The health of newly-arrived refugees in developed countries: what are some of the differences from the majority population?

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Summary

The social determinants of health, exposure to different environmental conditions and infectious diseases, lack of health infrastructure, ethnicity, undernutrition, and the sequelae of torture and trauma, are just some of the determinants likely to impact on the health of refugees after they arrive in developed countries. It is only when such differences in health issues are noticed, researched and published, that the established protocols and guidelines can take the particular issues that affect newly-arrived refugees into account. Without research to inform the evidence, the health care delivered to this vulnerable group of people is likely to be inadequate. This body of research aims to look at some pertinent clinical problems in newly-arrived refugees that are vastly different from the rest of the Australian population. It will focus on five issues where there is a gap in the research – Vitamin B12 deficiency, chronic suppurative otitis media and cholesteatoma, Helicobacter pylori and the determination of the age of refugee children.

There are many challenges for an Australian born-and-trained General Practitioner working in refugee health. Optimum health care and training for the health workforce relies on the existing literature, ongoing internal evaluations and the knowledge acquired from experienced practitioners. However publications and research that are able to inform screening, guide clinical decision-making and management guidelines for many illnesses unique to newly-arrived refugees are lacking. There is an assumption that the 'evidence' and 'guidelines' used for the majority population will be applicable to newly-arrived refugees after they have settled in a new country.

Most health professionals working in refugee health focus on clinical work rather than research or publishing. Many of the previous protocols for the screening and management of newly-arrived refugees are based on the clinical experience of these practitioners rather than on research. With a push for 'evidence-based medicine', screening and other guidelines will need to change, not because they are not accurate, but because they do not have the published evidence to validate

their use. This presents a dilemma for practitioners with experience in the field of refugee health, as their guiding documents may not reflect their experience.

My aim in this thesis has been to research some of the issues for which there is little literature in order to marry empirical knowledge and evidence. Screening and appropriate management for these conditions is not expensive or difficult, and is likely to save a great deal of morbidity and possible mortality, not to mention future expense to the health system.

Research into Vitamin B12 deficiency, chronic suppurative otitis media, cholesteatoma, Helicobacter pylori and age determination in refugee children are just some of the many unusual health problems I have noticed in my 15 years of working with newly-arrived refugees. This thesis is by publication with each chapter addressing one of these issues and presenting the literature I have previously published under that chapter heading. This body of work has affirmed that at least those issues I have researched have a different prevalence, presentation and need for follow-up to 'usual' practice.

Declaration

I certify that: 1) This thesis does not incorporate without acknowledgement any material previously submitted for a degree or diploma in any university;

2) To the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text;

3) Published works included in this thesis have been carried out conjointly with the listed co-authors; in each of those publications I participated in the initiation, conduct and direction of the conjoint research, data analyses and manuscript writing.

Signed 

Date: 4th September 2016

10 publications are included in this thesis

1. **Benson J**, Maldari T, Turnbull T (2010) Vitamin B12 deficiency – why refugee patients are at high risk. *Australian Family Physician* 39 (4) 215-217
2. **Benson J**, Phillips C, Kay M, Webber M, Ratcliff A, Correa-Velez I, Lorimer M (2013) Low Vitamin B12 levels in newly-arrived refugees from Bhutan, Iran and Afghanistan; a multicentre Australian study *PLoS One* 8(2):1-6
3. **Benson J**, Phillips C, Kay M, Hanifi H, Giri G, Leahy C, Lorimer M (2015). Low levels of Vitamin B12 can persist in the early resettlement of refugees: symptoms, screening and monitoring. *Australian Family Physician* 44(9):
   668-673
4. **Benson J**, Mwanri L. (2012)Chronic suppurative otitis media and cholesteatoma in Australia's refugee population. *Australian Family*
5. Mwanri L, **Benson J** (2013) Cases of Cholesteatoma in Refugee Populations in South Australia *Journal of Pharmaceutical and Biomedical Sciences* 37(37): 1915-1921
6. Abdul Rahim NR, **Benson J,** Mwanri L, Grocke K, Vather D, Zimmerman J, Moody T (2016) Prevalence of Helicobacter pylori in Newly-arrived refugees attending the Migrant Health Service. *Helicobacter* Sep 22. doi: 10.1111/hel.12360
7. **Benson J**, Abdul Rahim R, Agrawal R (2016) Newly-arrived refugee children with Helicobacter pylori are thinner than their non-infected counterparts. *Australian Journal of Primary Health.* 2016 Aug 5. doi: 10.1071/PY15187
8. **Benson J,** Williams J (2008) Age Determination in Refugee Children. *Australian Family Physician, 37(10), 821-824*
9. Vaska AI, **Benson J**, Eliott JA, Williams J (2016)Age determination in refugee children: A narrative history tool for use in holistic age assessment. *Journal of paediatrics and child health* 2016 May;52(5):523-8.
10. Sypek SA, **Benson J**, Spanner KA, Williams JL (2016) A holistic approach to age estimation in refugee children. *Journal of paediatrics and child health*. 2016 Jun;52(6):614-20

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I would like to acknowledge and thank all the co-authors and collaborators who have assisted me in putting together this body of research. In particular the health professionals at the Migrant Health Service in Adelaide and the other members of the Refugee Health Network of Australia, who shared my passion for collecting 'evidence' in order to inform refugee guidelines and protocols.

I would also like to thank all of the refugee patients who have taught me so much over the last 15 years. Their support and encouragement has been ever-present throughout my journey. I hope that this body of work brings us closer to health equity for the refugees of the future.

I am extremely grateful for all the wisdom, help and support given to me by my supervisors Prof Paul Ward, Dr Lillian Mwanri and Dr Julie Robinson.

Statements outlining the extent to which Dr Benson was responsible for each article in this thesis

Thesis chapter	Title	Nature and extent of candidates contribution
2	**Benson J**, Maldari T, Turnbull T (2010) Vitamin B12 deficiency – why refugee patients are at high risk. Australian Family Physician 39 (4) 215-217	This paper originated from my clinical observation of a high prevalence of Vitamin B12 in the newly arrived refugee patients I was seeing in my practice at the Migrant Health Service in Adelaide. After looking at the literature on the subject I realised that this had not been noted before in this population. I discussed the issue with my two colleagues who worked with me as General Practitioners at the Migrant Health Service and they began to screen their patients as well. We decided that this was an important problem and that, since it had not been noted before, I decided to publish an article in the Australian Family Physician. I performed the literature review, wrote the article and formatted it for submission. Drs Maldari and Turnbull contributed their data to the paper and reviewed the manuscript.
2	**Benson J**, Phillips C, Kay M, Webber M, Ratcliff A, Correa-Velez I, Lorimer M (2013) Low Vitamin B12 levels in newly-arrived refugees from Bhutan, Iran and Afghanistan; a	I presented at the national Refugee Health Conference on the findings published in my 2010 article. At the national meeting of the Refugee Health Network of Australia (RHeaNA) I asked if the other states would like to collaborate on a national study to look at the prevalence of Vitamin B12 deficiency throughout Australia. Not all of the states agreed, so Dr Phillips was from the ACT, Dr Kay from Queensland, Dr Webber from Newcastle in NSW and Dr Ratcliff from Tasmania. I had a small PHCRED grant to help with statistical analysis and collating data. I wrote up the Ethics application using the National Ethics Application Form (NEAF) and each state

	multicentre Australian study PLoS One 8(2):1-6	modified this for their own state. I collected all the data into one data-set and cleansed it. Dr Lorimer was the statistician who advised us and analysed the data. I did the literature review and wrote up the initial draft of the paper. This was reviewed mainly by Dr Phillips and Dr Correa-Velez, who also advised on the statistical analysis. I formatted the paper for a previous journal and then for PLoS One, and negotiated the publication of the paper.
2	**Benson J**, Phillips C, Kay M, Hanifi H, Giri G, Leahy C, Lorimer M (2015). Low levels of Vitamin B12 can persist in the early resettlement of refugees symptoms, screening and monitoring. Australian Family Physician 44(9): 668-673	This paper followed on from the previous prevalence article as I had many unanswered questions arising from the previous research. The concept was mine. I successfully applied for a larger PHCRED grant for this research and used this to pay for the statistician (Dr Lorimer) for reimbursement for the participants, for translation of the documents and for interpreters. Ms Hanifi is a nurse from Afghanistan who works at the Migrant Health Service and she assisted me with many of the Afghan participants, liaised with the Afghan and Iranian communities and advised on the cultural implications of the findings. Ms Giri is a community health worker from Bhutan who works at the Migrant Health Service. She similarly assisted me with the Bhutanese community. Because of the complexity of the research I also set up an advisory committee to assist me, which included Dr Leahy, Dr Phillips and Dr Kay. These three also assisted me with reading and advising on the draft of the paper before publication. I applied for ethics, performed the literature review, decided what tools to use and had them translated and back-translated, located the interpreters, collated the data and led the advisory committee in discussion about how to interpret the data. I also wrote the article, which was

		reviewed by the team and formatted it for two other journals before it was accepted by the Australian Family Physician for publication.
3	**Benson J**, Mwanri L. Chronic suppurative otitis media and cholesteatoma in Australia's refugee population (2012). *Australian Family Physician*; 41(12):978-80.	Due to my experience in Aboriginal health, looking in the ears of patients for chronic suppurative otitis media (CSOM) was part of my usual practice. At a clinical meeting at the Migrant Health Service I discussed my finding of a high prevalence of CSOM in adults, which I thought was unusual. The other clinicians were not aware of CSOM and after an education session, they too found a higher prevalence. I performed a literature review on the subject and found no literature at all on CSOM in refugees. I wrote up and gained ethics approval for an audit of the patients at the Migrant Health Service, had written permission from all of the doctors there to review their files and reviewed all the files for the 2 and ½ years of the study. Dr Mwanri is a Public Health Physician and was interested in this topic, especially aligning it with her experience in Africa. She contributed to the literature review and reviewed and advised on the draft of the article. I wrote the article, formatting it and successfully publishing it in the Australian Family Physician.
3.	Mwanri L, **Benson J** (2013) Cases of Cholesteatoma in Refugee Populations in South Australia *Journal of Pharmaceutical and Biomedical*	As part of looking at CSOM, I also noted the higher prevalence of cholesteatoma. Whilst preparing the previous research, Dr Mwanri and I decided to publish the two case studies of patients of mine with cholesteatoma. I applied for ethics approval for this to be added to the previous ethics application, gained written permission from the patients, wrote up the case studies, shoed the de-identified cases to the patients and advised on the final write-up of the paper.

	Sciences 37(37): 1915-1921	Dr Mwanri did an extensive literature review on cholesteatoma and wrote up the body of the paper, formatted it and successfully published it.
4	Abdul Rahim NR, **Benson J,** Mwanri L, Grocke K, Vather D, Zimmerman J, Moody T (2016) Prevalence of Helicobacter pylori in Newly-arrived refugees attending the Migrant Health Service. *Helicobacter* Sep 22. doi: 10.1111/ hel.12360	The concept for this research grew out of my clinical observation of a high prevalence of Helicobacter pylori (H.pylori) in refugee children with Vitamin B12 deficiency. The prevalence did not reach significance in the Vitamin B12 study, but as part of my literature review on the topic, I noted that there was very little literature on the prevalence of H.pylori in refugees. I discussed the logistics and relative cost of performing stool antigen with the local pathology laboratory and they were supportive of testing all newly-arrived refugees as part of their initial screening protocol at the Migrant Health Service. Stool samples were being collected from every patient for cysts, ova and parasites at the time. After collecting three years of data, I applied for ethics approval to audit it and set up a data-base in order to do this. University of Adelaide medical students needed to do a 'research project' that involved a small literature review of five papers and a two-page research proposal. Ms Grocke, Ms Vather, Ms Zimmerman and Ms Moody approached me and asked me if I would supervise them. I agreed and they became so enthusiastic about the project that they asked if they could be involved in the actual research. We gained approval from the Migrant Health Service for me to supervise them entering all the data from the 922 individual patient files into a spread-sheet which took them about 6 months. Midway through this they flew with me to Toronto to the North American Refugee Health Conference where they presented our interim findings. I then cleansed the

		data and re-organised it. At the time, I was co-supervising Dr Abdul Rahim as a Public Health Registrar in collaboration with Dr Mwanri. In order to complete the requirements to become a Public Health Physician, Dr Abdul Rahim needed to statistically analyse a data-set and write up the results. As her supervisor I sat in the same room as her so we had many conversations about this and the next study, including how we would analyse the data and which statistical tools would be most appropriate. We agreed that she would use this prevalence study for the purpose of her Public Health requirements. She performed another literature review, analysed the data, wrote up the paper and submitted it for publication. She then went on maternity leave and so I finalized the negotiations with the Journal and responded to the comments from reviewers.
4	**Benson J**, Abdul Rahim R, Agrawal R (2016) Newly-arrived refugee children with Helicobacter pylori are thinner than their non-infected counterparts. *Australian Journal of Primary Health* 2016 Aug 5.doi: 10.1071/PY15187	This publication is from a subset comprising the children from the previous prevalence study. I was alerted to the problem of thinness of children with H.pylori when I noticed that many of the refugee children in my practice who were struggling to put on weight, also had H.pylori. There was no literature on this problem in refugee children and only a small amount from developing countries. This was one of the original reasons I wanted to research H.pylori in the refugee population. Dr Agrawal is the paediatrician at the Migrant Health Service. Along with Dr Abdul Rahim, we discussed the best way to analyse the data in order to answer my question about thinness. I did an extensive literature review on the topic and Dr Abdul Rahim did the statistical analysis. I then wrote up the journal article and formatted it for three other journals before it was accepted in the Australian Journal of

		Primary Health.
5	**Benson J,** Williams J (2008) Age Determination in Refugee Children. *Australian Family Physician,* 37(10), 821-824	This article came out of a need for a publically available tool to determine the age of refugee children of uncertain age. I put together the Age Assessment Tool (AAT) for internal use at the Migrant Health Service, after an extensive literature review and discussions with the other doctors and nursing staff, in particular Ms Williams who is the Clinic Co-ordinator. I presented the Tool at the North American Refugee Health Conference in Toronto. The feedback was that this was an excellent tool that needed to be written up for public use and validated. I published this first article and the tool was used extensively both locally and internationally, by medical, government and legal bodies. We decided that the need for validation would involve two arms – one looking at how people from the refugee source countries determined age in their country, and the second refining and validating whether the tool we used was accurate.
5	Vaska AI, **Benson J**, Eliott JA, Williams J. Age determination in refugee children: A narrative history tool for use in holistic age assessment. *Journal of paediatrics and child health*. 2016	At the time I was discussing how we would validate the tool, I was approached by Mr Vaska, a medical student I had known for many years, asking if I would supervise him in an Honours year of his Medical degree and if I knew of any research he could do. I suggested this piece of research and asked Dr Eliott if she would co-supervise as she has particular experience in Qualitative research techniques. Along with Ms Williams and the community health workers at the Migrant Health Service, Mr Vaska and I discussed the feasability of doing this research with the communities. As his supervisor, I met with Mr Vaska regularly throughout the year of the research, discussed his literature review, read his transcripts, co-analysed his themes and reviewed

	May;52(5):523-8.	and advised on the writing up of this publication.
5	Sypek SA, **Benson J**, Spanner KA, Williams JL. A holistic approach to age estimation in refugee children. *Journal of paediatrics and child health*. 2016 Jun;52(6):614-20	Dr Sypek was a Paediatric registrar working at the Migrant Health Service who needed to do a research project in order to qualify as a Paediatrician. He asked if I knew of any projects he could take part in, I suggested the other half of this project. We set up a committee that also included Ms Williams and Ms Spanner, one of the other nurses at the Migrant Health Service. Ms Williams found the participants, blinded them to Ms Spanner and I and then we did the assessments using the AAT. Since I was Dr Sypek's supervisor throughout this project, the ethics application was in my name and I met regularly with Dr Sypek throughout the year. Dr Sypek collated the data, we all discussed it and he wrote up and published the paper. I reviewed and advised on the final version of the publication.

Chapter 1. Introduction

Background

The social determinants of health, exposure to different environmental conditions and infectious diseases, lack of health infrastructure, ethnicity, under-nutrition, and the sequelae of torture and trauma, are just some of the factors likely to impact on the health of refugees after they arrive in developed countries (1). It is only when such differences in health issues are noticed, researched and published, that the established protocols and guidelines can take the particular issues that affect newly-arrived refugees into account. Without research to inform the evidence, the health care delivered to this diverse and vulnerable group of people is likely to be inadequate. This body of research aims to look at some pertinent clinical problems in newly-arrived refugees that are vastly different from the rest of the Australian population. It will focus on four issues where there is a current gap in the published literature – Vitamin B12 deficiency, chronic suppurative otitis media and cholesteatoma, Helicobacter pylori and the determination of the age of refugee children.

There are many challenges for an Australian born-and-trained General Practitioner (GP) working in refugee health (2). At a clinical level many of the illnesses that are likely to be more common in newly-arrived refugees are rare in the Australian general population - examples may include malaria and schistosomiasis (3, 4). Others will be known to GPs but are much more common in refugees – examples will include hepatitis B, Vitamin D deficiency and Helicobacter pylori (5-7). Still others will be diseases that GPs might be familiar with in certain populations but that they might not consider worth screening for in newly-arrived refugees – examples will include chronic suppurative otitis media (common in Aboriginal people (8)), or Vitamin B12 deficiency (vegans (9)) (10, 11). Optimum health care and training for the health workforce relies on the existing literature, ongoing internal evaluations and the knowledge acquired from experienced practitioners (12-15). Beyond anatomy and physiology the Western medical curriculum is designed around the most

commonly occurring health issues and is slow to change given the globalisation of the world's population and recent changes to human migration. However publications and research that are able to inform screening, guide clinical decision-making and management guidelines for many illnesses unique to newly-arrived refugees is lacking (16, 17).

