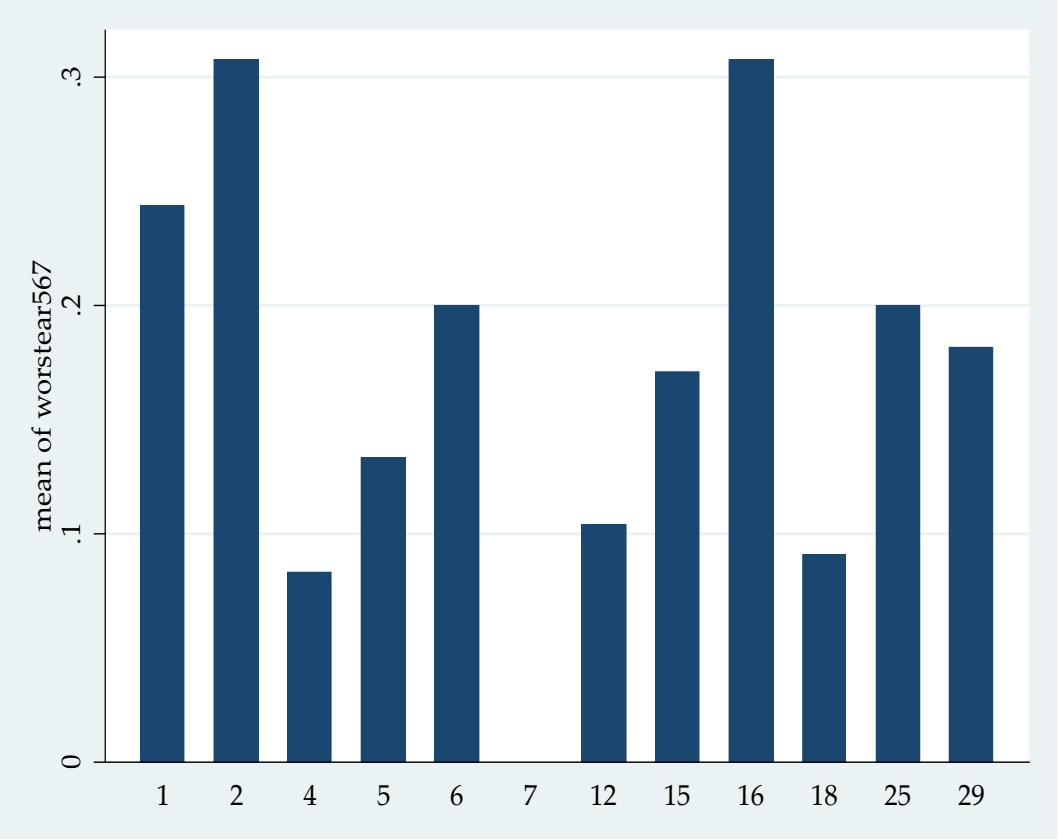
Acute otitis media with perforation	22	6 (4-9)
Dry perforation	4	1 (1-2)
Chronic suppurative otitis media	42	13 (9-16)
Any otitis media	**323**	**91 (88-94)**

There were 526 children aged 0-5 years seen and their results could be compared with the previous Child Health Check Initiative data from 2008 (see Table 4). The rates of all otitis media and the rates of each of otitis media were very similar for both the 0-30 month and the 0-5 years age categories.

Eleven of the 29 communities (38%) had children suffering from tympanic membrane perforation, with rates reaching as high as 30% in 2 communities (see Figure 2). All the communities where at least 15 children were examined had at least 1 child with a perforated tympanic membrane. All of these 10 communities met the World Health Organization criteria for middle ear disease being a massive public health problem requiring urgent attention.

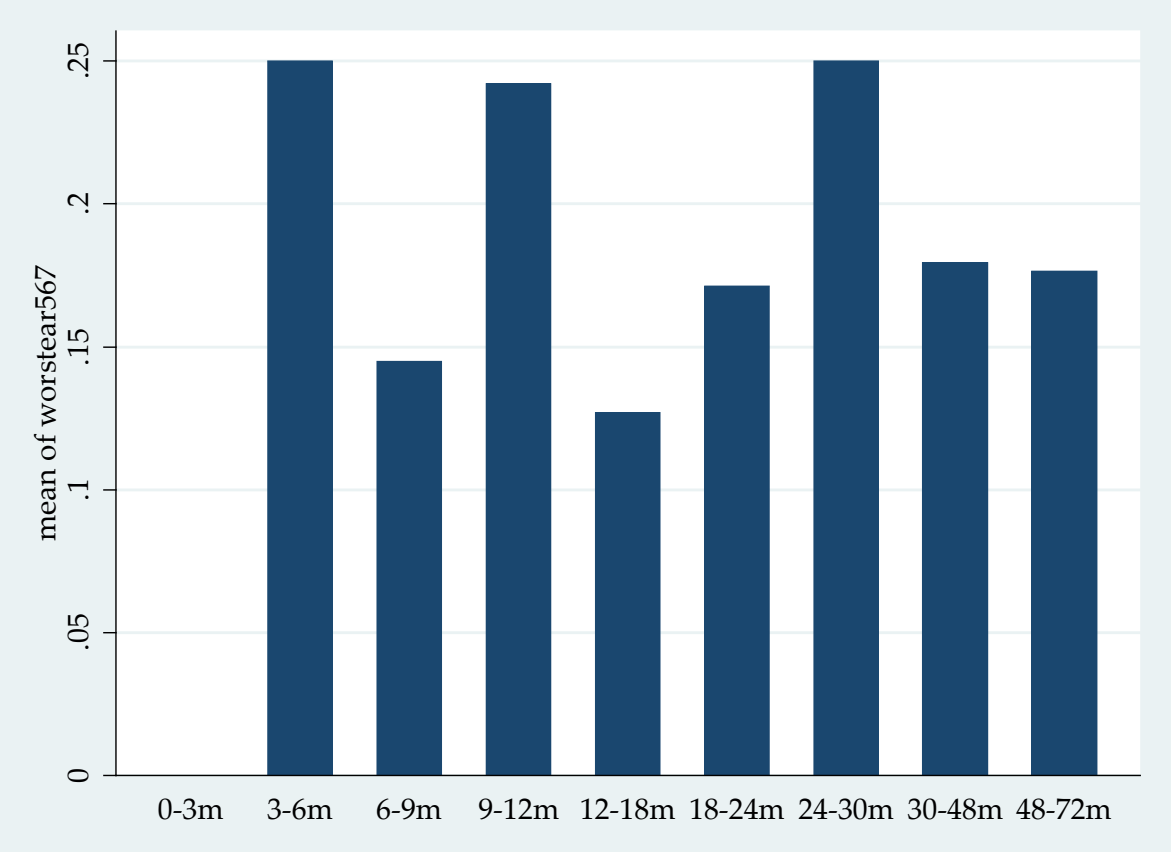
Figure 2. Proportion of children seen with diagnosis of tympanic membrane perforation (TMP) by community.



Unfortunately tympanic membrane perforation was detected in all age groups except babies less than 3 months of age. Rates of tympanic membrane perforation varied from 15-25% with no clear evidence of either an increase or decrease with age after 3 months (see Figure 3). Unfortunately,

nearly all of the tympanic membrane perforation were associated with ear discharge. Since the majority of children were aged between 6-30 months, estimates for these age groups will be most precise. Further analysis of these data will determine whether there has been progression or improvement with age for number of ears affected (unilateral or bilateral perforation) and size of the tympanic membrane.

Figure. 3 Proportion of children seen with diagnosis of tympanic membrane perforation (TMP), by age group.



The average of children seen was 18-24 months. The average birthweight was 3.0 kg (less than the Australian average and non-Aboriginal NT average). The varying clinical presentations of otitis media included otitis media with effusion (~33%), acute otitis media without perforation of the eardrum (~38%), acute otitis media with perforation (~6%), otitis media with dry perforation (~1%) and chronic suppurative otitis media (~13%) (see Figure 1, Table 3 and 4). The presence of cough (~20%), runny nose (~30-40%) and skin infection (~20%) were also common.

Data comparisons were made over the three year period (2008-10) for all children. As the amount of information for each child was not always complete, the denominators for each of the comparisons varied as shown (see Table 4). Otitis media risk factors that were assessed included crowding, child care, cigarette smoke exposure, campfire smoke exposure, breastfeeding, maternal education, and use of a pacifier. Most of the children seen in the study had been breast fed and had not used a pacifier. Mothers reported relatively low levels of education but the number engaging in further training or study after school appeared to increase over time (18 vs 33%). Child care attendance was uncommon but increasing (3% vs 20%). Exposure to cigarette and campfire smoke was common although it did vary significantly over time. Most children lived in crowded household with 8-9 occupants and 2-3 other young children. Over time there was a significant decrease in the taking of macrolide

antibiotics (36% vs 5%), but there was an overall increase in the prescribing of antibiotics in general (25% vs 36%).

Table 4. Characteristics by study year.