Most General Practitioners working in areas such as refugee health focus on clinical work rather than research or publishing (18). Many of the previous protocols for the screening and management of newly-arrived refugees are based on the clinical experience, and the empirical knowledge of these practitioners rather than on published research as might be expected in other areas of medicine. With this expectation that screening and other guidelines will be based on evidence, they will need to be updated as research is published to validate their use (19). This presents a dilemma for practitioners with experience in the field of refugee health, as their guiding documents at times may not reflect their personal experience and they may not have been taught the skills with which to challenge them (20).

My work in refugee health over 15 years has alerted me to many gaps in the literature, in particular around the four health issues on which this thesis is based. My particular work trajectory means that I also bring my experience of Aboriginal health and of working overseas in Nepal and Vanuatu to my knowledge of refugee health issues (21, 22). The clinical skills I learnt working with these populations and the gaps I have found means I have asked some of the questions that have formed the basis for my research.

One of the aims in my professional career has been to publish information, evidence and guidelines that are accessible to the GPs in Australia who are providing the health care for refugees (3-6, 10, 11, 23-26). My aim in this thesis is to research some of the issues for which there is little literature in order to marry empirical knowledge and evidence. Screening for these conditions and appropriate management is not expensive or difficult, and is likely to save a great deal of morbidity and possible mortality, not to mention future expense to the health system if not addressed in a timely manner.

Research into Vitamin B12 deficiency, chronic suppuratives otitis media, cholesteatoma, Helicobacter pylori and age determination in refugee children are just some of the many unusual health problems I have noticed in my 15 years of working with newly-arrived refugees. This thesis is by publication with each chapter addressing one of these issues and presenting the literature I have previously published under that chapter heading.

The Impact of the Social Determinants of Health on Refugees

The social determinants of health are 'the conditions in which people are born, grow, live, work and age, including the health system' …'Social determinants of health are mostly responsible for health inequalities – the unfair and avoidable differences in health status seen within and between countries' (27). Health inequity is known to differ across socio-economic groups, which is then reflected in parameters such as child and adult morbidity and mortality as well as quality of life (28). This is more pronounced amongst the urban poor than the rural poor and within countries there can be a wide differential based on such parameters as income, education, age, access to housing and transport, employment, social support and early life events (28, 29). The WHO-based Commission on Social Determinants of Health acknowledges that there are opportunities to address these inequities through policy and action at the 'local, national and global level' and that the costs of not acting in this way should be 'widely known and debated' (30).

It has been estimated that more than 200 million people, 2% of the world's population, live outside their country of birth (31). This migration is more obvious in countries such as Australia and Canada where up to 25% of the population are born overseas (32). The health of these new residents will be influenced by many factors, including the social situation in their country of origin, that of any transit countries and by the circumstances in which they live in the new country (33).

The 1951 Refugee Convention defined a refugee as someone who 'owing to a well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality, and is unable to, or owing to such fear, is unwilling to avail himself of the protection of that country' (34). In 2014 the United Nations High Commission for Refugees (UNHCR) estimated that there were more than 61 million 'uprooted persons' worldwide and 13 million refugees (35). Only about 1% of the 'people of concern' are submitted by the UNHCR for possible resettlement. In 2011, 62,000 refugees resettled in 22 industrialised countries (33). Who is settled in each country depends on the international political situation, decisions made by the UNHCR and the country's Government (36). Many have been in 'transit countries' living in refugee camps or unsafe and unstable conditions for many decades (33).

Refugees are forced migrants who leave their country in order to 'save their lives or preserve their freedom' (35). They are unprotected by their own country and usually leave with little preparation, very few belongings and little paperwork. Their future and even their freedom is usually uncertain (33). In contrast, migrants choose to move so as to improve their economic, career or education prospects. Asylum seekers are seeking international protection but have not yet had their claim for refugee status determined. Internally Displaced Persons (IDP) have been forced to flee from their home but have not crossed their country's border (33). The health profile of these different types of migrants is usually going to be vastly different and the health profile of one cannot be extrapolated to the other. For those who come as voluntary migrants, the social determinants of health are likely to be similar to those of the new country and they can prepare for their arrival by such activities as learning the language, establishing networks and ensuring their career is recognised. After resettlement in a developed country, the social determinants of health for refugees will certainly improve and there will be a 'catch-up' in their health status (23, 37). However there will still be a differential and their health and socio-economic status is still likely to be lower than the majority of the population in the new country as they

struggle with the transit as well as language difficulties, stigma and discrimination (25, 38).

Even those refugees who come from more developed countries have usually been denied health care, are in a vulnerable socio-economic as well as political position or the region has been in chaos. In a technology-rich country with easy access to affordable food, education, housing, water, sanitation, transport, immunisation, health and where even those who do not work are ensured of a basic income, the social determinants of health are often forgotten as a basic cause of health inequality (30).

Current Practices in Health Screening and Management of Refugees in Developed Countries

According to the UNHCR handbook, an initial post-arrival assessment should include physical, mental and social health as an essential requirement for a 'healthy start' in a refugee's new country (39). It goes on to say that 'as well as being a fundamental human right, optimal physical and mental health is a vital resource for integration, enhancing people's capacity to meet the inevitable challenges and stresses of the resettlement process. In contrast, poor health may act as a significant barrier to integration' (39). Optimising the opportunities for early intervention, will obviously be of benefit, not only to the people themselves, but also to the budgets of the receiving countries (39). Such assessments, if properly documented, collated and published, serve as a 'means of monitoring and documenting overall trends and issues for the purposes of professional development and ongoing service improvement' (39).

Pre-departure screening and/or treatment for UNHCR refugees addresses a small number of illnesses such as malaria and some intestinal parasites (40, 41). The use of a single dose of albendazole before departure was implemented in order to decrease the burden of intestinal parasites such as hookworm, roundworm and whipworm, however it is not adequate to treat schistosomiasis or strongyloides (42). Particular 'alerts' for areas or conditions of high risk (such

as poliomyelitis or Ebola), especially if there is a public health issue, are an important role of the Communicable Disease Control Branch of the receiving country.

Some health issues will be specific to certain populations, others common to all people of refugee background and others at a different prevalence than the rest of the population (42). Waves of refugees will reflect the areas of conflict in the world, and their health needs may change. The health system needs to be able to evolve to cater for the needs of this constantly changing population and be prepared to develop guidelines that are able to be adapted to cater for new and emerging issues (43). Health professionals working with newly-arrived refugees also need to be constantly on the alert as to different health profiles that might emerge(44). Examples would be the higher rates of malaria in African refugees, use of lead-based cosmetics in those from Burma, schistosomiasis in Africa and Asia and the higher prevalence of Vitamin B12 deficiency in those from Bhutan(11, 43, 45).

It is not only the prevalence of infectious diseases, nutritional deficiency and immune dysfunction that are influenced by the social determinants of health. Chronic diseases such as cardiovascular disease, diabetes, hypertension and some cancers are also more common (46). These diseases with more long-term, chronic or insidious morbidity may not be at the forefront of the minds of either refugees or health professionals soon after arrival.

The development of evidence-based guidelines and screening protocols is likely to be difficult, time-consuming and expensive. One of the controversies in refugee health is the relative cost of 'on-shore' screening and vaccination versus the cost 'off-shore' (47). Similarly the cost of screening needs to be balanced against the cost of undiagnosed disease and so guidelines need to be updated regularly in order to reflect the demographics of incoming refugees(48).

According to Tugwell and the Canadian Collaboration for Immigrant and Refugee Health (CCIRH), developing guidelines needs to take into account the prevalence of the condition, specific clinical considerations, screening or treatments at the time of migration, screening post-migration, treatments available and

implementation issues such as cost (49). Canada have begun to address this by investing in the health of their vulnerable populations (50). They have developed evidence-based screening guidelines for both acute and chronic conditions in newly-arrived refugees(51-54).

Appropriate health-care of newly-arrived refugees will not only improve their immediate health but is also likely to decrease the long-term health burden on the individual, their family, the society and the health system. If refugees are only given 'routine' health care, their health is likely to be suboptimal and this will further compound their difficulties in resettling in the new country (48). This could potentially lead to increased morbidity over the person's lifetime, mortality and escalating costs to the health system in the future (55). The imperative is not only about the individual and their place in their new society, but deeper issues of inequity of health care (17).

Newly-arrived Refugee Health Screening and Management in Australia

After World War II, most of Australia's refugees came from post-war Europe where their health status was probably similar to that of much of the post-war Australian population. In the 1970s, 80s and 90s refugees from Vietnam, Latin America and then the Balkans came from war-torn regions that had previously had a reasonable standard of living and education (56). Refugees from the Middle East, in particular Afghanistan and Iraq began to arrive in the 1990s (56). Many of these people had come from environments of protracted instability over a long period of time. In 1999, 80% of refugees arriving in Australia were from the former Yugoslavia or the Middle East. In the 2000s most of the refugees who came were from Africa with a peak of 80% in 2005 (43). Not only did they come from a region with a greater burden of exotic infectious diseases, but also health, education and the other social determinants of health had been neglected, sometimes for decades. Currently, refugees are mostly from countries and regions such as Bhutan, Burma, Central Africa, the Horn of Africa, Afghanistan,

Iraq and Syria (57). They are likely to have a similar health status to those people from their country of origin or transit, vastly different to the health status of those born in Australia.

One of the challenges for resettlement countries such as Australia is how to ensure that those who arrive have a level of health that is not going to put the rest of the population at risk and that is not going to cost an exorbitant amount of public money. Everyone applying for a Humanitarian visa has a health check, including a Chest X-ray for Tuberculosis (TB) if over the age of 11 and an HIV (Human Immunodeficiency Virus) test if over the age of 15 (58). Those who are deemed to have costly illnesses such as severe disability or a need for major surgery have their humanitarian visas rejected. It was on this basis that those with HIV and with amputations were previously rejected. In the last few years, the ceiling for the estimated cost of health-care has been increased, and so some of those with amputations, disabilities and HIV are now granted visas. Those with active (infectious) TB need to be successfully treated before their visa can be granted and those with latent TB are given a visa with a 'Health Undertaking' meaning they need to see a Chest Physician soon after arrival. In addition, before departure, the International Organisation for Migration (IOM) offers a voluntary 'fitness to fly' assessment which includes malaria, a measles-mumps-rubella vaccination and empirical treatment for intestinal parasites (36). During the outbreaks of poliomyelitis in Syrian refugees and Ebola virus in those from West Africa, the Australian Government set up special protocols after arrival in order to protect public health (59).

Along with most other medical organisations, the Australian Medical Association (AMA) believes that asylum seekers and refugees should receive 'the same level and quality of health care as other Australians' (60). The position statement goes on to say that

> '*More research is needed into the health status and health care of asylum seekers and refugees…to assist medical practitioners in the care of these groups, and the development of appropriate services*' (60).

The need for the identification of health disparities, the collection and publishing of data and the ongoing evaluation of the changes has been identified internationally (61). However it is also acknowledged that this is not the case as specific ethnic and cultural groups are likely to be lumped together under such heading as 'Middle-Eastern' or 'Asian' without recognition of their past history as a refugee (61).

Deborah Zion et al in examining 'The Ethics of Researching Asylum Seeker Health in Australia' asks the question about how we 'investigate the lives of those who are politically, socially, and economically marginalized in a way that may bring them back into the human circle as rights-bearing participants?' (62). Her discussion is not directly related to physical health, but the idea that people who come to Australia deserve to begin their lives here as equals, will also apply to their health.

For most of the rest of Australia it is difficult to relate to the poverty, fear, trauma, isolation and lack of previous social determinants of health or health care experienced by refugees. Similarly for the health profession, the diseases of poverty and overcrowding are rare, and being rare, are not routinely screened for (63). There is limited exposure in many Australian medical schools to teaching on the social determinants of health (64). Doctors who have worked with other vulnerable patient groups are more likely to be aware of the impact of the social determinants of health on disease profiles. Otherwise the assumption is likely to be made that once refugees have settled in Australia, their health profile will match that of the rest of the Australian population.

Hence when seeing a patient from a refugee background, particularly if they are newly-arrived, screening should be different to that for the rest of the Australian population (16). However, unless health practitioners are aware of their particular needs, the health care provided to a newly-arrived refugee is likely to be similar to that for the rest of the health professional's patients (2). Clinical decision-making in refugee health is complex and will involve a variety of different activities. As well as looking at the national guidelines to see if they are relevant, it is important to look at specific refugee health guidelines, but might

also involve a review of the literature, discussing the issue with other refugee health practitioners or doing internal audits.

When deciding whether to screen for an illness as part of a preventive health strategy, evidence-based guidelines such as those from the Royal Australian College of General Practitioners (RACGP), can guide decision-making (63). These guidelines might also direct screening for higher risk patients, for example, Vitamin D in those with dark skin or who wear extensive covering for cultural reasons, or Hepatitis B in those who come from high prevalence countries, regions or ethnicities. Refugee health guidelines such as those written by the Australasian Society for Infectious Diseases (ASID) suggest screening for higher risk infections such as malaria and schistosomiasis (16). However, such guidelines will only be written based on the evidence published in peer-reviewed journals and many community GPs will not be familiar with the more specific recommendations for screening in newly-arrived refugees (2). In the few studies asking GPs about their needs in regards to refugee health, knowledge about the conditions they are likely to encounter is a high priority (1, 2). The ASID guidelines have recently been rewritten to include the evidence that has been gathered since the first edition was published in 2009 (19).

In Australia the health services offered to newly-arrived refugees have been described as 'piecemeal' with different combinations of a specialist refugee health service, community health centres, tertiary hospital infectious disease or paediatric clinics and private GPs in each state (1, 2, 14, 65-67). Who does the initial screening and care for refugees is different in every jurisdiction. In South Australia about half are seen by the specialised refugee health service (the Migrant Health Service) and half are seen by private GPs. The protocols in use at the Migrant Health Service are in use by some of these private GPs in the community but the majority of those working outside the Migrant Health Service do not use them and rely on what they can find in the public domain (1). For example, during the four years that a specific Medicare item number was in existence to claim for a Refugee Health Assessment (Item 714), fewer than half of the newly-arrived refugees who qualified received an assessment using this item number (45). Even though Australia has one of the best free interpreter services

in the world, doctors are underutilising this service which will certainly impact on the healthcare of those with very limited English such as newly-arrived refugees (68). Hence one of the barriers to people receiving equitable health care is that health providers may not be aware of issues specific to refugees (2, 12, 66).

Children and adolescents make up about 50% of the current refugee cohort in Australia. Caring for refugee children is a particular imperative and there is much more at stake if deficiencies and acute and chronic diseases are left undetected and untreated. Screening has documented otherwise unidentified chronic health problems such as developmental delay, infectious diseases, lack of immunisation, Vitamin D deficiency and anaemia (65, 66, 69). Importantly, even those diagnoses of unequivocal public health importance such as malaria and TB were often found to be asymptomatic or the parents were unaware of the importance of the symptoms in the children in these studies (65). This may be because the parents had 'normalised' the problem in an environment where health care was not available, but also because there were competing priorities on arrival such as education, transport, finances, food, language etc. Children receive very limited pre-departure screening and a comprehensive health assessment soon after arrival will improve short-term and long-term health outcomes (14). However, appropriate screening for children after arrival is not guaranteed. For instance, in NSW, only one in five refugee children are assessed by a specialist refugee health service (14).

In 2005 the Communicable Disease Network of Australia asked the Australasian Society for Infectious Diseases (ASID) to develop post-arrival screening and treatment guidelines at a time when about 70% of newly-arrived refugees were from Sub-Saharan Africa. In 2009, I was part of the team of eleven health professionals who published the 'Diagnosis, management and prevention of infections in recently arrived refugees' (16). They were written based on the literature at the time and from the experience of the authors, all of whom were clinicians working in refugee health. As the patterns of international migration shift, the health profile of newly-arrived refugees changes and the protocols for pre-departure screening and treatment need to be reviewed, so the post-arrival

screening will need to be monitored and changed. In 2014 the Refugee Health Network of Australia (RHeaNA) decided to rewrite the Australian guidelines because of the change in the demographics of the newly-arrived refugee population and the recent literature (42). RHeaNA is a national group of over 150 refugee health service providers in all states and territories who meet and collaborate on refugee health issues (45). The new guidelines were published on the ASID website in May 2016 (19).

This combination of past social determinants of health, exposure to infectious diseases, lower socio-economic status in the new country, less access to culturally appropriate healthcare, lack of research and limited teaching in medical school is likely to translate into a different health-care profile for newly-arrived refugees in Australia. Despite the diverse and ever-changing countries of origin, their flight from an environment that has often been unstable and chaotic for a long period of time means that many aspects of their health profile are likely to be similar to that of other refugees.