	2008	**2009**	**2010**	
n	63	183	191	437
Birth weight (kg)	2.914	3.063	2.963	
n	63	167	187	
Gestational age (weeks)	37.5	38.07	38.00	
n	67	204	255	
Mean age (months)	18.97	16.86	24.4	
Antibiotics (5 weeks) n	65	195	242	
any	25%	23%	36%	**p=0.007**
betalactam	64%	83%	82%	p=0.284
macrolide	36%	13%	5%	**p=0.005**
topical	na	19%	22%	p=0.124
male	52%	47%	50%	
Ear Status				
n	65	195	250	
Normal	11%	3%	15%	
OME	26%	38%	36%	p=0.214
AOMwoP	40%	41%	31%	p=0.093
AOMwiP	8%	6%	6%	
Dry Perforation	0	2%	2%	
CSOM	15%	12%	10%	p=0.387
No. children with TMP	N=15	N=37	N=43	N=95
Other health measures				
n	**59**	**196**	**253**	
Any cough	18%	12%	22%	
Runny nose	39%	20%	39%	
Any skin condition	12%	19%	19%	
Risk factors				
n	~63	~195	~250	
People per house	9.35	8.72	8.45	
Children < 5 yo per house	2.63	2.47	2.20	
% with >7 people	78%	66%	62%	p=0.064
Child care (any)	3%	10%	20%	**p<0.001**
Cig smoke – mum	38%	61%	56%	p=0.006
Child near campfire	49%	27%	30%	**p=0.003**
Mum education	18%	24%	33%	**p=0.022**
Breastfed	88%	95%	92%	p=0.075
Pacifier	16%	21%	24%	p=0.397

The rates of all otitis media and the different types of otitis media did not vary significantly over time. There was less acute otitis media without perforation and chronic suppurative otitis media detected in 2010 but this difference was not statistically significant (see Table 4).

When comparing children with tympanic membrane perforation (n=78) and children without tympanic membrane perforation (n=346) the only significant differences were increased use of topical antibiotics (as expected for discharging ears) and increased rate of runny nose detection (nasal discharge visible from a distance of 3 feet) (see Table 5). Children with tympanic membrane perforation lived in more crowded houses and were more likely to be exposed to cigarette smoke. However, these differences were not statistically significant. There was no protection apparent from breast feeding or harm apparent from pacifier use or child care attendance.

Table 5. Comparison of children with and without tympanic membrane perforation (TMP)

	No TMP	**TMP**		
n	**346**	**78**		
Birth weight (kg)	2.99	3.02		
n	**331**	**74**		
Gestational age (weeks)	37.95	38.05		
n	**415**	**95**		
Mena age (months)	20.6	21.5		
Antibiotics (5 weeks) n	**394**	**92**		
any	27%	38%		
betalactam	80%	83%		
macrolide	10%	8%		
topical	9%	53%		
	415	**95**		
male	50%	44%		
Other health measures				
n	**411**	**94**		
Any cough	17%	20%		
Runny nose	29% [25 to 34]	44% [34 to 54]	15% [4 to 26]	p=0.007
Any skin condition	16%	23%		
Risk factors				
n	**400**	**93**		
People per house	8.53	9.17		
Children < 5 yo per house	2.30	2.68		
% with >7 people	64% [59 to 69]	73% [64 to 82]	9% [-1 to 19]	p=0.115
Child care (any)	19%	14%		
Cig smoke – mum	54% [49 to 59]	63% [53 to 73]	9% [-2 to 20]	p=0.134
Child near campfire	32%	29%		
Mum education	29%	25%		
Breastfed	93%	89%		
Pacifier	21%	23%		

Conclusion

Approximately 90% of young children surveyed who were living in the remote communities of the Northern Territory and the Torres Strait Islands had some form of otitis media. This rate is similar to that reported Northern Territory in 2006 (from a study conducted in 2001).[1] In some communities, tympanic membrane perforation rates were more than 30%. While the overall rate of otitis media is not decreasing, there is possibly a modest decrease in CSOM over time. Further surveillance with larger numbers of children will be required to confirm this. The high rates of all forms of otitis media found in this survey highlight the urgency needed in providing treatment and management of this chronic disease in children within remote Northern Territory communities.

The rates of otitis media described in this surveillance project were much greater than figures reported in 2008 by the Emergency Health Check Initiative.[2] The difference in the overall prevalence of otitis media between previous research studies and the Emergency Response Child Health Check Initiative is likely to reflect different assessment methods and inclusion of children from outside remote Aboriginal communities in the Child Health Check Initiative.

CONCLUSIONS

Project 1 (*NHMRC Proposal)*
The proposed randomised controlled trial will provide an important contribution towards the assessment of clinical interventions for otitis media in Indigenous children. Unfortunately, in the Northern Territory this remains a common disease which potentially has a profound adverse effect on child hearing and development. This proposed research project will address 2 medical treatment options, both of which are used commonly but are not consistent with most current clinical practice guidelines. The trial will result in the best available evidence to guide the medical management of chronic suppurative otitis media in high-risk children. The results will have important implications for all disadvantaged populations suffering this disease, especially for Indigenous Australians (where rates are unacceptably high). The usefulness of training and educational materials for Aboriginal Health Workers will also be examined. These resources should also support other workers in disadvantaged populations. This aspect is especially important for the ongoing management of this chronic disease.

The design and scope of this study will lead to more robust data surrounding issues of effective clinical management of chronic suppurative otitis media in high-risk children. The study also meets the goals of the 'Close the Gap' initiative in Indigenous health that identifies hearing health in the Northern Territory as a priority.

Project 2 *(Systematic Review)*
Adherence to treatment is a major issue in the effective clinical management of otitis media. The systematic review, which followed the NHMRC guidelines of systematic reviews, found some evidence to suggest that regular SMS messaging (sent via mobile phones to persons who have conditions that require daily therapy and ongoing medical follow-up to improve adherence) is effective. However care should be taken in its application. Important individual, family, treatment and health service characteristics can affect the effectiveness of SMS leading to improved adherence. These factors represent real or perceived barriers to adherence. While the results of the systematic review are encouraging, further randomised trials involving Indigenous Australians are needed.

Project 3 *(Randomised Controlled Trial)*
This pilot randomised controlled trial was the first of its kind in a remote Indigenous setting to determine the acceptability and efficacy of using MMS (video messaging) and texting to promote behavioural change in an Australian Indigenous population. In this small study, there were no benefits from MMS'ing or texting in terms of clinical improvement or attendance rates. It is possible however, that short, simple text messages with appointment times and/or treatment at home reminders without the video messaging would be more effective in encouraging short term behaviour change. Furthermore, a study conducted over a longer time period would potentially be more effective.

While MMS offers health care providers and health promoters an accessible, acceptable and novel approach for engaging families in remote Aboriginal communities, further research is needed. It will be important to explore a broader range of characteristics (within the context of MMS'ing and texting) which may potentially promote clinic attendance and/or improves health outcomes.

Project 4 *(Prevalence Study)*
Different rates of otitis media have been reported for children living in the remote Northern Territory communities. The variation between the rates has been significant. Prevalence data over a three year period confirmed that approximately 90% of children in these areas will have some form of otitis media. In some communities, tympanic membrane perforation rates were as high as 30%. This has

major implications for 'whole of community' and their children's well being in terms of later learning and development. This is in community areas that are already suffering significant disadvantage. It was also confirmed in this data gathering that the rate is not decreasing. The difference in the overall prevalence of otitis media between previous research studies and the Emergency Response Child Health Check Initiative is likely to reflect different assessment methods and inclusion of children from outside remote Aboriginal communities.

The high rates of all forms of otitis media in Indigenous children highlight the extreme urgency needed in providing clinical treatment and ongoing management of this chronic disease. More effective prevention, earlier identification, better treatment, and more monitoring are especially needed for acute otitis media with perforation and chronic suppurative otitis media.

Summary

The four projects have been conducted by the Menzies School of Health Research Ear Health Team as part of their broader research program. The focus on chronic suppurative otitis media (CSOM) is appropriate. CSOM remains the most disabling form of otitis media and it continues to present a major challenge to Australian Aboriginal families and their health care providers. Unfortunately, there is a lack of high quality research addressing this condition. Project 1 has resulted in a NHMRC funding submission for the largest randomised trial of treatment for CSOM in Aboriginal children. The treatments to be tested are both identified as research priorities by the experts contributing to the Technical Advisory Group of the updated Clinical Care Guidelines. The development of the funding application is a critical first step in linking high quality research studies to better clinical practice in remote Aboriginal communities.

Projects 2 and 3 have addressed the potential role of mobile phones in improving health outcomes for Aboriginal children with CSOM. The systematic review identified a small number of trials that were conducted in different populations and addressed different conditions. While the results were encouraging, further high quality research will be needed. Project 3 describes the first randomised controlled trial involving Australian Aboriginal families. The study demonstrated that text and MMS messages are acceptable to Aboriginal families from 2 remote Aboriginal communities. However, use of these messages did not substantially improve clinical practice.

Project 4 has provided the latest data on the burden of CSOM in a range of Aboriginal communities in the Northern Territory. Unfortunately, the very high rates of all forms of otitis media persists. The good news is that the data are consistent with a reduction in the overall rates of CSOM in young children. This information, along with current evidence-based treatment recommendations and training, is disseminated to remote community staff by the Menzies Ear Health team and the visiting Northern Territory Government Tele-Otology Outreach Team. Project 4 also highlights the importance of diagnostic accuracy in studies reporting the prevalence of all forms of otitis media. Large differences in estimates of burden of disease are possible if different methods of diagnosis are used. For high risk Aboriginal children, there is a need for a consistent diagnostic approach that utilises appropriate technology (tympanometry and video otoscopy) in order to ensure estimates of burden of disease are not misleading.

CSOM in remote Aboriginal communities is essentially a disease of poverty. While improvements in the social determinants of health are likely to be beneficial, better primary health care is needed to minimise the impact of this disease on children who have already been affected. These projects have contributed important new information about the current burden of disease and identified some important opportunities for better health in the future.