What might be the most appropriate model of primary care for newly- arrived refugee has been the subject of much academic and political debate. A study by Joshi et al in 2013 looked at the literature on the current different models in Australia and overseas and found that a specialised service with co-ordinated care ensured that important issues such as adequate access and quality of care were addressed (70). Some of the advantages of such a model are 'improved physical and mental health' (70). Similarly a study by Johnson et al in 2008 found that GPs' 'awareness of and experience managing health conditions unique to refugees, and the multiple and complex nature of refugee health conditions' were significant challenges to caring for refugees in a mainstream general practice (2).

The Lack of Evidence and Best Practice for Refugee Health Issues

A group in Ontario, Canada, first used the phrase 'Evidence-based Medicine' as recently as 1992 (71). The Evidence-Based Medicine Working Group said that 'Evidence-based medicine de-emphasises intuition, unsystematic clinical

experience, and pathophysiologic rationale as sufficient grounds for clinical decision making and stresses the examination of evidence from clinical research'(71). The authors go on to say that 'At the same time, systematic attempts to record observations in a reproducible and unbiased fashion markedly increase the confidence one can have in knowledge about patient prognosis, the value of diagnostic tests, and the efficacy of treatment' (71, 72). Since then 'evidence' has become the established method for problem-solving and decision-making in the care of patients. However, critical appraisal of the literature will involve an appraisal of whether the evidence can be extrapolated to include the particular circumstances of the individual being cared for. Evidence must always be enhanced by the experience of practitioners who are able to examine the applicability and practicality of the data and its statistical significance (72).

A search for articles on 'refugee health' on PubMed in October 2014 from 2007-2014 yielded 1964 hits, only 0.17% of those for 'health' in the same timeframe with 1188613 hits. In a previous review of the literature on refugee health in Canada 66% were found to be on mental health and acculturation, 21.8% on communicable disease, 3 % on health screening and 1.5% on nutrition (73). Conditions specific to refugees are likely to remain 'invisible' in most population-based statistics and research. Most medical research is done on the majority population in Western developed countries and the limited research done in developing countries is rarely extrapolated to refugees and migrants when they resettle in developed countries (73). Reasons might include: language, culture, complexity, small numbers, lack of exposure to researchers and clinicians and 'invisibility' in the new country.

The 10/90 research gap posits that 'only 10% of global health research is devoted to conditions that account for 90% of the world's disease burden' (74). Similarly, refugees in developed countries are likely to carry a higher burden of acute and chronic infectious diseases that may be undiagnosed at the time of arrival (16). Refugees are not only affected by the epidemic and endemic nature of the infectious diseases to which they might have been exposed, but also to other factors which would adversely affect their physical health such as poverty,

overcrowding, lack of adequate health-care, lack of sanitation, poor nutrition and torture and trauma (42).

New and emerging issues in refugee health are very difficult to research and studies in this area tend to be underfunded (75). Refugees tend to be a 'hidden population' when looking at national data-sets as their numbers are low and are not 'readily distinguished or enumerated' from the majority population (76). The demographics of refugees and asylum seekers changes regularly, depending on socio-political issues in the world and initially the numbers in the receiving country will be small and spread throughout the country. Senior clinicians in refugee health services need to be aware of the risks for each new cohort, use their clinical knowledge and experience, and discuss with colleagues nationally and internationally. On the other hand, those who are working with refugees are best placed to do research as they have relationships with the communities, as well as being aware of their needs (76).

The WHO acknowledges that for many of the poorest countries of the world, there is a lack of data on the burden of disease, its distribution, or even on the impact of the available health system (30). Most newly-arrived refugees come from areas with poor health infrastructure or research or data collection facilities, so their specific health risks may not be known. For example, both the Centre for Disease Control and Prevention in the USA (CDC) (www.cdc.gov) and the World Health Organization (www.who.int) have maps of schistosomiasis prevalence that do not include Afghanistan, Burma or Bhutan, three of the common source countries for refugees. Refugee health services throughout the world know from experience that refugees who come from these areas have been exposed to schistosomiasis and so need to be screened and treated for this important disease (3).

Understanding the different health needs of refugees at the time of settlement into developed countries such as Australia, Canada, Europe and the USA, as compared to the rest of the population and other migrants, is a recent field (73). It is only really since the influx of refugees from Africa in the 2000s that Australian clinicians have begun to document the different physical health needs

of refugees. The mental health issues have been known and explored for a lot longer. For instance the Forum of Australian Services for Survivors of Torture and Trauma (FASSTT) has been in existence for more than 25 years. Although there has been a decrease in acute infectious diseases such as malaria, tuberculosis and parasites since that time, 'neglected' chronic health conditions such as Vitamin B12 deficiency, chronic suppurative otitis media and Helicobacter pylori infection have received scant attention in the literature of the source countries or in research after resettlement (44). These conditions will not usually come to the attention of a health professional unless they are screened for, as they are likely to be asymptomatic or the symptoms may have been 'normalised' (39, 77) and do not appear in the screening protocols of many countries. For instance in the large study in the GeoSentinel Clinics in the USA from 1997-2009, none of these illnesses were mentioned out of the 62 diseases screened for in 7792 refugees (55). However, in their cohort only 5% were reported as being 'healthy' (78).

In newly-arrived communities the data from post-arrival assessment is the only way of collecting information about unique and novel issues that will need ongoing screening (55). A flexible health service that allows a clinician's enquiring mind to screen for diseases based on suspicion and then clarify an audit with ethical research, will help gather answers for some of the questions about new and emerging diseases. As Johnston et al (2012) said in their audit of the Darwin Refugee Health Service 'Accurate data on the health of refugees in primary care is vital to inform clinical practice, monitor disease prevalence, influence policy and promote coordination' (79). Smaller health jurisdictions such as the health service in Darwin will struggle to gather enough data to inform guidelines, especially as the source countries change with variation in the areas of conflict and disadvantage. Some screening will not prove to be useful and so regular audits are essential. For instance, in the year 2000 a 2 year-old Sudanese child died of lead poisoning in the USA (80). Similar high lead levels had been found in other refugee health services throughout the world (81). However, after two years of screening all newly-arrived children at the Migrant

Health Service for lead levels, only one child had a mildly elevated level and it was decided not to continue this screening.

The use of the empirical clinical knowledge of those who are directly involved with newly-arrived refugees to inform screening about refugee health is of the utmost importance. As discussed in a report from the WHO Commission on the Social Determinants of Health,

> *'Often the richest sources of data on how things work in the real world can be found by tapping into the tacit knowledge of those working most closely with the targeted communities'* (37).

Such knowledge can guide health practitioners to screen for treatable problems that might otherwise have a high morbidity or even mortality. Practising medicine in this manner might be couched as a 'realistic intervention' – one that 'captures the linkages between the context, the mechanisms and the outcomes' of an issue or intervention in a particular context (37). Formal research and publication of findings will build a body of evidence on the unique health issues of newly-arrived refugees. However as with any research addressing issues associated with the social determinants of health, generating evidence involves methodological diversity and a multi-disciplinary approach (37).

Flexibility to adequately address the evolving needs of newly-arrived refugees should be an essential element of their early assessment (13, 44). The social, economic and public health consequences of these chronic diseases with higher prevalence in developing countries are also becoming increasingly important in the many developed countries to which people migrate (44). There is no international consensus on what is needed for screening, often because of the wide variations in health infrastructure and financial support given to newly-arrived refugees in receiving countries, but mostly because of the lack of evidence and devaluing of clinical knowledge and experience about the prevalence of endemic non-infectious diseases.

My Contribution to the Research on Refugee Health

Until the ASID guidelines were published in 2009, there was very little information in the peer-reviewed journals to inform GPs about clinical issues in newly-arrived refugees. Between 2004 and 2009, I published a series of case studies in the Australian Family Physician (AFP) with accompanying literature review, discussion and practical assessment and management guidelines to assist GPs in better caring for their newly-arrived refugee patients (3-6, 23, 26). The Australian Family Physician (AFP) is a peer-reviewed journal published each month by the RACGP. It has a circulation of 43,000 and its target audiences are GPs, GP registrars, international medical graduates and physicians. The AFP is Medline listed and easily searchable and although it only has an Impact Factor of 0.7 based on its citations, it is read by about 70% of Australian GPs (82). I was then part of the team who wrote the ASID guidelines for the 'Diagnosis, management and prevention of infections in recently arrived refugees' (16), which for the first time collated evidence and expertise on refugee health and brought it into the public domain.

After the publication of the ASID guidelines I began to address some of the other health problems I had noticed in my clinical practice, for which there was little or no literature.

This thesis aims to address some of the issues that seem pertinent to the ongoing health and well-being of newly-arrived refugees to Australia. Until my recent publications, Vitamin B12 deficiency, chronic suppurative otitis media, cholesteatoma and Helicobacter infection causing growth problems in children, had not been recognized in newly-arrived refugees and there was no practical protocol in the international public domain for the determination of the age of refugee children.

The second chapter of the thesis reports my research on Vitamin B12 deficiency in refugees to Australia. My initial publication entitled 'Vitamin B12 deficiency. Why refugee patients are at high risk' in 2010 was the first alert that this might be an issue and the literature has grown rapidly since that time (24). Our

national collaboration through RHeaNA on 'Low Vitamin B12 levels among newly-arrived refugees from Bhutan, Iran and Afghanistan: a multicentre Australian study' in 2013 was published at about the same time as a short paper in the Morbidity and Mortality Weekly Report (MMWR) from the Communicable Disease Control Department (CDC) in the USA and also showed an alarmingly high prevalence of Vitamin B12 deficiency in this cohort (11). A further paper in 2015, 'Low levels of Vitamin B12 can persist in the early resettlement of refugees: symptoms, screening and monitoring' followed those with borderline Vitamin B12 deficiency over 6 months and monitored their symptoms (83). There have been 21 citations of these papers by July 2016.

The third chapter looks at chronic suppurative otitis media and cholesteatoma in the newly-arrived refugee patients I serviced at the Migrant Health Service in South Australia from 2009-2011. Despite the common occurrence of these conditions in the Australian Aboriginal population and in developing countries, refugees have previously not been identified as being at higher risk. The initial paper published in the Australian Family Physician on 'Chronic suppurative otitis media and cholesteatoma in Australia's refugee population' was a way of alerting GPs to investigate the possibility of diagnosing this problem in adult refugees as well as in children (10). The follow-up paper, 'Cases of Cholesteatoma in Refugee Populations in South Australia', discussed two cases of cholesteatoma, an otherwise very rare disease (84).

The fourth chapter presents my research on Helicobacter pylori in newly-arrived refugees. Despite a well-known association of H.pylori with gastric carcinoma and growth retardation in children in developing countries, until the publication of Sarah Cherian's research on Helicobacter in African children in Melbourne in 2008 there was limited research on its prevalence or morbidity in newly-arrived refugees (7). My first paper, 'Prevalence of Helicobacter pylori in newly-arrived refugees attending the Migrant Health Service', reports the prevalence from a large cohort of newly arrived refugees from 2013-2014 (85). The second paper looks at the paediatric subset of this study and reports on the finding that 'Newly-arrived refugee children with Helicobacter pylori are thinner than their non-infected counterparts' (86). The study of the epidemiology and morbidity

associated with Helicobacter pylori in refugees is also a newly emerging area and hopefully my papers will be the beginning of an increased awareness of this problem.

The fifth chapter outlines the protocol and tool for the determination of age in refugee children whose age is unknown that I wrote in 2008 and the two subsequent studies carried out in order to validate this protocol (26). Knowing a correct age is important for schooling, vaccinations, and many other health and social reasons and has previously only been determined by the use of X-rays. Initially it was important to establish what age means in some different cultures. The paper 'Age Determination in Refugee Children: Developing an Evidence-based Narrative History Tool' clarified some of these issues (87). The other piece of research entitled 'An Holistic Approach to Age Estimation in Refugee Children' reported the successful validation of the original protocol (88). My first paper has been cited 14 times and quoted in several government policies. The protocol to determine the age of refugee children has been modified at the Migrant Health Service based on this research.

The Discussion will outline how this body of work adds to the limited research on the health of newly-arrived refugees. As the social determinants of health and the areas of conflict and disadvantage in the world change over the coming years, new issues will emerge that will impact the health of refugees. The struggle to develop evidence-based guidelines to inform screening and management will continue to be a challenge, both at an international and a local level. New research such as the articles constituting this thesis will add to the body of literature needed to develop such guidelines, and to assist practitioners in understanding how the health of newly-arrived refugees to developed countries differs from the majority population.

Chapter 2. Vitamin B12

Background

Vitamin B12 is mainly found in animal-source foods (such as meat, eggs and milk) and it is well-established in the literature that deficiency is common in the developing world (89). Even after arrival in a developed country, many people of refugee background are not able to afford, or choose not to eat, meat, eggs or milk.

Vitamin B12 is an essential vitamin for neural and blood development and B12 deficiency has been associated with a variety of symptoms including depression, fatigue, memory loss, irritability, parasthesiae, peripheral neuropathy and anorexia. If the deficiency is severe and for a prolonged period of time, it can cause irreversible subacute combined degeneration of the spinal cord.

The established teaching in medical schools throughout the world is that Vitamin B12 deficiency is rare and can be predicted from macrocytosis in red blood cells, symptoms such as parasthesia, or neurological signs. Because Vitamin B12 is stored for five years in the body and animal-source foods are plentiful in the diet of developed countries, only those with absorption problems or who eat a vegan diet are deemed to be at high risk. Using this line of thinking would not put newly-arrived refugees at continued risk of Vitamin B12 deficiency after arrival and would not justify initial or subsequent screening. However this had not been tested before my studies were done.

As well as the risk of morbidity in the affected patient, there is an increased risk of neural tube defects in the babies of women with Vitamin B12 deficiency. The Birth Defects Registry in South Australian (SA) Health has recently published a paper citing our research, identifying an increase in neural tube defects in women in Adelaide who were originally from developing countries (90). Vitamin B12 deficiency is an independent risk factor for neural tube defects but folate deficiency is more common in developed countries and so health promotion and research has focused on folate levels. The women in their cohort had normal folate levels and their Vitamin B12 levels had not been collected. This is an

urgent issue and the identification of Vitamin B12 deficiency in women of child-bearing age from developing countries will be taken up by this group after discussions with me.

After the publication of the first paper, there was only one other international study examining Vitamin B12 deficiency in refugees after arrival in a developed country. The Centers for Disease Control and Prevention (CDC) in the USA was very concerned about the high numbers of Bhutanese refugees arriving in the USA with Vitamin B12 deficiency and sent a team to the refugee camps to investigate. The results from 2008-2011 were written up in the Morbidity and Mortality Weekly Report in 2011 (91). This report was published just as I was setting up the national study.

There is no international consensus for testing, screening or treatment for Vitamin B12 deficiency. Those studies used to inform the current guidelines have not been done on people who are likely to have other deficiencies because of dietary reasons or in those of different ethnicities to the majority populations of Western countries. However the WHO has recommended that a level below 150mmol/L constitutes Vitamin B12 deficiency and most would not dispute this.

The first paper comprises two brief case reports, a review of the literature and discussion. The second paper is a cross-sectional quantitative descriptive study and the third is a mixed methods cohort study assessing B12 levels and symptoms at two points after arrival.

I was originally alerted to the fact that Vitamin B12 might be important in people from Nepal in 2005-2006 when I was working in the remote area of eastern Nepal at the B.P.Koirala Institute of Health Sciences in Dharan. This area is close to the refugee camps where Bhutanese refugees have lived in Nepal for the last 15 years.

In Nepal, people often complained of fatigue, irritability and ‘jham-jham’ (parasthesia particularly in the arms). Jham-jham was also seen as a way of alerting a physician as to whether a patient might have depression. It was seen as a type of ‘neurasthenia’ but not identified as Vitamin B12 deficiency in most

people as the investigation was expensive and so the deficiency was not formally diagnosed. Dharan and the surrounding area are very isolated with very limited access to nutritious food either in the villages or in the camps. There was also a long-standing civil war in the region at the time, with the Maoist rebels often blockading the roads so that food supplies from outside could not be brought in.

In Adelaide, I found that the newly-arrived Bhutanese refugees who were complaining of the same symptoms also had Vitamin B12 deficiency. An initial audit of the whole newly-arrived refugee population revealed a high prevalence of Vitamin B12 deficiency in other groups as well. After publication of an article in the Australian Family Physician in 2010 outlining some of these pilot results (24), other refugee health services in Australia also began to screen for Vitamin B12 levels. They reported that they too found a higher prevalence of B12 deficiency than expected and we decided to set up a multi-centre trial.

Successfully gaining ethics approval for the national study was difficult as one of the states' ethics committee said that there was no evidence that refugees had higher rates of Vitamin B12 deficiency and that it was assumed that people's B12 levels would return to normal after settlement in a developed country where they had easy and cheap access to animal-source foods. It took much longer to achieve ethics approval in that state, as we had to reapply with more information about the gap in the literature we were hoping to address.

There were some difficulties with the cohort study when the Bhutanese health worker went on extended leave, the number of newly arrived refugees dropped dramatically and the assistant researcher from the Horn of Africa found the symptom questionnaire too confronting to continue the study. Many of the participants in this study found it difficult to understand the idea of a Likert scale and the questions generated a long narrative rather than an ability to tick a box. This made interpretation by the interviewer demanding. This study was also underpowered to determine whether symptoms were linked to Vitamin B12 levels, especially in the face of the many other complex risk factors experienced by newly-arrived refugees.