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Project 1

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APPENDIX 1

Table 1: Excluded studies and reasons for exclusion

Author/s	Pub Date	Title	Reference	Intervention	Reason for exclusion
Ammassari A, Trotta MP, Shalev N, Tettoni MC, Maschi S, Di Sora F , *et al.*	2011	Timed short messaging service improves adherence and virological outcomes in HIV-1-infected patients with suboptimal adherence to antiretroviral therapy	Journal of Acquired Immune Deficiency Syndromes, 2011 58:4 (e113-e115)	Automated time SMS reminders at the time of dosing. 9-month intervention period.	Study design is 'single-arm open-labelled'. Inclusion offered to all patients reporting any degree of suboptimal adherence according to identified measures. No control arm. Limited information - Letter to Editor.
Bos A, Hoogstraten J, Prahl-Andersen B.	2005	Failed appointments in an orthodontic clinic.	American Journal of Orthodontics and Dentofacial Orthopedics, 2005 Mar;127(3):355-7.	Intervention was a reminder for a single appointment. 4 study arms. i) Telephone, ii) mail, iii) SMS, iv) control. Reminder 1 day before the appointment.	All booked patients over a 3-week period were 'divided' into 4 groups. For the 'follow-up" component of the study ' 30 "random subjects" from each group were interviewed. Intervention was a reminder for a single appointment.
Chen ZW, Fang LZ, Chen LY, Dai HL.	2008	Comparison of an SMS text messaging and phone reminder to improve attendance at a health promotion center: a randomized controlled trial.	Journal of Zhejiang University SCIENCE B, 2008 Jan;9(1):34-8.	Intervention was a reminder for a single appointment. Randomised to 3 groups: i) SMS reminder, ii) telephone contact, iii) control - no reminder. Reminder 72 h prior to the appointment.	Study concerned improving attendance for periodic appointments for preventative health screening checks.

da Costa TM, Salomao PL, Martha AS, Pisa IT, Sigulem D.	2010	The impact of short message service text messages sent as appointment reminders to patients' cell phones at outpatient clinics in Sao Paulo, Brazil	International Journal of Medical Informatics, 2010 Jan; 79 (1): 65-70	SMS text message sent 24 h before appointment to all patients. 11 month study.	Not RCT. Intervention was a reminder for a single appointment.
Fairhurst K, Sheikh A.	2008	Texting appointment reminders to repeated non-attenders in primary care: randomised controlled study.	Quality & Safety in Health Care", 2008 Oct;17(5):373-6.	Randomised to two groups: i) SMS text message sent, ii) Control (no reminder)). A text message reminder of the appointment sent between 0800-0900 on the morning preceding afternoon appointments and between 1600-1700 on the afternoon preceding morning appointments. Reminders for Monday morning sent on Friday afternoon.	Attendance for single appointment only. Participants were patients who failed to attend two or more routine appointments in the preceding year. All appointments made by these patients over a six month period were included in the study. Patients with no mobile phone or were unable to provide a mobile telephone numbers were subsequently excluded.
Fischer HH, Moore SL, Ginosar D, Davidson AJ, Rice-Peterson CM, Durfee MJ, MacKenzie TD, Estacio RO, Steele AW.	2012	Care by Cell Phone: Text Messaging for Chronic Disease Management	American Journal of Managed Care, 2012 Feb; 18 (2): e42-7	Participants received text message prompts in their choice of English or Spanish over a 3-month period. Messages requesting fasting BSL readings were sent to each patient at 7.15am 3 times a week. Appointment reminder sent 1-day before appointment.	Patient response to SMS message required. Intervention a text communication system to improve self management of diabetes. A feasibility study - not sufficiently powered.
Franklin VL, Waller A, Pagliari C, Greene SA.	2006	A randomized controlled trial of Sweet Talk, a text-	Diabetic Medicine, 2006 Dec;23(12):1332-8.	Randomised to i) conventional insulin therapy, ii) conventional therapy and	Patient response to SMS message required. Intervention offered a means of contact and

		messaging system to support young people with diabetes.		Sweet Talk, or iii) intensive insulin therapy and Sweet Talk. Goal setting at clinic visits was reinforced by daily text-messages from the Sweet Talk software system, containing personalized goal-specific prompts and messages tailored to patients' age, sex and insulin regimen. Participants to respond to texts by sends BSLs and Insulin dose.	support between clinic visits.
Grodzicki T, Wizner B, Gaciong Z, Narkiewicz K.	2009	Education using SMS increases efficacy of treatment of hypertensive patients	Nadcisnienie Tetnicze, 2009 13:3 (147-157)	Randomised into 2 groups differing frequency of text messages sent (once or twice weekly) Each SMS contained 2 modules, i) a reminder about medication; ii)information about life style modification. 6 month study.	A translated abstract available only. No control group.
Guy R, Hocking J, Wand H, Stott S, Ali H, Kaldor J.	2012	How effective are short message service reminders at increasing clinic attendance? A meta-analysis and systematic review	Health Services Research, 2012 47:2 (614-632)	18 reports (10 controlled observational studies, 8 RCTs). Reviewed studies which involved a comparison of appointment attendance rates between patients who did and did not receive attendance reminders.	Study designs other than RCT included. Focus on attendance for one-off appointments.
Hardy H, Kumar V, Doros G, Farmer E, Drainoni ML, Rybin D, Myung D, Jackson J, Backman E, Stanic A,	2011	Randomized Controlled Trial of a Personalized Cellular Phone Reminder system to Enhance	AIDS Patient Care & STDs, 2011 Mar; 25(3): 153-61	Randomized to personalised text messages daily or reminder beep at the time of dosing. 6 week study.	No control group. Patient response by text message required.

Skolnik PR.		Adherence to Antiretroviral Therapy			
Hasvold, PE, Wootton R.	2011	Use of telephone and SMS reminders to improve attendance at hospital appointments: a systematic review	Journal of Telemedicine & Telecare, 2011; 17 (7): 358-64	29 Studies included (counted as 33 studies because 4 studies had 2 different intervention arms). Focus non-attendance for appointments in health care settings.	Focus on attendance for one-off appointments. Of 29 studies, 9 were RCTS, design of the rest not known.
Kim YS; Cho S.J	2007	Mobile phone message versus postal reminders to increase treatment adherence after lipid lowering therapy among hyperlipidemic patients in primary care	Value In Health, Volume: 10 Issue: 3 Pages: A57-A57	Compared mobile phone messaging and postal reminders as means of increasing the follow-up attendance rate	Focus on attendance for one appointment at 24 weeks post therapy. Abstract for conference presentation or poster only.
Koury E, Faris C.	2005	Mobile phones and clinic appointments: the start of a beautiful new friendship?	British Journal of Healthcare Computing & Information Management, 2005; 22(8): 18-20.	Conference abstract only. RCT was conducted to assess the feasibility and effect of using SMS text messaging as a means of reminding patients of their appointments at an NHS OPD	Focus on attendance for one appointment.
Kunawararak P, Pongpanich S, Chantawong S, Pokaew P, Traisathit P, Srithanaviboonchai K, Plipat T.	2011	Tuberculosis treatment with mobile-phone medication reminders in northern Thailand.	The Southeast Asian Journal of Tropical Medicine and Public Health, 2011 Nov;42(6):1444-51.	Multi-drug resistant (MDR) and non-MDR-TB patients randomised into either Model 1 (DOTS conventional treatment strategy) or Model 2 (DOTS + phone call reminder to take	Intervention consisted of telephone call reminder and not text message.

				medication)	
Leong KC, Chen WS, Leong KW, Mastura I, Mimi O, Sheikh MA, Zailinawati AH, Ng CJ, Phua KL, Teng CL.	2006	The use of text messaging to improve attendance in primary care: a randomized controlled trial.	The Journal of Family Practice, 2006 Dec;23(6):699-705.	Two intervention arms consisted of text messaging and mobile phone reminders 24-48 hours prior to scheduled appointments. Control group - no intervention.	Focus on attendance for one appointment.
Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, *et al*	2010	Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial	The Lancet, 2010 Nov 27;376 (9755):1838-45	Randomised to i) SMS intervention or ii) standard care. Intervention group received weekly SMS messages and required to respond in 48 h.	Patients were required to respond within 48 h.
Liang X, Wang Q, Yang X, Cao J, Chen J, Mo X, Huang J, Wang L, Gu D.	2011	Effect of mobile phone intervention for diabetes on glycaemic control: A meta-analysis	Diabetic Medicine, 2011 28:4 (455-463)	22 Studies - 12 studies used SMS + Internet. 8 Studies SMS alone (interactive + patient report of BSLs). 2 studies compared mobile phone verses web based interaction.	Interventions very hetrogenous. Included Type 1 and Type 2 diabetic patients.
Liew SM, Tong SF, Lee VK, Ng CJ, Leong KC, Teng CL.	2009	Text messaging reminders to reduce non-attendance in chronic disease follow-up: a clinical trial.	British Journal of General Practice, 2009 Dec;59(569):916-20.	Randomised to 3 groups, i) text messaging reminder, ii) telephone reminder, iii) control. Reminder was sent 24-48 hours prior to the appointment.	Focus on attendance for single appointment.
Miloh T, Annunziato R, Arnon R, Warshaw J, Parkar S, Suchy FJ, Iyer K, Kerkar N.	2009	Improved Adherence and Outcomes for Pediatric Liver Transplant Recipients by Using Text	Pediatrics, 2009 Nov; 124(5):e844-50	Patients' records reviewed comparing the year before and year after the intervention.	Not RCT.