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Low Vitamin B12 Levels among Newly-Arrived Refugees from Bhutan, Iran and Afghanistan: A Multicentre Australian Study

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Abstract

Background: Vitamin B12 deficiency is prevalent in many countries of origin of refugees. Using a threshold of 5% above which a prevalence of low Vitamin B12 is indicative of a population health problem, we hypothesised that Vitamin B12 deficiency exceeds this threshold among newly-arrived refugees resettling in Australia, and is higher among women due to their increased risk of food insecurity. This paper reports Vitamin B12 levels in a large cohort of newly arrived refugees in five Australian states and territories.

Methods: In a cross-sectional descriptive study, we collected Vitamin B12, folate and haematological indices on all refugees (n = 916; response rate 94% of eligible population) who had been in Australia for less than one year, and attended one of the collaborating health services between July 2010 and July 2011.

Results: 16.5% of participants had Vitamin B12 deficiency (<150 pmol/L). One-third of participants from Iran and Bhutan, and one-quarter of participants from Afghanistan had Vitamin B12 deficiency. Contrary to our hypothesis, low Vitamin B12 levels were more prevalent in males than females. A higher prevalence of low Vitamin B12 was also reported in older age groups in some countries. The sensitivity of macrocytosis in detecting Vitamin B12 deficiency was only 4.6%.

Conclusion: Vitamin B12 deficiency is an important population health issue in newly-arrived refugees from many countries. All newly-arrived refugees should be tested for Vitamin B12 deficiency. Ongoing research should investigate causes, treatment, and ways to mitigate food insecurity, and the contribution of such measures to enhancing the health of the refugee communities.

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Introduction

Among countries with formal refugee resettlement programs, Australia ranks third after the U.S. and Canada in the size of the annual intake of refugees, with 13750 refugees entering in 2010/11. The Australian government has increased the refugee resettlement program to 20,000 places in 2012/13. Refugees are a heterogeneous population who share the experience of being displaced through conflict and human rights abuse in their home countries. Chronic food insecurity – the inability to ensure basic nutritional needs of the population – has emerged as one of the pressing problems resulting from, and in turn reinforcing, political instability in many refugee-source countries [1] . Many refugees who arrive in Australia through the humanitarian program come from countries at extreme and moderate risk of food insecurity (Table 1).

Nutritional deficiencies among newly arrived refugees, particularly iron and Vitamin A deficiency, have been well-described in the national and international literature [2,3,4]. Refugees from countries with compromised food supplies, and particularly those where intake of animal source food (ASF) is limited, are also at risk of Vitamin B12 deficiency. Although there is a deficit of national data, surveys in some refugee source countries, such as Iran [5], Nepal [6,7] and Kenya [8] (where many South Sudanese refugees live) have demonstrated high rates of Vitamin B12 deficiency.

Despite this, Vitamin B12 is not part of most recommended screening protocols for newly arrived refugees [9]. Emerging data suggest that at least some refugee populations may be at particular risk of Vitamin B12 deficiency. In a study of 326 refugees undertaking post-arrival screening in Minnesota, Texas and Utah, 27% of those from Bhutan and 12% from Somalia had Vitamin

Table 1. Top ten source countries for refugees in the Australian off-shore resettlement program and risk of food insecurity.

	2010		2011	
	Top ten refugee-source countries, Australian off-shore humanitarian intake [37]	Risk of food insecurity [38]	Top ten refugee-source countries, Australian off-shore humanitarian intake [39]	Risk of food insecurity [40]
1	Burma	Moderate	Iraq	Low
2	Iraq	Low	Burma	Moderate
3	Bhutan	Moderate	Afghanistan	Extreme
4	Afghanistan	Extreme	Bhutan	Moderate
5	Congo (DRC)	Extreme	Congo (DRC)	Extreme
6	Ethiopia	Extreme	Ethiopia	Extreme
7	Somalia	Extreme	Sri Lanka	Moderate
8	Sudan	Extreme	Iran	Low
9	Liberia	Extreme	Sudan	Extreme
10	Sierra Leone	Moderate	Somalia	Extreme

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B12 deficiency [10]. Case study data in Australia has demonstrated extremely low Vitamin B12 levels without associated macrocytosis in some newly arrived refugee patients [11]. The U.S. three-state study [10] is the largest study yet reported on Vitamin B12 deficiency in newly arrived refugees in a resettlement country, but one-third of this population were from Burma, and with the exception of Somalia, African countries were under-represented.

Although no internationally agreed threshold exists above which a prevalence of low Vitamin B12 is indicative of a population health problem, McLean and colleagues [12] used a threshold of 5% in their review of folate and Vitamin B12 deficiencies worldwide. Accordingly, we hypothesised that Vitamin B12 deficiency is greater than 5% among newly arrived refugees, and that prevalence might be higher among women, who may have reduced access to ASFs. There are precedents for systematic under-recognition of significant health issues among newly arrived refugees. For example, the high prevalence of Vitamin D deficiency among refugees was under-recognised, or often misdiagnosed as somatisation, for many years in resettlement countries [13,14], resulting in long delays in the development of policy approaches to manage this health risk. Emerging health problems among refugees can be missed because they are resettled into small geographically diverse populations, demographic indicators that might reliably identify refugees on datasets are lacking, and overworked health care services often have little capacity to undertake service-based research [15,16]. The Refugee Health Network of Australia (RHeaNA) was established to share information across all service providers who work in refugee health, allowing rapid identification and response to emerging health problems [16].

In this paper we report the prevalence of low Vitamin B12 levels across newly arrived refugees in five states and territories in Australia.

Methods

Ethics Approval

This study was approved by the Human Research Ethics Committees of: Australian National University, Hunter New England Health Local Health District, Mater Health Services, South Australian Department of Health, Tasmania Department of Health and Human Services, and University of Adelaide.

Participating Sites

Australia uses a decentralised model for resettlement of refugees, and does not have a central national health screening service, as for example, New Zealand does. Initial screening of refugees is voluntary, and conducted by general practitioners working in community health services, hospital-based health assessment services, NGOs or private general practices. Participating services and groups in this study were the following members of the Refugee Health Network of Australia: the Migrant Health Service (Adelaide, South Australia), Companion House Medical Service (Canberra, ACT), Refugee Health Queensland (Brisbane), Refugee and Humanitarian Arrival Clinic (Royal Hobart Hospital, Tasmania), Migrant Resource Clinic (Launceston, Tasmania) and the Hunter New England Refugee Health Program (Newcastle, NSW).

Study Population

Refugees from all age groups who arrived in Australia on humanitarian visas, with residence in Australia of less than 12 months, and who attended one of the participating refugee health centres between 1 July 2010 and 21 July 2011.

Data Collection

All refugees who presented to one of these services were asked for their consent for screening. In the case of children, consent was sought from their parent or adult guardian. An information sheet outlining the importance of Vitamin B12 and the purpose of the data collection was interpreted verbally for each patient by a professional interpreter. Baseline demographic data included date of birth, gender, date of arrival in Australia, date of test, country of birth and cultural identity. As part of the usual testing arranged for newly-arrived refugees, these health services collected haemoglobin (Hb), mean corpuscular volume (MCV), Vitamin B12 levels and folate levels. Results were collated and de-identified by the clinicians at each site, then provided to the central researcher (JB).

Definitions

The World Health Organisation (WHO) has recommended that a level of <150 pmol/L (<203 pg/mL) be used as the threshold for defining Vitamin B12 deficiency [17]. This measure was chosen for its clinical relevance, since levels below 150 pmol/

L are associated with health consequences. Other measures that might confirm true Vitamin B12 deficiency such as holotranscobalamin, homocysteine or methylmalonic acid (MMA) are expensive and are not used in the clinic setting [17]. Anaemia was defined as a haemoglobin <120 g/L.

Measurement

Serum Vitamin B12 levels were measured using the Abbott Architect automated assay in five sites, and the Beckman Unicel DxI 800 Analyser in one site. Full blood count, including MCV, was measured using automated machines at each site which have been evaluated and approved by the National Association of Testing Authorities (NATA).

Analysis

For analysis Vitamin B12 category was dichotomised (<150 pmol/L, ≥150 pmol/L). Where appropriate, chi square analysis was used for binary categorical variables. For the high prevalence countries, the probability of Vitamin B12 deficiency was modelled using separate logistic regressions for age and gender. All analyses were tested for significance at the 5% level. Odds ratios (and 95% confidence intervals) are presented for each predictor of interest.

Results

The study population consisted of 916 persons (427 females, 489 males). Two were excluded as there was no date of birth. Fifty-four persons declined to be screened, or did not have Vitamin B12 tested, resulting in a participation rate of 94%. The age distribution of the population by gender is presented in Figure 1. Compared to the overall population of humanitarian arrivals to Australia during the study period, there is a slight over-representation of people under 30 years of age in our sample (71%, compared to 63% in the national sample) and women (47%, compared to 42% in the national sample) [18]. Most participants were examined shortly after they arrived in Australia. Sixty-six per cent had arrived in Australia within the previous month, with only 6% having a duration of stay recorded of more than four months.

Vitamin B12 Deficiency

Overall16.5% of newly arrived refugees had results consistent with Vitamin B12 deficiency (<150 pmol/L). Low levels of Vitamin B12 were least prevalent among those under 14 years of age (11.5%), compared to those aged 15–29 years (18.3%), 30–49 years (19.9%) and over 50 years (19.6%) ($p<0.001$;). Fourteen per cent of females and 18.6% of males in the cohort had levels below 150 pmol/L ($p = 0.006$). Among women of reproductive age (>15 years) 17% of had Vitamin B12 deficiency, though contrary to expectation older males (19.6%) also had Vitamin B12 deficiency.

Persons from Bhutan, Iran and Afghanistan had the highest rates of low Vitamin B12, with approximately one-third of participants from Bhutan and Iran and one-quarter from Afghanistan having levels below 150 pmol/L (Table 2). There was a significant association between Vitamin B12 deficiency and advancing age in Bhutan, but not in Afghanistan or Iran (Table 3). In addition, there was no association between Vitamin B12 and gender for any of these high prevalence countries (Table 3).

Anaemia and Red Cell Indices

Results of full blood counts were available for 913/916 participants. Of these, 16.4% had anaemia, with eight having haemoglobin levels below 90 g/L. Patients with Vitamin B12 deficiency were no more likely to have anaemia than patients without deficiency. The prevalence of anaemia (Hb<120 g/L) in the study population was 18.5% (28/151) in cases with Vitamin B12<150 pmol/L, and 16.0% (122/762) in cases with levels ≥150 pmol/L ($p = 0.5$). Macrocytosis (MCV>95 fL) was reported in 4.6% (7/151) of cases who also had Vitamin B12<150 pmol/L, and 0.9% (7/762) of cases with Vitamin B12 levels ≥ 150 pmol/L ($p = 0.004$), indicating a sensitivity of 4.6% for macrocytosis in detecting Vitamin B12 deficiency. None of the cohort had folate deficiency.

Discussion

This study has shown that Vitamin B12 deficiency is prevalent among newly-arrived refugees to Australia, particularly those from Bhutan, Iran and Afghanistan. Low Vitamin B12 levels were also more prevalent in males, and in older age-groups in some countries. Few population-based surveys have assessed Vitamin B12 status throughout the world and this dearth of data has made it difficult to estimate the magnitude of Vitamin B12 deficiency at both regional and global levels [12]. Nationally representative surveys have reported high prevalence of Vitamin B12 deficiency among children aged 1 to 6 years in Mexico (7.7%) [19], school-aged children in Venezuela (11.4%) [20], women of reproductive age in Germany (14.7%) [21], Vietnam (11.7%) [22], and the United Kingdom (11%) [23], pregnant women in Venezuela (10.9%) [20], and in the elderly in New Zealand (12%) [24]. There are no nationally representative surveys for Australia. The very few surveys that have investigated this issue in refugee source countries have been based on local- or district-level data. These surveys have reported high prevalence of Vitamin B12 deficiency among school-aged children in Kenya (where many Sudanese refugees live) (40%) [25], and pregnant women in Nepal (where Bhutanese refugees have lived since the early 1990 s), ranging from 28% [26] to 49% [6].

To our knowledge, only one study has previously investigated Vitamin B12 status in a refugee population [10]. It found Vitamin B12 deficiency in 64% (63 of 99) of specimens obtained during overseas medical examinations from adult Bhutanese refugees, 27% (17 of 64) of post-arrival medical screenings collected by three state health departments in the U.S., and 32% (19 of 60) of resettled Bhutanese refugees screened at a health clinic in the U.S. The study also reported post-arrival serum Vitamin B12 concentrations among 326 resettled refugees from 12 countries of origin, including Bhutan. Other than the Bhutanese, only refugees from Somalia were found to have Vitamin B12 deficiency (10 of 82, or 12%) [10]. Our study, which is based on a larger sample ($n = 916$) and is drawn from large community-based screening services for newly-arrived refugees distributed across five of the seven states and territories in Australia, confirms the U.S. findings of the high prevalence of Vitamin B12 deficiency in Bhutanese refugees, and provides further information on deficiency among patients from Iran and Afghanistan. This study also confirms that very few refugees with Vitamin B12 deficiency have macrocytosis and therefore macrocytosis is of little use as a tool for screening for Vitamin B12 deficiency in this population.

Despite food insecurity in their country of origin, our African participants reported lower prevalence of Vitamin B12 deficiency compared to participants from Bhutan, Iran and Afghanistan. High levels of anaemia and micronutrient deficiencies found in refugee camps, including Kakuma refugee camp in Kenya, has led the United Nations World Food Program (WFP) and UNHCR to improve the quality of the diet available including the addition of micronutrient powders (MNP) [27]. A MNP sachet (1 g) contains

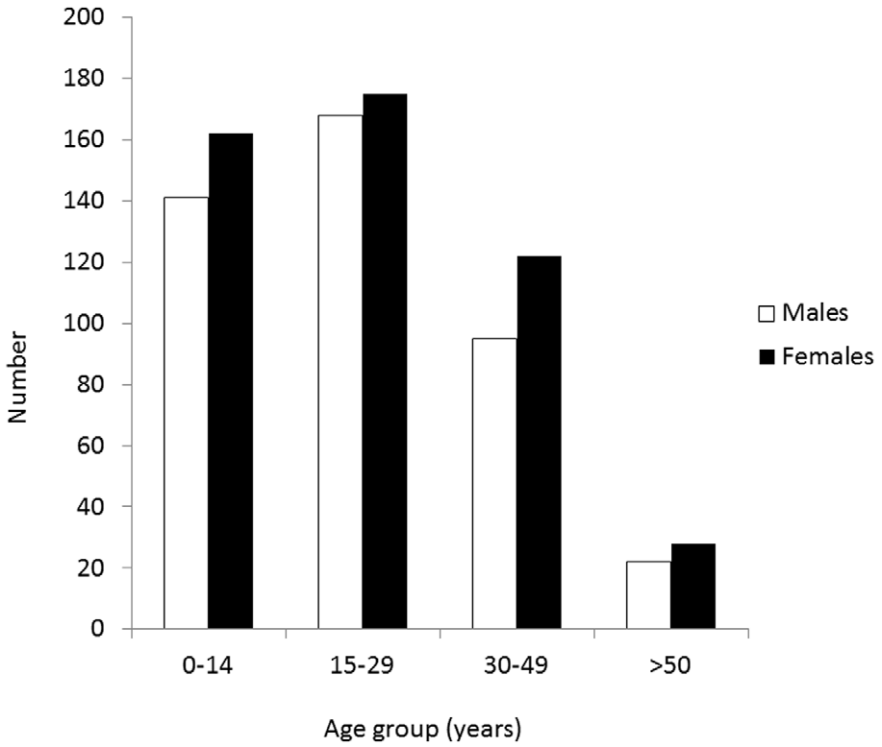

Figure 1. Age and gender distribution of newly arrived refugees who participated in the study (n = 916).
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0.9 μg of Vitamin B12. Our findings suggest that these programs are having a positive impact on reducing Vitamin B12 deficiency and should be a common practice in refugee camps worldwide.

The Bhutanese customarily do not consume animal source foods and supplementation may be necessary for this population. Although people from Iran and Afghanistan do consume meat, many of those who have fled their countries of origin due to war and human rights violations have not been in refugee camps and so would not have received micronutrient supplementation. It is

Table 2. Country of origin of refugees and Vitamin B12 results.

Country of origin	Total number of refugees	Vitamin B12 level			Median Vitamin B12 level	Interquartile range for B12 levels
		<150 pmol/L	150 – 240 pmol/L	>240 pmol/L		
		n (%)	n (%)	n (%)		
Afghanistan	159	39 (24.5)	61(38.4)	59 (37.1)	207	150, 291
Bhutan	196	61 (31.1)	82 (41.8)	53 (27.0)	188	137.5, 249
Burma	113	2 (1.8)	8 (7.1)	103 (91.2)	412	312, 532
Iraq	70	14 (20)	27 (38.6)	29 (41.4)	216	164, 308
Iran	48	14 (29.2)	17 (35.4)	17 (35.4)	176	145.5, 255.5
Sri Lanka	23	0	5 (21.7)	18 (78.3)	315	242, 373
Horn of Africa[1]	104	11 (10.6)	37 (35.6)	56 (53.9)	250.5	187, 338
Central Africa[2]	145	5 (3.5)	23 (15.9)	117 (80.7)	374	282, 510
West Africa [3]	13	0	1 (7.7)	12 (92.3)	492	399, 701
East Africa[4]	32	3(9.4)	6 (18.8)	23 (71.9)	355.5	236.5, 440
Other[5]	13	2 (15.4)	2 (15.4)	9 (69.3)	267	208, 288

[1]Includes: Somalia, Ethiopia, Eritrea.
[2]Includes: Congo (DRC), Rwanda, Burundi.
[3]Includes: Sierra Leone, Liberia.
[4]Includes: Sudan, Kenya.
[5]Includes: Bangladesh, Pakistan, China (Uyghur), India, Zimbabwe.
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Table 3. Low Vitamin B12 levels by age and gender, respectively, for each high prevalence country.

	Bhutan (n = 196)		Iran (n = 48)		Afghanistan (n = 159)	
	<150 pmol/L	Odds Ratio (95% CI)	<150 pmol/L	Odds Ratio (95% CI)	<150 pmol/L	Odds Ratio (95% CI)
Age Category	**P = 0.048**		**P = 0.54**		**P = 0.32**	
0–14 years	16.1%	1 (Ref)	23.1%	1 (Ref)	34.9%	1 (Ref)
15–29 years	35.8%	2.92 (1.22, 6.96)	25.0%	1.11 (0.22, 5.73)	21.8%	0.52 (0.23, 1.19)
30–49 years	38.5%	3.26 (1.32, 8.08)	40.0%	2.22 (0.43, 11.60)	18.8%	0.43 (0.15, 1.28)
≥ 50 years	38.1%	3.21 (1.04, 9.98)	0	0	16.7%	0.37 (0.04, 3.50)
Gender	P = 0.40		P = 0.62		P = 0.18	
Female	28.1%	1 (Ref)	33.3%	1 (Ref)	30.9%	1 (Ref)
Male	33.6%	1.30 (0.70, 2.39)	26.7%	0.73 (0.20, 2.59)	21.2%	0.60 (0.29, 1.26)

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possible that their Vitamin B12 levels may return to normal in a country with ready access to a wide variety of foods.

However, it should not be assumed that residence in Australia will necessarily result in a rapid improvement in dietary quality and quantity. In a study of 31 refugees who had settled in Perth, Gallegos and co-authors [28] found that 71% had experienced 'running out of food'. A 2007 study also found that immigrant women who have spent less than half their life in the U.S. were at higher risk of food insecurity [29].

Our results raise the question of whether or not refugees with Vitamin B12 deficiency who do not report symptoms should be treated. Since their study, the Center for International Health in Minnesota has developed a policy of administering Vitamin B12 500–1000 mcg orally to all asymptomatic Bhutanese patients. All other newly arrived refugees have their Vitamin B12 tested and where levels are low or borderline, a protocol for oral treatment is followed (personal communication Dr Ann Settgast and Dr Michael Westerhaus, Center for International Health, Minnesota).

Low maternal levels of Vitamin B12 appear to be an independent risk for neural tube defects [30]. A recent finding in South Australia is an increase in the prevalence of neural tube defect affected pregnancies in women from the Middle East and South and Central Asia (personal communication Dr Wendy Scheil, Public Health Physician, Head Pregnancy Outcome Unit, SA Health, Government of South Australia). There is an evolving debate about whether Vitamin B12 should be added to folic acid as a supplementation, or be routinely checked for and supplemented in pregnancy [31,32,33].

Recently it has been argued the measurement of Vitamin B12 levels lacks sensitivity or specificity and that biomarkers such as elevated levels of methylmalonic acid (MMA) and homocysteine, two Vitamin B12-dependent enzymes, are a more sensitive measure of Vitamin B12 deficiency [34], although this is still subject to much debate [35]. It is possible that the true rate of subclinical Vitamin B12 deficiency, if measured using biomarkers, may be significantly greater than reported here.

Our study has a number of limitations. First, this is a cross-sectional descriptive study that has assessed Vitamin B12 status on newly-arrived refugees from all age groups who attended one of the five collaborating refugee health services over a one year period. Although we cannot claim that our sample is representative of all humanitarian arrivals to Australia during the study period, the study involved participants from five of the seven Australian states and territories, and had a high participation rate of 94% of eligible participants. Importantly, the population described in our study is broadly representative of the major countries of origin of refugees resettled across the UNHCR's resettlement program. In 2011, UNHCR reported that the leading countries of origin for refugees seeking resettlement were Iraq, Burma, Bhutan, Somalia, the Democratic Republic of Congo, Iran and Afghanistan [36]. Our findings are therefore of relevance to other resettlement countries. Second, we have not reported clinical examination findings of patients with Vitamin B12 deficiency, as standardising examination protocols across the refugee health services was beyond the scope of the study. The recent U.S. three-state study was triggered by reports that physicians were seeing an increased number of patients with peripheral neuropathy. Of the 141 Bhutanese refugees seen at the refugee clinic in St Paul Minnesota, 60 were tested for Vitamin B12 levels, 19 (32%) were Vitamin B12 deficient, and two (11%) had peripheral neuropathy [10]. Third, in dichotomising B12 levels into low (<150 pmol/L) and normal (≥150 pmol/), we may have simplified a complex picture; Vitamin B12 levels between 150–240 pmol/L are borderline results which some authors have argued may also include patients with true Vitamin B12 deficiency [34].

Policies to enhance the health of refugees after resettlement, including screening, require evidence. There are structural difficulties in gathering data that can inform clinical practices for small, vulnerable populations who are not readily identifiable in standard datasets. A further challenge for refugee health policy-makers is that the refugee populations resettled in Australia constantly change in response to international geopolitical events. Individual refugee services are usually too small and overworked to produce datasets of sufficient size and quality to demonstrate emerging conditions among refugee populations. Both the U.S. and our Australian studies investigating Vitamin B12 deficiency among resettled refugees were initially triggered by clinicians' observations in a few services, but confirmed by the combined data of a network of services working together for a common purpose. Refugees, like other vulnerable populations, require networks of services that can undertake rapid research on emerging conditions, and guide policymakers on the appropriate responses to meet these emerging conditions.

Although a health assessment is recommended as soon as possible after a refugee resettles in their host country, evidence for best practice in the delivery of refugee health care to newly-arrived refugees is still in its infancy. Currently there is no consensus about Vitamin B12 testing in this population though this has been performed in a few centres in Australia. This multicentre study has

shown that low Vitamin B12 levels are common in newly arrived refugees from a number of countries. Ongoing research is needed to investigate effective approaches to treat Vitamin B12 deficiency and mitigate food insecurity, and to understand the contribution of such measures to enhancing the health of the refugee communities.

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Author Contributions

Conceived and designed the experiments: JB CP MK MW AR IC ML. Performed the experiments: JB CP MK MW AR IC. Analyzed the data: ML CP. Wrote the paper: JB CP MK MW AR IC ML.

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Benson J, Phillips C, Kay M, Hanifi H, Giri G, Leahy C, Lorimer M. Low levels of Vitamin B12 can persist in the early resettlement of refugees: symptoms, screening and monitoring. Aust Fam Physician 2015;44(9):668–73.

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Discussion

Screening of Vitamin B12 levels in our Australian cohort of 916 of newly-arrived refugees from six sites delivered the surprising result that a third of newly-arrived refugees from Bhutan and Iran, and a quarter of those from Afghanistan had dangerously low Vitamin B12 levels (11). Such a study had not been done before in a refugee population in a developed country. These figures were much higher than expected. It also confirmed that macrocytosis is not a useful marker for Vitamin B12 deficiency.

In contrast to the usual teaching, the follow-up study showed that B12 levels could not be predicted by symptoms or other blood parameters, and that they did not improve after arrival (83). It was originally intended that this second study would tease out some of the symptomatology such as irritability and paraesthesiae that anecdotally improved as Vitamin B12 levels normalized. This study was only done in an Adelaide population of 135 people and may not have had the power to show any significance with these symptoms. However the fact that none of the symptoms reached significance with relation to Vitamin B12 levels highlights that Vitamin B12 could not be predicted from the symptoms. In both the initial trial and this subsequent study, macrocytosis was not associated with Vitamin B12 levels and did not even change significantly as the Vitamin B12 level improved.

It was an unexpected finding from this second study that 11% of those with borderline levels dropped their Vitamin B12 to dangerously low levels 4-6 months after arrival. As previously mentioned, most people would assume that Vitamin B12 would improve after arrival in Australia where animal-source foods are cheap and readily available. The conclusion we made from this study was that all newly-arrived refugees should be screened for Vitamin B12 levels, regardless of symptoms and that their levels should then be followed for at least 12 months, including those with borderline B12 deficiency.

An Honours student I was supervising, looking at the diet of refugees in the 6-12 months after arrival, has just completed a further study. Using qualitative techniques she aimed to build up a picture of what the diet of Bhutanese and

Middle Eastern people is like after they have settled in Australia and hence whether our assumption that people will be eating more animal-source foods might not be correct. Again the results have been surprising and have shown that it is not food insecurity or poverty but taste, personal preference and family pressure that mean that generally people do not eat enough animal-source foods. This seems to apply to younger people as well as the older generation.

This important information about the high risk of Vitamin B12 deficiency in newly-arrived refugees has been disseminated internationally by discussions with the CDC in the USA and refugee health clinicians in the USA and the UK, presentations at national and international conferences and the publication in PLOS ONE, a journal with a high Impact Factor of 3.73.

The national study highlights the benefits of a multi-centre trial in a population where individual cities do not have large enough numbers. The results of this study are ground-breaking and have already led to further interest in this field. The other two studies are more pilots, as the numbers are small. However, the outcomes will be of great interest to others who are exploring Vitamin B12 deficiency and hopefully will lead to larger studies that will clarify what we have found.

Many more unanswered questions have flowed from this research, primarily focusing on the need for screening as compared to testing those with symptoms or signs of Vitamin B12 deficiency and whether Vitamin B12 would naturally improve after resettlement and so further testing would not be necessary.

Research on Vitamin B12 deficiency in refugees is very new and the issues we have grappled with in these studies have not been researched previously. They highlight areas that need further research with more numbers so that symptomatology of Vitamin B12 deficiency might reach significance and dietary factors can be further explored.

Vitamin B12 deficiency is cheap to diagnose and treat, and it could be argued that the high morbidity of missing a diagnosis justifies screening and management in this high-risk population. Until economic modeling is done

however this cannot be confirmed. I have begun building an evidence base on which future clinicians can make management decisions and future researchers can continue to build up a more complete picture of the issues surrounding Vitamin B12 deficiency, and how they differ in newly-arrived refugees from the rest of the majority population.

Chapter 3. Chronic Suppurative Otitis Media and Cholesteatoma

Background

Chronic suppurative otitis media (CSOM) and cholesteatoma are diseases of poverty and disadvantage. They are widespread in the developing world and CSOM is the most common cause of hearing impairment worldwide. They are rare in the majority of the population of developed countries and the recognition and management of both of these conditions are unlikely to be an integral part of undergraduate or postgraduate training outside the Indigenous health curriculum.

There is no national or international literature on the prevalence of CSOM or cholesteatoma in refugees and very little from their countries of origin. It is the most important cause of preventable hearing loss in the world but in those cultures where it is more common it has been 'normalised' and is unlikely to be a symptom that will take people to see the doctor.

The other problem with CSOM is that until recently it has been difficult to manage as the main causes are poverty and overcrowding, there are no oral antibiotics available to treat the staphylococcus and pseudomonas that cause the discharge and middle ear destruction, and the only topical antibiotic was ototoxic and so could not be used if there was a perforated tympanic membrane.

In 2006 Ciprofloxacin ear-drops were registered in Australia for the treatment of CSOM in Aboriginal people and in 2009 the Pharmaceutical Benefits Scheme (PBS) listing was extended to include others under the age of 18 with CSOM. I ran education sessions for the other GPs at the Migrant Health Service to upskill them on the identification and management of CSOM and cholesteatoma and wrote ear examination into our internal screening protocol.

Screening should always follow the WHO Principles of Screening, one of which is that there is a cost-effective treatment available for the condition (92). Hence it was only when Ciprofloxacin ear-drops were available on the PBS that screening all newly-arrived refugees for CSOM could be justified.

The first article was an audit of the prevalence of CSOM and cholesteatoma at the Migrant Health Service and the second a detailed presentation of two case studies of patients with cholesteatoma.

Having worked since 2002 in Aboriginal health and since 2007 in remote Aboriginal communities, I am familiar with the morbidity associated with diseases that are more common in this population such as chronic suppurative otitis media (CSOM), rheumatic heart disease and trachoma. Australian Aboriginal people have the highest rate of CSOM and rheumatic heart disease in the world and Australia is the only developed country that still has endemic trachoma. 'The National Guide to a Preventive Health Assessment for Aboriginal and Torres Strait Islander people' recommends screening for these conditions but they are not part of the 'RACGP –Redbook Guidelines for preventive activities in general practice' or the ASID 'Diagnosis, management and prevention of infections in recently arrived refugees' (16, 63, 93).

With this experience I had been examining my own refugee patients for evidence of CSOM, rheumatic heart disease and trachoma as part of their initial health assessment. I found no trachoma and only very rare rheumatic heart disease. However, screening all patients with otoscopic examination revealed a high rate of CSOM, and four confirmed cases of cholesteatoma.

In discussion with other refugee health practitioners, I realised that others had never diagnosed CSOM or cholesteatoma, as ear examination does not appear in any refugee screening guidelines. Unless they have worked in Aboriginal health, General Practitioners (GPs) may never have seen CSOM and most will not diagnose a cholesteatoma in their lifetime.

When all the GPs at the Migrant Health Service were screening everyone for CSOM the numbers of people diagnosed jumped dramatically. An unusual finding in this cohort was the large number of adults with CSOM, as the disease is usually seen more commonly in children. This reflected the lack of resources in the countries of origin of newly-arrived refugees as the condition had not been diagnosed or treated in the past. All of the adults were deaf in the affected ears.

There is limited research on CSOM or cholesteatoma from the countries of origin of Australia's refugees and no previous research on CSOM or cholesteatoma in refugees in developed countries. However, this is an important disease to diagnose and treat as early as possible as the long-term morbidity associated with deafness is preventable.

Hence the importance of doing an internal audit and publishing the findings in a peer-reviewed journal that is easily accessible to the GPs who are seeing patients of refugee background (10).

The following article has been removed due to copyright restrictions:

Benson J, Mwanri L. Chronic suppurative otitis media and cholesteatoma in Australia's refugee population. Aust Fam Physician 2012;41(12):978–80.

You can freely access the full text of this article at
http://www.racgp.org.au/afp/2012/december/suppurative-otitis-media/

JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

Mwanri Lillian & Benson Jill. **Cases of Cholesteatoma in Refugee Populations in South Australia.** *Journal of pharmaceutical and biomedical sciences (J Pharm Biomed Sci.)* 2013 December; 37(37): 1915-1921.

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Case study

Cases of cholesteatoma in refugee populations in South Australia

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Core idea: Cholesteatoma is a serious health condition and can lead to severe complications including meningitis, brain and extradural abscesses and death. While it is not an uncommon in developing countries, the cholesteatoma occurrence is rare in Australia. Many health professionals in Australia have not seen cholesteatoma cases in their practice. This paper analyses the occurrence of a few cases in a newly arrived refugee populations. Findings highlight the need to educate health professionals about the higher than the expected cases in newly refugee populations. The findings are highly transferable to other countries similar to Australia where refugee population from developing countries is increasing.

Authors contribution: Both the author contributed equally to this paper.

Abstract: *Purpose:* This paper aims to describe the unusually high prevalence of cholesteatoma in refugees, and to advocate for the preparation of health systems including educating clinicians and other health professionals about conditions that are more common in refugee populations.
Methods: An audit of patient records from the Migrant Health Service in Adelaide was conducted from June 2009 to November2011 to identify Chronic Suppurative Otitis Media (CSOM) and cholesteatoma cases.
Results: In the 2.5 year timeframe of the study, 20 patients were diagnosed with CSOM, including 13males (65%) and seven females (35%). Two cases of Cholesteatoma were also identified during the same study period. Details of CSOM have been published elsewhere[1]. In the current paper, we report two cases of Cholesteatoma in recently arrived refugee populations in South Australia.
Discussion: Both cholesteatomas and CSOM are diseases of poverty and rare conditions in the general Australian population. In the past two decades, Australia has received an increasingly high flow of migrants from across the world with significant proportions arriving with refugee backgrounds. Refugees have multiple risk factors for cholesteatoma: were having commonly been victims of torture, trauma and head injury and mostly coming from a background of severe and long-standing socio-economic disadvantage. Advocacy and education are needed to improve the preparedness of clinicians, other health workers and health systems to address the unique needs of this vulnerable group of people to ensure that they have optimum health as they settle into Australia.

Key words: Recently arrived refugee populations; Cholesteatoma; Medical and health workers' education; addressing health inequalities.

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INTRODUCTION

A cholesteatoma is a slow-growing, cystic non-malignant but destructive lesion consisting of stratified squamous epithelium and filled by keratin. Cholesteatomas can affect any area of the temporal bone leading to significant intracranial and extracranial complications[2]. They may invade skull and adjacent structures through mechanisms including mechanical compression, osteoclastic action, production of proteolytic enzymes and cytosines[3].Complications include meningitis, brain abscess, thrombophlebitis of the lateral sinus and extradural abscess, peripheral facial paralysis and death[4-8].