		Messaging			
Nelson TM, Berg JH, Bell JF, Leggott PJ, Seminario AL.	2011	Assessing the effectiveness of text messages as appointment reminders in a pediatric dental setting	The Journal of the American Dental Association, 2011 Apr; 142 (4): 397-405	Randomly assigned to 2 groups i) SMS reminder, ii) voice message (control)	Focus on attendance for one appointment.
Perron NJ, Dao MD, Kossovsky MP, Miserez V, Chuard C, Calmy A, Gaspoz JM.	2010	Reduction of missed appointments at an urban primary care clinic: a randomised controlled study.	BMC Family Practice, 2010 Oct 25;11:79.	Randomised to 2 groups. 1. Sequential intervention starting 48 hours prior to appointment. Sequence = i) phone call (fixed or mobile); ii) SMS if no response after 3 attempts if patient had mobile phone; iii) if no response postal reminder. 2. Control - no intervention. 3 month intervention time period.	Focus on attendance for one appointment.
Prasad S, Anand R.	2012	Use of mobile telephone short message service as a reminder: the effect on patient attendance.	International Journal of Dentistry, 2012 Feb; 62(1):21-26.	Randomised to SMS reminder or Control. Reminder sent 24 h prior to appointment.	Focus on attendance for one appointment.
Taylor NF, Bottrell J, Lawler K, Benjamin D.	2012	Mobile telephone short message service reminders can reduce nonattendance in physical therapy outpatient clinics: a randomized controlled	Archives of Physical Medicine and Rehabilitation, Jan;93(1) :21-6	Randomised to SMS reminder or Control. SMS reminder sent 2-days before appointment if the appointment was made more than 3 days before the appointment or the day before the appointment if the	Focus on attendance for one appointment.

		trial.		appointment was within 2 days.	
Wei J, Hollin I, Kachnowski S.	2011	A review of the use of mobile phone text messaging in clinical and healthy behaviour interventions	Journal Of Telemedicine And Telecare, Volume: 17 Issue: 1 Pages: 41-48	Literature Review. 24 studies included (16 RCTs, 8 Clinical Management, 8 clinical management, 9 health-related behaviour modification).	Wide range of study designs included, including before and after with no control. No meta-analysis. Studies included various outcome measures.
Yang Y, Sangasubana N, Bentley S I, Thumula V, Mendonca C.	2008	Randomized controlled trial of telephone, email and text messaging reminders on patient compliance with antibiotic regimen	Value In Health, Volume: 11 Issue: 3 Pages: A104-A104	Randomized to telephone, email, SMS follow-up or control groups. Email, SMS, telephone call made on 4th day of antibiotic regimen.	Conference extract only.

Table 2: A list of the six studies eligible for inclusion

Author/s	Pub Date	Title	Reference	Study Characteristics	Main Findings
da Costa TM, Barbosa BJ, Gomes e Costa DA, Sigulem D, de Fátima Marin H, Filho AC, Pisa IT.	2012	Results of a randomized controlled trial to assess the effects of a mobile SMS-based intervention on treatment adherence in HIV/AIDS-infected Brazilian women and impressions and satisfaction with respect to incoming messages	International Journal of Medical Informatics, 2012 Apr;81(4):257-69	Randomised Controlled Trial. Study context: Brazil Randomised to standard care or standard care plus SMS messaging. Intervention delivered over 4-months. The SMS message automatically sent on Saturday and Sunday and alternate days through the working week. Participants were required to own a mobile phone and be experienced SMS users. No participant response required. 29 participants were randomised (Control n = 15 and Intervention n=14). Of those allocated to the intervention, only 9 received the allocated intervention (5 did not receive the intervention due to phone theft or loss, change of number or leaving the broadcast area). Eight participants in the Intervention group were included in the analysis. Two participants from the control group are reported as 'lost to follow-up' and were excluded from the analysis. 5 of 8 study quality measures met.	Outcomes measured included – self reporting, counting of pills and microelectronic monitoring via pill bottle lids. Adherence measured as exceeding 95% of participants. *Self reporting:* 100% participants in the Intervention group adherent (n = 8) compared to 85% participants in the Control group (n = 11) adherence. *Counting of Pills:* 3 participants (38%) in the Control group and 4 participants (50%) in the Intervention group were measured as adherent using this method. *Microelectronic monitoring*: 6 participants in the control group (46%) compared with 6 participants in the intervention group (75%) were measured as adherent using this method. The study was under powered.

Horvath T, Azman H, Kennedy GE, Rutherford GW..	2012	Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection	Cochrane Database, DOI: 10.1002/14651858.CD009756	Systematic Literature Review & meta-analysis (2 Randomised Control Trials) Studies' context: Kenya. In 1 study all participants provided with mobile phones & no response from patients required; in the other study patients required access to own mobile phone and a response from patient required within 48 h. Studies conducted over 48-52 wks.	In meta-analysis of both trials, any weekly text-messaging (i.e. whether short or long messages) was associated with a lower risk of non-adherence at 48-52 weeks (RR 0.78, 95% CI 0.68 to 0.89). The effect of short weekly text-messaging was also significant (RR 0.77, 95% CI 0.67 to 0.89).
Pop-Eleches C, Thirumurthy H, Habyarimana JP, Zivin JG, Goldstein MP, de Walque D, MacKeen L, Haberer J, Kimaiyo S, Sidle J, Ngare D, Bangsberg DR.	2011	Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text messagereminders.	AIDS, 2011 Mar 27;25(6):825-34.	Randomised Controlled Trial. Study context: Kenya Randomised to 4 SMS reminder interventions (short daily SMS (n=70), long daily SMS (n=72), short weekly SMS (n=73), and long weekly SMS (n=74)) or control (n=139). Messages sent out at 12pm. Study conducted over 48 wks. 7 out of 8 study quality measures[1] clearly met.	Proportion of at least 90% adherence according to intervention by intention-to-treat at 48 weeks: Control (n=139) - 0.40; Daily (all) (n=142) - 0.41 (*p* 0.92); Weekly (all) (n=147) – 0.53 (*p* 0.03); Short (all) (n=143) – 0.47 (*p* 0.27); Long (all) (n=146) – 0.47 (*p* 0.24). Participants in groups receiving weekly reminders were significantly less likely to experience treatment interruptions exceeding 48 h during the 48-week follow-up period than participants in the control groups (81 vs 90%, P = 0.03)
Sharma R, Hebbal M, Ankola AV, Murugabupathy V.	2011	Mobile-phone text messaging (SMS) for providing oral health education to mothers of preschool children in Belgaum City	Journal of Telemedicine and Telecare, Volume: 17 Issue: 8 Pages: 432-436	Randomised Controlled Trial. Study context: India 150 children randomised to text message group or the pamphlets group. 3 text messages per day sent and 3 pamphlets sent home with	143 out of 150 children and their mothers completed the study. Pamphlets group (n=72) and text message group (n=71). The Visible Plaque Index (VPI) score was not significantly different between the

				children each day. Messages were repeated weekly. Study conducted over 4 wks.3 out of 8 study quality measures[1] clearly met.	groups – Difference 1.81% (*p* 0.27, 95%CI -1.39-5.01).
Strandbygaard U, Thomsen SF, Backer V.	2010	A daily SMS reminder increases adherence to asthma treatment: a three-month follow-up study.	Respiratory Medicine, 2010 Feb;104(2):166-71.	Randomised Controlled Trial. Study context: Denmark 26 participants randomised to SMS reminder or Control. Reminders sent 10am daily. Study conducted over 12 wks. 4 out of 8 study quality measures[1] clearly met.	22 of 26 participants completed the study (Intervention n=12, Control n=14). Analysis not by intention-to-treat. The absolute difference in mean adherence rate between the 2 groups after 12 weeks was 18%, (95% CI 3 - 32.%, $p = 0.019$)
Ting TV, Kudalkar D, Nelson S, Cortina S, Pendl J, Budhani S, Neville J, Taylor J, Huggins J, Drotar D, Brunner HI.	2012	Usefulness of cellular text messaging for improving adherence among adolescents and young adults with systemic lupus erythematosus	The Journal of Rheumatology, 2012 39:1 (174-179)	Large study with sub-study. i) Observational study: visit adherence SMS intervention (n=70, 7% (n=5) male) – observational study; SMS sent to all participants 7 days, 3 days, and 1 day prior to each scheduled follow-up clinic appointment. ii) RCT: medication (1 medication type) adherence SMS intervention involving subgroup of participants (n=41). Randomised to SMS group (n=19) and Standard of Care (SOC) (n=22). SMS group received a standardised daily SMS for HCQ medication as prescribed in addition to the printed information sheet given to the SOC group. Study conducted over 14 mths 2 out of 8 study quality measures[1] clearly met.	No patients with adherence >80% - SOC n=6 (27%), SMS n=7 (37%) Serum HCQ levels SOC mean = 0.46 (SD 0.55), SMS mean = 0.64 (SD 0.45), Total participants (n=41) mean = 0.54 (SD 0.51). With blood levels of HCQ ≥ 900mg/ml reflecting adequate exposure to HCQ 10 out of 41 (25%) participants had sufficiently high levels. 12 out of 41 (29%) participants had undetectable levels. Mean self reported adherence rates across both groups were 80% (SD 20%). Cellular text message reminders (CTMR) did not influence adherence to HCQ medication over time.

[1] Eight quality measures include; randomised; concealment of allocation; used appropriate controls; follow-up of patients or episodes of care; blinded assessment of 1º outcome; baseline measurement; reliable primary outcome measure; protection against contamination.