Cholesteatomas are categorised as congenital or acquired with only 2% to 5% known to be congenital[9].The majority of cholesteatomas in adults are acquired, with evidence suggesting that significant proportions can develop in individuals with chronic suppurative otitis media (CSOM) [10,11], an inflammatory disease involving the middle ear usually associated with a purulent discharge through a perforated tympanic membrane. The World Health Organisation (WHO) estimates that between 65 and 330 million people across the world are affected by CSOM, with the majority being in the developing world including Sub-Saharan Africa, where its prevalence is as high as 0.4-4.2%[12]. In developed countries including Britain, the prevalence of CSOM is very low, only 0.9% in children and 0.5% in adults. However, in Indigenous populations throughout the world, the prevalence of both CSOM and cholesteatoma is higher than in the general population with figures of CSOM of up to 12%[13]. For example, in some remote Aboriginal communities in Australia, 50% of children have CSOM[11]. The prevalence of cholesteatoma in the adult population in Australia is extremely low, in the order of 6/100,000[11,14]
Similar to the risk factors for CSOM, socio-economic factors including overcrowding, frequent upper respiratory tract infections, inadequate nutrition, poverty, low literacy rate and inadequate sanitary facilities have been reported as determinants ofcholesteatoma[12,14-17]. Both CSOM and cholesteatoma are influenced by poverty and not ethnicity[14,18].

A rarer cause of acquired cholesteatoma is after trauma, with presentations known to occur up to 24 years after the original injury[19].Mostly this is in relation to a confirmed fracture of the temporal bone or a severe injury such as a gun-shot wound. However diastasis of the suture lines or tears in the tympanic membrane has been known to cause implantation of foci of squamous epithelium which go on to produce cholesteatomas[19].

Australia is increasingly becoming the most diverse population in the world, and in the past two decades has received a steady flow of migrants, many of whom come as refugees or asylum seekers. In 2010-2011, Australia accepted 13,750 humanitarian refugees and the numbers are increasing annually. These populations are significantly diverse with the top ten source countries in 2010 being Burma, Iraq, Bhutan, Afghanistan, Congo, Ethiopia, Somalia, Sudan, Liberia and Sierra Leone. Every year the source countries change according to the areas of conflict and human rights abuses[20]. Most refugees come from environments with meagre food choices, high infectious diseases rates, poverty, overcrowding and limited health-care facilities and many have been subjected to torture, trauma and violence, with estimates of up to 64% having sustained a head injury[21]. Because of these backgrounds, refugees and asylum seekers may bring new, complex, unique and challenging health conditions not previously encountered by Australian health workers and health systems.

The focus of this paper is to describe two cases of cholesteatoma diagnosed in newly arrived refugees in South Australia. The aim is to present our experiences of cholesteatoma and to highlight the unusually high occurrence of this condition in refugee populations compared to the general population in Australia. Information derived from this paper can inform policies and practices that will improve the health of refugee populations in Australia and in similar populations in other developed countries.

METHODS

The Migrant Health Service (MHS) of South Australia is a State funded community health service where newly arrived refugees are seen by a multi-disciplinary team for the first 12 months after arrival. Approximately half of Adelaide's refugee population is screened at the MHS soon after arrival, the remainder being seen by other health services including General Practitioners (GPs) around Adelaide. Unlike other health workers across the state, health workers including

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GPs at the MHS are involved in regular education sessions updating them about refugee issues and most have post-graduate qualifications in cross-cultural health. As such they are more able to identify new and challenging health conditions that are generally not feasible to identify in the Australian general health system.

Four adults have been diagnosed with cholesteatoma over the last 10 years, confirmed by CT of head and requiring surgery. This is over 100 times the predicted prevalence in the Australian population. The description of two cases of cholesteatoma diagnosed at MHS in South Australia, presented in the current paper, sheds light on some of the risk factors in this population. Case identification methods for these cases were similar to recently published article on CSOM for these populations[1].

ETHICAL CONSIDERATIONS

The Manager, clinic coordinator and individual GPs gave permission for the research to occur and individual written consent was given by both patients whose cases are described. However their identity has been subtly de-identified. Ethics approval to conduct the research was obtained from SA Health HREC.

CASE REPORT A

Fatima (pseudonym), aged 18, arrived in Australia in October 2011 from Afghanistan with her mother and two young brothers to join her father who had been in Australia for two and a half years. The family had moved to Pakistan eight years earlier after they had been attacked by the Taliban and, amongst other injuries to the family, Fatima had been badly beaten around the head. Just five months before leaving for Australia the Taliban attacked the family again and kidnapped two brothers aged 16 and 14. They had not been seen since that time.

Since the attack Fatima had pain in both ears with occasional discharge, sometimes of blood; dizziness and deafness. She had been given drops in Pakistan and once had suction that caused severe pain rendering her unconscious for several hours.

At her initial screening assessment on arrival to Australia, the GP noted a central perforation of the right tympanic membrane, as well as a smaller perforation in the attic, with visible granulomatous tissue and other debris; and a large, almost total, perforation of the left tympanic membrane. There was no mastoid tenderness or lymph nodes present.

A diagnosis of chronic suppurative otitis media with possible cholesteatoma was made and Fatima was given Ciprofloxacin ear drops and sent for audiometry. A CT scan of the head was also ordered and she was referred to a teaching hospital.

Audiometry confirmed a left-sided moderate to severe mixed hearing loss and a right-sided severe mixed hearing loss (Fig. 1). CT of the head suggested bilateral cholesteatomas with the right tympanic membrane unable to be identified (Fig. 2). Ear swab grew no pathogens.

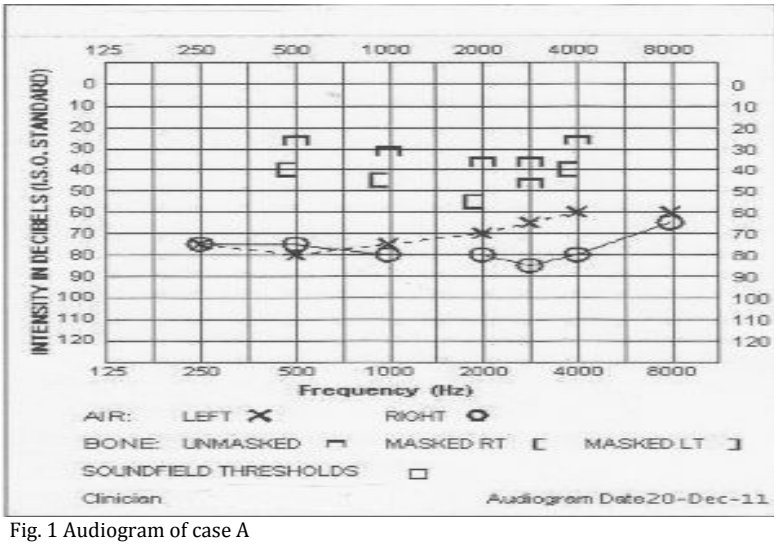

Fig. 1 Audiogram of case A

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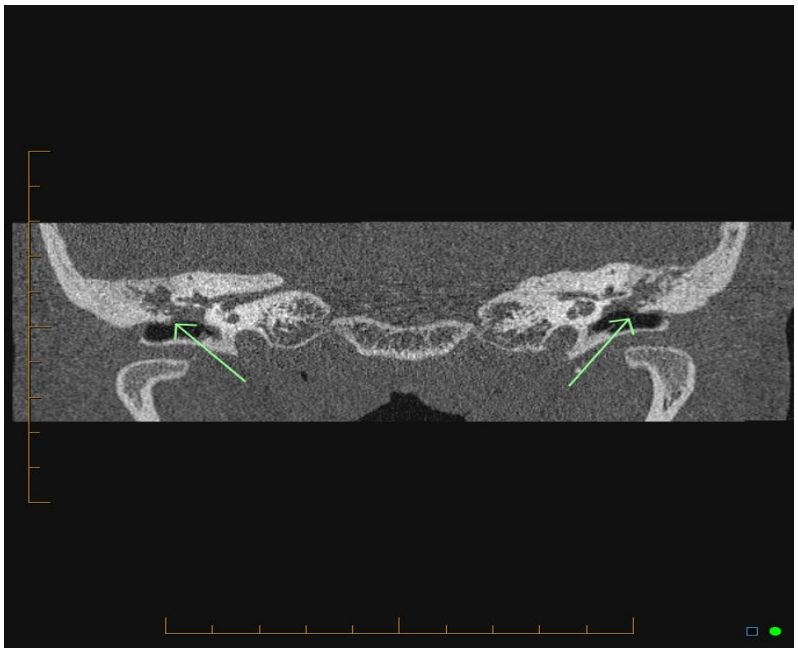
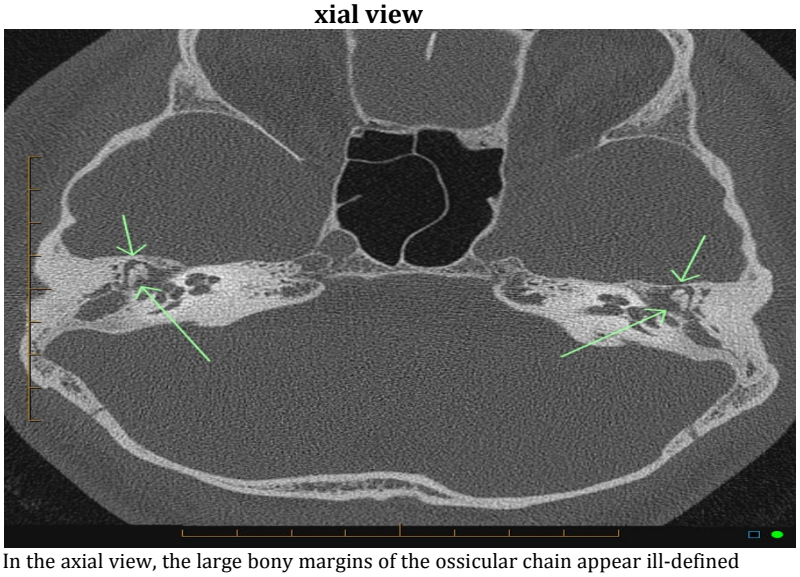
Coronal view



In the coronal view, there is extensive soft tissue opacification of the attic of the middle ear cavities and the mastoid air cells on both sides. On the left side the tympanic membrane appears deficient in its mid portion while on the right side the tympanic membrane is not specifically identified. Ruptured or retracted. There is the impression of some erosion of the scutum on both sides particularly the right. The arrows are pointing to the soft tissue and erosion of the scuta on both sides.

xial view



In the axial view, the large bony margins of the ossicular chain appear ill-defined with the arrows pointing to the soft tissue surrounding the ossicular chain

Fig. 2 CT of case A

The first hospital ENT specialist Fatima saw cleaned out her ear and gave her ear-drops containing triamcinolone, neomycin, gramicidin and nystatin, with no follow-up organised, and no letter sent to the referring GP. She was referred to a private ENT specialist who removed copious fungal debris from the right ear revealing a total tympanic membrane perforation and middle ear

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squamous debris. He confirmed the GP's suspicion of cholesteatoma and referred her directly to another teaching hospital.
In June 2012, Fatima underwent an Examination under anaesthesia of her right ear with a modified Radical Mastoidectomy. The head of the malleus and incus were removed along with squamous debris and a cholesteatoma (5x2x1mm) confirmed by histopathology.
Fatima was fitted with bilateral Xtreme 121 bone conductor hearing aids, which improved her 'speech in noise testing' from 0% to 70%. When last seen she was learning English, had minimal pain or dizziness. Along with permission to publish her case, she sent a letter in English, thanking the GP for her support.

CASE REPORT B

Mohammed (pseudonym), aged 50, a Kurdish journalist, and his wife, travelled from Iraq to Australian waters in 2002. The boat in which they were travelling sank and Mohammed was hit on the head and found unconscious in the water. They were taken to a detention camp on Nauru where they lived for the next three years. They were moved to Adelaide in July 2005 on Temporary Protection Visas and in April 2008 were given visas to stay in Australia permanently.
In Iraq, Mohammed had limited access to health care and had been arrested and beaten many times. He had had a right discharging ear associated with hearing loss and dizziness since 1998.
In Nauru, Mohammed was diagnosed with 'chronic otitis media and externa' and given Amoxycillin and ear-drops containing framycetin, gramicidin and dexamethasone. An ear swab showed *staphylococcus aureus*.
After arrival in Adelaide in July 2005, Mohammed was seen by a community GP who continued the above ear-drops and added Cefuraxime and bethistine.
In February 2006 he was seen at the Migrant Health Service and referred urgently to the local teaching hospital because of suspicion of cholesteatoma. Limited right atticotamy, tympanoplasty, and mastoidectomy, with resection of the posterior bony wall of the external auditory canal as well as the ossicles were performed in May 2006. Cholesteatoma was found in the epitympanum and facial recess. Recovery was slow and associated with severe dizziness.
Mohammed was reviewed regularly and in May 2009 was found to have a recurrence of the right cholesteatoma arising from the posterior margin of the postero-superior perforation. The chorda tympani was enveloped in disease but the tegmental wall was intact.
Mohammed's right ear continued to discharge on occasions and in September 2011 an Examination under anesthesia revealed ear canal adhesions, which were divided. It was thought that the adhesions were the cause of recurrent otitis externa.
Mohammed has continued to have problems of dizziness and pain and recent ENT review and CT scan revealed a granuloma in his right mastoid cavity.

DISCUSSION

There is no current literature on the rate of cholesteatoma in newly arrived refugee populations in Australia, but most come to Australia from environments which favour the development of CSOM and cholesteatoma[20]. The identification of four cases in the small number of refugees seen at MHS may reflect the multiple risk factors of increased frequency of CSOM and head injury[1]. It is also indicative of a higher frequency of these conditions in newly arrived migrants especially refugees compared to the general population of Australia or other developed countries.

According to the ABS[22], most migrant populations live in mainland state metropolitan areas. Given that cholesteatomas are very rare in the Australia[11,14] health workers including general practitioners and other clinicians (including ENT specialists) are less likely to be aware of their unique features for ease of diagnosis. Furthermore it may be even more challenging to diagnose and treat cholesteatomas in newly arrived refugee populations as they may tolerate diseases and their complications well into their adult life[23,24]. In addition, it has been described that that one of the challenges of working with refugee populations is the lack of evidence pertaining to their unique health issues[1,25]. Medical and other health care staff with limited previous experience of diagnosing and managing cholesteatomas will need to ensure that they are able to properly identify and manage patients with these conditions as the consequences of no diagnosis, misdiagnosis and mismanagement are likely to be severe.
Both cases had a history of a traumatic head injury. There is a very limited literature on

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cholesteatoma after head injury but many refugees arriving in Australia come from countries with high prevalence of violence leading to head injuries[21]. Untreated head injuries coupled with factors associated with poverty such as poor nutrition and high prevalence of infection, malnutrition and chronic stress; may result in middle ear and other serious infections[16]. Middle ear infections for example in the case in CSOM have been recognised as causes of cholesteatoma[1,11].

In the current study the diagnosis of both cases was confirmed by CT scanning following referrals of patients to hospitals in South Australia. This is consistent with best practice in the management of cholesteatoma.

As with many issues affecting new and vulnerable populations, the presence of cholesteatoma in these populations in Australia is likely to make resettlement more challenging because of the resulting poor quality of life and potential severe consequences including brain abscesses. These cases illustrate the need for concerted efforts in promoting the awareness of cholesteatoma to all clinicians and other health service providers to these new migrants in Australia and other developed countries. Health workers especially clinicians and public health practitioners should be aware of conditions such as cholesteatoma in these disadvantaged populations. The length of time to diagnosis and treatment and the lack of awareness of health professionals to the possibility of serious illness are exemplified in these case studies. The importance of continued monitoring of hearing and for recurrence is also highlighted.

Along with other diseases of poverty and trauma, management protocols and guidelines for all newly arrived refugees should have cholesteatoma listed as a significant health issue prevalent in these populations. Advocacy and education are also needed to improve the preparedness of health workers and health systems to address the unique needs of this vulnerable group of people to ensure that they have optimum health as they settle into Australia.

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Competing interest / Conflict of interest
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Discussion

In my audit the prevalence of chronic suppurative otitis media was 2.07%, which meets the WHO definition of 'high', especially in the adults where the prevalence was 2.64%. This is obviously very different to the prevalence in the rest of the Australian population that will be low, except in Aboriginal and Torres Strait Islander people (10).

The prevalence of cholesteatoma in the population I saw at the Migrant Health Service was about 100 times higher than would be expected (84). This is probably a direct consequence of the high rate of CSOM but there may be other contributing factors such as head injury. We decided to publish this research as case studies based on two of the refugee patients I had seen. After gaining ethics approval and written permission from the two patients, I interviewed them, accessed their clinical files, Xrays, audiograms etc. Dr Mwanri performed another literature review and wrote up the discussion of the cases for the peer-reviewed journal.

The morbidity and even possible mortality that can result from untreated CSOM and cholesteatoma and the fact that refugees may not present with symptoms of these diseases, mean that otoscopy should be included in the screening protocols for all newly arrived refugees. It is also important that clinicians have training in order to be able to recognise these conditions and are aware of the particular treatment for CSOM.

Since the publication of these articles, doctors working in other refugee health services in Australia have become more aware of the possibility of high prevalence of CSOM and cholesteatoma in newly-arrived refugees. Otoscopy has been included in their internal screening protocols and anecdotally there has been an increase in the detection of CSOM and cholesteatoma in their clientele.

CSOM is not difficult to diagnose or treat, but the consequences of missing a diagnosis will leave a person with deafness and ear discharge. This is likely to affect their education, socialization, acquisition of language and work prospects. Cholesteatoma is more difficult to diagnose and treat, but can be fatal. The

publication of these two papers is the first alert to those working with refugees that these conditions are much more common than the rest of the majority population.

Chapter 4. Helicobacter pylori

Background

Helicobacter pylori (H.pylori) is a bacteria that can infect the gastrointestinal tract, causing symptoms, signs, morbidity and mortality across the life-span. It is an emerging health issue internationally and has been identified as a preventable cause of gastric carcinoma and peptic ulcer. It is generally acknowledged that its prevalence will increase in the presence of overcrowding, low socioeconomic status and poor sanitation. There is scant literature on people of refugee background, either from their source countries, in their country of resettlement or across a spectrum of ethnicities. The literature has usually identified extremely high rates, for instance 82% in asymptomatic African children in Western Australia (7)

A recent major change in the H.pylori arena has been the validation of stool H.pylori antigen (Ag) as a gold standard test for identification and follow-up. Previous to this, only Urea breath tests were validated for active infection as H. pylori antibody (Ab) in serum only identifies exposure and not current infection. Many of the previous studies had only used H.pylori Ab and so their use in identifying prevalence is of H.pylori is of doubtful significance.

This cross-sectional study was conducted at the Migrant Health Service in Adelaide. It involved an extensive literature review, collection of a large data-set and complex statistical analysis.

All newly arrived refugees at the Migrant Health Service have stool collected as part of their initial screening in order to detect parasites. After discussion with the local pathology laboratory, H.pylori Ag was added in 2010.

As the Senior Medical Officer at the Migrant Health Service, I needed to make a decision about whether we should screen all newly-arrived refugees for H.pylori Ag. An extensive literature review revealed mainly studies that had been done on the general population in developed countries. For those studies done on children, they were mostly done on severe gastrointestinal symptoms or signs.

An initial audit of my patients found that the prevalence of H.pylori was not as high as was found in Western Australia or from source countries. If there is a prevalence of over 80% it is not cost-effective to screen a population. However if it's lower and there are significant sequelae of a positive test, it would be appropriate to screen. Initially I was also concerned that those with H.pylori were more likely to have Vitamin B12 deficiency but this was not confirmed by our Vitamin B12 study, even though this connection has been found in other international trials.

As well as a formal collection of data to establish the general prevalence of H.pylori in newly-arrived refugees, I decided to look at the height and weight of children with and without H.pylori. Children of refugee background are known to be shorter and thinner than their Australian counterparts. The aetiology of this is likely to be complex but is assumed to be due to previous poverty and undernutrition. However I noticed that in some children, their weight did not seem to improve in an environment of food security and that often these children had symptoms of anorexia and early satiety and were positive for H.pylori Ag. There was no current literature on an association of thinness with H.pylori in refugee children though there has been a small amount of research from developing countries about 'growth retardation' in children with H.pylori (94-96).

Medical students at the University of Adelaide need to be part of a research project as an essential requirement of their course in 3rd year. I have taught refugee health at both the University of Adelaide and Flinders University for many years and a group of students asked if I would supervise them for their research project. I decided that I would do a large descriptive study looking at the H.pylori data over several years and the students agreed to help me collect the data.

I gained Ethics approval from the University of Adelaide and SA Health and then over the next 18 months the four students entered data from 927 patients into an Excel spreadsheet. This involved many hours of supervised access to the clinical software system at the Migrant Health Service. When they were about

halfway through collecting the data they did a short literature review, prepared a power point presentation and presented our interim findings at the North American Refugee Health Conference in Toronto in Canada. They were the only medical students to present at the conference and were widely praised. They are co-authors on the 'Prevalence of Helicobacter pylori in Newly-arrived refugees attending the Migrant Health Service' article.

I was supervising Dr Razlyn Abdul Rahim's placement at the Migrant Health Service as a Public Health registrar. She needed to do statistical analysis of a dataset as part of her training and we had just completed the collection of the H.pylori data. How to interpret the data involved extensive discussions about such issues as whether it would be better to use univariate or multivariate analysis and whether to do a nested case-control study or a cohort study for the children. We made the decisions that the cohort study would have more power and that we would use multivariate analysis.

The statistical analysis was quite complex, especially, the Z scores for the 'Newly-arrived refugee children with Helicobacter pylori are thinner than their non-infected counterparts' article. We involved Dr Rishi Agrawal, the visiting Paediatrician at the Migrant Health Service in this process and he has continued to be part of the publication of the second article.

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ORIGINAL ARTICLE

WILEY Helicobacter

Prevalence of *Helicobacter pylori* infection in newly arrived refugees attending the Migrant Health Service, South Australia

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Abstract

Background: To determine the prevalence of *Helicobacter pylori* infection in the refugee population attending the Migrant Health Service, South Australia, identify demographic factors associated with infection and compare prevalence of infection in refugees with that of the nonrefugee population in Australia.

Materials and Methods: Cross-sectional study conducted between October 2010 and August 2013. Monoclonal stool antigen testing for *H. pylori* infection is performed as part of a comprehensive health assessment for newly arrived refugees. The sample population included 922 adults and children. Outcome measures were (i) prevalence of *H. pylori* infection (ii) association between demographic factors such as sex, ethnicity and age, and *H. pylori* infection.

Results: *H. pylori* infection was detected in 198 (21.5%) participants (95% CI 18.9%–24.3%). The odds of infection were lower in females OR 0.71 (95% CI 0.51–0.98) compared to males. Compared to Middle Eastern participants, the odds of infection were 1.75 (95% CI 1.17–2.62) times higher in African and 1.90 (95% CI 1.10–3.26) times higher in Burmese participants. Infection was not associated with age.

Discussion and Conclusion: *H. pylori* infection is common among newly arrived refugees. The long latency of infection to development of complications and the availability of testing and relatively effective eradication regimens all add weight to a decision to screen in this population.

KEYWORDS
epidemiology, prevalence, refugees

Helicobacter pylori (*H. pylori*) is a common bacterial infection associated with gastrointestinal and extra-gastrointestinal diseases. Commonly acquired in childhood,[1,2] the organism is transmitted via person-to-person contact and through consumption of contaminated water.[3] Infections are more common in developing countries with reported prevalence of as high as 90%.[4,5] There are limited studies on the prevalence of *H. pylori* in the source countries of refugees. However, research on those with symptoms shows high rates, for example, 48% in Burma[6] and 73.4% in Bhutan.[7] Factors contributing to increased exposure to the organism include increasing age, large family size, low socioeconomic status, overcrowding and poor sanitation as well as having an infected sibling.[4,5,8]

Gastrointestinal manifestations include gastritis, atrophic gastritis and peptic ulcers.[2,9] *Helicobacter pylori* infections have been acknowledged to contribute to the majority of gastric carcinoma cases worldwide.[9] Growth retardation and nutritional deficiencies particularly iron deficiency anemia, resulting from impaired gut iron absorption in children, have also been associated with *H. pylori* infections in developing countries.[1,3]

Of the 51.2 million forcibly displaced people worldwide, 16.7 million are refugees.[10: p 2] The top three countries of origin are

Afghanistan, Syrian Arab Republic, and Somalia, while Pakistan, Islamic Republic of Iran, Lebanon, Jordan, and Turkey receive the highest numbers of refugees.[10: pp 2,3] Over 98 000 people identified as refugees were subsequently resettled in 21 countries in 2013, with approximately 90% of official UNHCR refugees admitted into the USA, Canada, and Australia.[10: p 21] Given that refugees live in conditions that enhance the transmission of *H. pylori,* we aim to quantify the burden of infection in this population in order to contribute to available evidence informing the need for targeted screening. Screening and treatment for *H. pylori* are associated with a reduction in risk of gastric cancer and development of peptic ulcer disease and prevents anemia.[11] Furthermore, a high-risk population screening strategy with stool antigen, treatment of positive cases, and retesting is shown to be relatively cost-effective.[12] It is acknowledged that, if a prevalence of 75% is assumed, such a screening strategy can avert 3.0 cases of gastric cancer and 22.8 cases of peptic ulcers per 1000 people managed, with a cost saving of US $111 800 per cancer case prevented.[12] Whereas if 25% prevalence is assumed, the strategy potentially prevents 1.0 cancer case and 7.6 ulcers per 1000 people managed, with an estimated cost saving of US $193 900 per cancer case.[12]

1 | METHODS

1.1 | Study setting

Our study was conducted at the Migrant Health Service of South Australia. Of the total number of humanitarian entrants resettled in the state (1369 individuals in 2013–14),[13] approximately half access primary health care at this facility. Newly arrived refugees undergo a comprehensive health assessment within the first few weeks of entry to Australia at a nurse-led New Arrival Clinic. A suite of routine screening tests is performed to detect various communicable and noncommunicable diseases. *Helicobacter pylori* stool antigen is one of the investigations conducted.

1.2 | Testing methods for *H. pylori*

Invasive and noninvasive methods are available to detect *H. pylori* infection. Our discussion will focus on noninvasive testing methods namely serology, urea breath test (UBT), and stool antigen test. *H. pylori* IgG antibody serology is the most frequently used test in primary care with relatively low cost and higher availability.[14] Test sensitivity range from 90% to 97% and test specificity range from 50% to 96%.[15] However, serology is less reliable in children and does not differentiate between previous and active infection.[15,16] The UBT identifies the presence of active infection by detecting bacterial urease activity.[14,17] The test has both a sensitivity and specificity between 95% and 97% and high negative and positive predictive values.[15,17] Although recommended for posteradication testing, it is not widely available.[14] The stool antigen test detects the presence of active infection by enzyme immunoassay.[14,17] It has a pooled sensitivity and specificity of 94% and 97%, respectively.[15] The negative and positive predictive values are also high.[17] It is recommended for use in pretreatment diagnosis and posteradication monitoring and is easily administered compared to the UBT.[15,17] Redeen and colleagues report the accuracy of UBT and serology as 96% and 86%, respectively, when compared against the gold standard test of bacterial culture.[18] The accuracy of the UBT was comparable to other invasive tests.[18] Stool antigen test is comparable to UBT thus both can be used interchangeably for diagnosis of *H. pylori* infection.[17] Hence accounting for the high validity and ease of application, stool antigen testing appears favorable over serology for diagnosis of *H. pylori* in primary care settings.

Diagnosis of *H. pylori* infection was made by monoclonal fecal antigen enzyme immunoassay (MFAT) (ImmunoCard STAT!®HpSA kits (Meridian Bioscience Inc)). The stool antigen test has been used at the Migrant Health Service since October 2010.

1.3 | Data collection and analysis

Data on all patients attending the Migrant Health Service between October 2010 and August 2013 for the comprehensive health assessment were extracted from the electronic patient records onto MS Excel. Information on date of birth, sex, weight, height, hematological indices including hemoglobin (Hb) and mean corpuscular volume (MCV), ferritin, iron, and vitamin B12 level as well as the presence of *H. pylori* infection collected during the initial comprehensive health assessment was obtained.

Data analysis was conducted using Epi Info™ (version 7.1.4.0, Centers for Disease Control and Prevention, Atlanta, USA) and Stata 12 (StataCorp LP, TX, USA). Associations between categorical independent variables and *H. pylori* infection status were initially analyzed using chi-squared test or chi-squared test for trend. Logistic regression was then performed to examine the effect of independent variables on *H. pylori* infection. Lastly, multivariate logistic regression was used to examine the effect of covariates namely sex, ethnicity, and age on *H. pylori* infection. The significance level was set at 5%. The Middle Eastern ethnicity was set as the reference group for comparative data analysis.

The study was approved by the SA Health Human Research Ethics Committee and University of Adelaide Human Research Ethics Committee (SSA reference: SSA/12/SAH/51).

2 | RESULTS

The sample size included 923 subjects, one excluded due to the absence of a stool sample for *H. pylori* testing. Of the remaining 922 subjects, 510 (55.1%) were male (Table 1). Ethnicities represented are Middle Eastern (39%), African (27.1%), Bhutanese (21.5%), Burmese (9.7%), and others (2.7%) (Table 1). The median age was 19.3 years with an age range from 0 to 82 years. *H. pylori* infection was detected in 198 (21.5%) participants (95% CI 18.9%–24.3%).

Bivariate analysis showed males and females were similarly affected (P=.16). A difference in prevalence was observed between ethnic groups (Table 2). The odds of infection were 1.57 (95% CI 1.06–2.31) times higher in African participants compared to the

TABLE 1 Demographic characteristic of attendees at the Migrant Health Service, South Australia, October 2010 to August 2013

Variable	Number (%)
Sex	
Male	509 (55.2)
Female	413 (44.8)
Ethnicity	
Middle Eastern	360 (39.0)
African	250 (27.1)
Burmese	89 (9.7)
Bhutanese	198 (21.5)
Others	25 (2.7)
Age group in years	
0–9	151 (16.4)
10–19	329 (35.7)
20–29	183 (19.9)
30–39	135 (14.7)
40–49	63 (6.8)
50–59	37 (4.0)
60 and above	23 (2.5)

Middle Eastern group (Table 2). Similarly, the odds of infection in the Burmese participants were 1.74 (95% CI 1.02–2.97) times compared to our reference group (Table 2). There was no association between age and *H. pylori* infection (Table 2).

The effects of these variables were assessed further in a multivariate logistic regression model presented in Table 3. Independent variables included in the model were sex, ethnicity, and age. Those categorized as "Other" ethnicities were excluded because this group comprised small numbers of individual from a variety of geographic locations. Hence, the remaining sample size is composed of 897 subjects.

Multivariate analysis shows that after adjusting for ethnicity and age, the odds of *H. pylori* infection were lower in females with OR 0.71 (95% CI 0.51–0.98) compared to males (Table 3). The association between ethnicity and infection was enhanced after adjusting for sex and age. Compared to Middle Eastern participants, the odds of infection were 1.75 (95% CI 1.17–2.62) times higher in African and 1.90 (95% CI 1.10–3.26) times higher in Burmese participants. The odds of infection in Bhutanese refugees were comparable to the reference group.

TABLE 3 Adjusted odds ratios of demographic factors tested for association with *Helicobacter pylori* infection

Variables	Odds ratio	95% CI	*P*
Sex			
Male	Reference		
Female	0.71	0.51–0.98	.04
Ethnicity			
Middle Eastern	Reference		
African	1.75	1.17–2.62	.01
Burmese	1.90	1.10–3.26	.02
Bhutanese	1.13	0.72–1.79	.60

3 | DISCUSSION

Refugee populations are at increased exposure to *H. pylori* due to poor living conditions characterized by overcrowding, large family sizes, and poor sanitation. In this study, infection was observed in approximately one-fifth of the refugee population attending the Migrant Health Service from the period of October 2010 to August 2013. Male sex and Burmese and African ethnicity were found to be associated with *H. pylori* infection.

We compare our findings to the epidemiology of *H. pylori* infection in the Australian population available from peer-reviewed literature. It is important to note that individual studies vary in participant demography and method of detecting infection. Serology is the most frequently used method but as mentioned previously, does not distinguish between active and previous infection. Hence, it is likely that the prevalence of active infection in the general Australian community is overestimated and is probably much lower compared to the refugee population. Our study findings are therefore most comparable to

TABLE 2 Association between demographic characteristics of participants with *Helicobacter pylori* infection

Variable	N	*H. pylori* positive n (% of row)	Odds ratio	95% CI	*P*
Sex					
Males	509	118 (23.2)	Reference		
Females	413	80 (19.4)	0.80	0.58–1.10	.16
Ethnicity					
Middle Eastern	360	66 (18.3)	Reference		
African	250	65 (26.0)	1.57	1.06–2.31	.02
Burmese	89	25 (28.1)	1.74	1.02–2.97	.04
Bhutanese	198	39 (19.7)	1.09	0.70–1.70	.69
Others	25	3 (12)	0.61	0.18–2.09	.43
Age	922	198 (21.5)	1.00	0.99–1.01	.69

others that utilize either the UBT or stool antigen test in participants regardless of the presence or absence of symptoms.

Within the broader Australian community, estimates of prevalence in the population range from 15% to 38%.[5,19–24] Ages of participants in these studies range from 16 to 80 years[5,19,20,22–24] with the exception of one that included subjects aged 1–59 years,[21] which yielded the lowest prevalence estimate. The crude prevalence in our participants of 21.5% is nearly 1.5 times that of the Australian population's estimate when both adults and children are included. The proportion of adults above 20 years that are *H. pylori* positive in our study sample is comparable to estimates in the Australian adult population. Two studies focussing on children aged 0–14 years (N=147) and 4 months to 2 years (N=52) each reported prevalence of 14% and 44%, respectively.[25,26] The proportion of children less than 15 years of age infected with *H. pylori* in our study is about 1.6 times higher than that reported by Hardikar and Grimwood[25] yet half the burden of that reported by Ritchie et al.[26] However, this should be interpreted with caution as participant characteristics and settings are not entirely comparable. The former study recruited asymptomatic children, had no Aboriginal representation and measured *H. pylori* serology; while the second utilized UBT and stool antigen on Aboriginal children admitted for acute diarrheal illness. Cherian et al.[4] reported prevalence of 82% in 182 African refugee children aged less than 16 years old who undertook stool antigen testing during initial health assessment following resettlement in Western Australia. Their findings were approximately 3.5 times higher than the proportion affected in our subjects aged below 15 years (data not shown).

We did not find an association between age and *H. pylori* infection in our study. In contrast, the burden of *H. pylori* infection is observed to increase with age in the Australian community. Moujaber et al.[21] performed serology on over 2400 samples of randomly selected sera sent to major laboratories around Australia for diagnostic testing and reported seropositivity rates of 4.0% in those between ages 1 and 4 years and 23.3% between ages 50 and 59 years. Similarly, Lin and colleagues, also utilizing serology on randomly selected Caucasian adults in the community, described age-stratified prevalence of 18% in those aged between 20 and 30 years, and 53% in those over 70 years old.[23] The observed age gradient of *H. pylori* infection is postulated to be due to a cohort effect and the lower prevalence within the younger age groups due to improvements in socioeconomic status and living conditions in Australia.[23,25] Contrastingly, living conditions such as overcrowded refugee camps are experienced by our study population of all ages. Another probable explanation for the lack of association between age and *H. pylori* infection in our study is the relatively small number of participants representing the older age groups, resulting in a lack of statistical power to detect a difference between the age groups if there was one. This reflects the age distribution of humanitarian entrants in Australia where people over the age of 50 years comprise approximately 10% of those granted visas.[27]

Australian studies have shown variances in the burden of *H. pylori* infection in different ethnicities or birth region. In a study of 1316 randomly sampled adults, participants born outside Australia or New Zealand were more likely to be *H. pylori* positive with the highest prevalence ratios seen in people born in Africa or South America followed by Asia and the Pacific.[5] This is similar to our findings whereby, compared to other ethnicities, African ethnicity was more likely to be a predictor of *H. pylori* infection. In another study carried out in 1995, 25.8% of children of migrants from developing countries tested positive compared to 5.9% of children of Caucasian Australian and Western European background.[25] A study on Aboriginal peoples had also reported high prevalence of infection, reflecting the health inequalities experienced by this group compared to other Australians. Windsor and colleagues described an overall prevalence of 76% in 520 Aboriginal participants both adults and children in Western Australia using the UBT.[28] The presence of symptoms was not specified in the study participation criteria. Aboriginal people are more likely to experience overcrowded living conditions and poorer access to adequate sanitation hence contributing to the relatively high burden of infection.

Most Australian-based studies report no difference in occurrence of infection between the sexes. The association between male sex and infection as observed in our study has been previously reported.[23,28] However, the clinical significance and reason for this are unknown.[23]

We acknowledge study limitations attributed by the absence in the dataset of pre-arrival inhabitants per household ratio, dwelling types, and clinical features, for example, gastrointestinal symptoms. These could allow further characterization of those likely to be at higher risk of infection and may potentially explain the disparity of infection between ethnicities hailing from different geographic locations or dwellings types such as refugee camps or houses. History of dyspepsia could be correlated with current infection to determine whether dyspepsia is a reliable predictor of current infection. This would contribute to evidence on whether population-level screening should be performed or whether the current refugee guidelines of "test and treat" approach should be maintained.[16]

The use of stool antigen testing in this study permitted accurate measurement of prevalence in our cohort as it measures current infection. Its advantage over the rapid urease test or the UBT is that patients on antibiotics and proton-pump inhibitors do not have to cease treatment to be tested[15]; hence, such patients were not excluded from our study. None of the patients in this study were on treatment for *H. pylori*. The noninvasive nature and relative ease in administration further promote the use of stool antigen as the more acceptable test in adults and children. As has been shown by Schulz et al.,[12] the cost per cancer case in a refugee population would justify the screening of newly arrived refugees. Such screening in primary care as a preventive strategy is also much more cost-efficient than screening to detect an advanced stage of disease.[29]

Finally, the large sample size of the study has resulted in a robust estimate of the prevalence of infection in this population.

4 | CONCLUSION

Our study shows that *H. pylori* infection is common in this population and equally affects adults and children, with some ethnicities more likely to be impacted than others. Moreover, the long latency between

infection and development of well-known complications, the availability of accurate, acceptable, and easily accessible tests such as the stool antigen test, and the availability of relatively effective eradication regimens all add weight to a decision to screen for this organism in newly arrived refugees in Australia.

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Research

Newly arrived refugee children with *Helicobacter pylori* are thinner than their non-infected counterparts

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Abstract. The hypothesis of this study was that those refugee children with *Helicobacter pylori* are thinner than their non-infected counterparts. This cross-sectional study investigated the height and weight of newly arrived refugee children up to age 19 years, who were screened for *H. pylori* using a stool antigen test at the Migrant Health Service in Adelaide between August 2010 and October 2013. Of 460 children, 21% were infected with *H. pylori*. After adjusting for vitamin B12 and iron levels, ethnicity, age and sex, the odds of being thin in the 10- to 19-year-old age group was 4.28-fold higher (95% CI 1.48–12.4) if they were *H. pylori* positive compared with those who were *H. pylori* negative. The difference between the two groups is statistically significant ($P = 0.01$). Screening and treatment for *H. pylori* in the general population in developed countries is not recommended unless there are symptoms such as dyspepsia or risk of peptic ulcer, duodenal ulcer or gastric cancer. Given the findings of this study, a recommendation could be made that newly arrived refugee children who are thin should be tested for *H. pylori*. Thinness in children may influence their cognitive ability, school performance, physical endurance and hence their ability to successfully settle into their new country.

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Introduction

Australia accepts ~13 000 refugees each year from countries such as Afghanistan, Bhutan, Iraq, Burma, Iran and Africa (Department of Immigration and Border Protection 2014). Although their countries of origin, countries of transit and ethnicity differ, their health issues are similar and are likely to be different to that of the rest of the Australian population. Refugees settling in developed countries usually come from a background of lower socioeconomic status, higher rate of infectious diseases and different chronic disease profile (Phillips *et al*. 2011).

Newly arrived refugee children are more likely to be thinner and shorter than the rest of the Australian population, reflecting the demographics of their country of origin or transit (Mutch *et al*. 2012). However, it is expected that their weight and height will improve once they have access to more reliable food sources, clean water, safe housing with no overcrowding, education, less stress and after any parasites have been treated (Mutch *et al*. 2012).

Helicobacter pylori is a bacterial infection of the gastrointestinal tract that has been associated with peptic ulcer disease, gastric carcinoma, atrophic gastritis, gastritis, vitamin B12 deficiency, iron deficiency and growth retardation in children (Marshall and Warren 1984; De Vries *et al*. 2008; Malfertheiner *et al*. 2012). It is more common in developing countries because of the increased contaminated water and person-to-person transmission due to overcrowding and poor sanitation (Malaty 2000). It is usually contracted in childhood and without treatment is likely to become a chronic infection with a 15% risk of peptic ulcer disease and an increased risk of gastric carcinoma in adulthood (Malaty 2000; Torres *et al*. 2000).

Many of the source countries for refugees have a high prevalence of *H. pylori*, and refugees coming to developed countries are more likely to have *H. pylori* than the rest of the population (Cherian *et al*. 2008; De Vries *et al*. 2008). For example, in those with symptoms who live in Myanmar (Burma), the prevalence was 48% (Myint *et al*. 2015), and in Bhutan, it was 73.4% (Shiota *et al*. 2013). In developed countries, the prevalence of infection in children and adolescents is well below 10% and increases with age (Koletzko *et al*. 2011). In contrast, the majority of those people infected in developing countries contract *H. pylori* at a young age from their family, so there is little difference in the prevalence across the age span (Myint *et al*. 2015).

Many studies have used serology for screening, which detects past as well as current exposure to *H. pylori*, and is not recommended for screening in children (Koletzko *et al*. 2011). Rather, urea breath tests or stool antigen tests, which indicate only current infection, are more reliable (Cherian *et al*. 2008). A stool antigen test is a validated, cost-effective and non-invasive method for detecting *H. pylori*. It is recommended as a screening tool and proof of eradication in both children and adults (Koletzko *et al*. 2011; Malfertheiner *et al*. 2012).

Thinness in adults is defined as a body mass index (BMI) <17. When this is applied to children, the cut-off point sits at a *z*-score of –2 or the fifth centile of BMI (Cole *et al*. 2007).

What is known about the topic?

- *Helicobacter pylori* is more common in newly arrived refugees who come to Australia than in the rest of the Australian population and screening is cost-effective for the prevention of peptic ulcer and gastric carcinoma in high-risk populations.

What does this paper add?

- Newly arrived refugee children aged 10–19 years with *H. pylori* are significantly thinner than their non-infected counterparts, independent of other risk factors such as iron deficiency, vitamin B12 deficiency, age, sex or ethnicity.

The hypothesis of this study was that refugee children with *H. pylori* are thinner than their non-infected counterparts.

Methods

This retrospective cross-sectional study investigated the height and weight of all newly arrived refugee children up to age 19 years, with and without *H. pylori* infection, who were screened at the Migrant Health Service (MHS) in Adelaide between August 2010 and October 2013.

The MHS sees approximately half of the 1300 refugees who come to Adelaide per year for initial screening and a comprehensive health check and management plan. Since 2010, all newly arrived refugee patients have blood, urine and stool investigations for parasites and for the *H. pylori* antigen. Other parameters collected were age, sex, ethnicity, haemoglobin (Hb), mean corpuscular volume (MCV), vitamin B12, iron and ferritin levels, height and weight.

The monoclonal faecal antigen enzyme immunoassay (MFAT) (Immuno*Card* STAT! HpSA kits, Meridien Bioscience Inc., Cincinnati, OH, USA) was used to diagnose of *H. pylori*.

Ethics approval was granted by the SA Health Human Research Ethics Committee and the University of Adelaide Human Research Ethics Committee (HREC/12/SAH/48).

Statistical analysis

Height-for-age Z (HAZ) scores, weight-for-age Z (WAZ) scores and percentiles were determined for all children up to age 19 years using the World Health Organization (WHO) Child Growth Standards and WHO Reference 2007 (see http://www.who.int/childgrowth/en/ and the Growth Reference from http://www.who.int/growthref/en/, accessed 27 June 2016). These standards were developed based on a reference population that combined samples from six participating countries, thereby representing an international benchmark and suggesting 'how children should grow' if nutrition and health status are adequate (Wang and Chen 2012). Binomial outcome variables indicating growth retardation were derived from the Z scores and percentiles namely 'Stunting' – defined as HAZ scores less than –2 for children and adolescents; 'Wasting' – defined as WAZ scores less than –2 for children under 10 years old; and 'Thinness' – defined as a BMI-for-age less than the fifth percentile in those aged 10–19 years (Wang and Adair 1999).

Associations between the categorical independent and outcome variables above were analysed using a Chi-Square test. Logistic regression was then performed to examine the effect of independent variables on the growth outcome variables. Multivariate logistic regression was used to examine the effect of covariates including *H. pylori* infection status, age, sex, ethnicity and vitamin B12 and iron levels. The significance level was set at 5%.

Data analysis was conducted using Epi Info (ver. 7.1.4.0; Centers for Disease Control and Prevention, Atlanta, GA, USA) and Stata 12 (StataCorp LP, College Station, TX, USA).

Results

There were 460 participants aged between 0 and 19 years. Reflecting Australia's humanitarian intake during 2010–2013, this sample includes 47% Middle Eastern, 30% African, 12% Bhutanese, 8% Burmese and 3.5% other refugees.

The overall prevalence of *H. pylori* antigen positivity was 21%, with no significant difference across the age spectrum or between sexes. Table 1 shows the prevalence of *H. pylori* antigen positivity stratified by ethnicity.

The difference in prevalence of *H. pylori* infection between the different ethnicities represented was not statistically significant ($P = 0.055$).

Helicobacter pylori infection was not found to be associated with stunting in children and adolescents aged 0–19 years. Nor was there any association with wasting or thinness for children less than 10 years old (Table 2). Children and adolescents aged 10–19 years who were *H. pylori* positive were 2.97-fold (95% CI 1.22–7.24) more likely to be thin than those who were *H. pylori* negative ($P = 0.02$; Table 2).

After adjusting for vitamin B12 and iron levels, ethnicity, age and sex, this association was further enhanced; those aged 10–19 years who were *H. pylori* positive were 4.28-fold (95% CI 1.48–12.4) more likely to be thin than those who were *H. pylori* negative ($P = 0.01$).

Discussion

Screening and treatment for *H. pylori* in the general population in developed countries is not recommended unless there are symptoms such as dyspepsia or risk of peptic ulcer, duodenal ulcer or gastric cancer (Malfertheiner *et al*. 2012). It has been suggested that high-risk populations be screened and treated for *H. pylori* in order to prevent gastric carcinoma and peptic ulcer (Arboleda *et al*. 2013). The prevalence of *H. pylori* in the Australian population under the age of 19 years is low, and would not constitute a high-risk population for screening purposes. However, in countries such as China where there is a high rate of gastric cancer (26 per 100 000), screening of 20-year-olds was found to be cost-effective (Schulz *et al*. 2014). In considering if it is appropriate to screen paediatric populations, one should consult international guidelines, as they recommend an assessment of the risk of *H. pylori*-associated cancer as well as of 'other healthcare priorities' (Koletzko *et al*. 2011; Schulz *et al*. 2014). Screening for *H. pylori* is not currently included in the national guidelines for screening newly arrived refugees (Murray *et al*. 2009).

There has been limited evidence collected about the prevalence of *H. pylori* in asymptomatic children of refugee

background. Cherian *et al*. (2008) found a prevalence of 82% in the 193 African children in their study in Western Australia (Cherian *et al*. 2008). This is much higher than the 27.7% found in African children in our study. There are numerous factors that could contribute to this difference, including the local social determinants of health, environmental conditions, country of origin and time in a refugee camp.

Without treatment, *H. pylori* infection may persist for decades and cause life-long chronic illness (Schulz *et al*. 2014). Studies vary as to the spontaneous elimination rates in children, which ranged from 0.3% per year to 7% per month (Torres *et al*. 2000). Gastric cancer occurs in 0.1–3% of those chronically infected and there is an increased risk in those who acquire *H. pylori* at an early age (Tolia 1999; Schulz *et al*. 2014). Gastric cancer is the second most common cause of cancer death in the developing world (Schulz *et al*. 2014). There is an increased prevalence in developed countries in those who have spent their childhood in developing countries where the prevalence is higher (De Vries *et al*. 2008). The death rate for gastric cancer in Australia is 3.8 per 100 000.This is significantly lower than the death rate in the source countries of many of the refugees who come to Australia; for example, the rate is 24.5 per 100 000 in Bhutan, 10.2 per 100 000 in Myanmar, 17.1 per 100 000 in Afghanistan and 16.5 per 100 000 in Iran (Ferlay *et al*. 2015).

As well as the better-known symptoms of epigastric pain, bloating and nausea, the broad definition of dyspepsia includes the more non-specific symptoms of anorexia, early satiety and fullness (Mutch *et al*. 2012; Suzuki and Moayyedi 2013). Children may not volunteer symptoms of dyspepsia and may need specific questioning to ascertain the presence of such symptoms (De Vries *et al*. 2008; Koletzko *et al*. 2011).

The association of *H. pylori* with symptoms is controversial. *H. pylori* has been shown to be present in 22.5% of symptomatic children, as compared with 14.1% of children without gastrointestinal symptoms (Tolia 1999). In some studies, eradication of *H. pylori* has a statistically significant effect on dyspeptic symptoms (Malaty 2000; Suzuki and Moayyedi 2013); however, even those infected children without symptoms have been found to have gastritis with chronic inflammatory cell infiltrates at endoscopy (Torres *et al*. 2000). In the original publication by Marshall and Warren (1984) on gastritis with *H. pylori*, only 'burping' was voluntarily associated with infection.

A previous study reported symptoms such as anorexia in 65% of children in the general population with *H. pylori*, as compared with 15% of non-infected children (Franceschi *et al*. 2014). Ghrelin is a hormone produced in the stomach and is involved in the hypothalamic regulation of appetite. Infection with *H. pylori* can decrease ghrelin levels, with a consequent reduced appetite and early satiety (Suzuki and Moayyedi 2013; Franceschi *et al*. 2014). Similarly, high levels of leptin have been found in those with *H. pylori*, which can inhibit gastric ghrelin secretion and decrease appetite (Franceschi *et al*. 2014). It could be hypothesised that the decreased weight in older children in our study may represent chronic gastritis or the long-term effects of *H. pylori* infection on ghrelin and leptin levels.

Studies in developing countries have identified that children infected with *H. pylori* are more likely to have other manifestations such as iron deficiency, diarrhoea, malabsorption and growth retardation independent of confounders such as socioeconomic status, diet or other parasites (Bravo *et al*. 2003; Queiroz *et al*. 2013). Children infected in infancy are more likely to be thin, short or have growth faltering (Bravo *et al*. 2003; Thomas *et al*. 2004; Mera *et al*. 2006; Queiroz *et al*. 2013) and in one study it was associated with a decrease in cognitive function (Queiroz *et al*. 2013). There is evidence of beneficial effects on growth after treatment of the *H. pylori* (Goodman *et al*. 2011; Queiroz *et al*. 2013). Other theories suggest that children with *H. pylori* are more likely to have decreased resistance to other bowel pathogens with associated malabsorption (Thomas *et al*. 2004).

Table 1. *Helicobacter pylori* (*H. pylori*) antigen status by ethnicity of children

$P = 0.055$ for all ethnicities

Ethnicity	*H. pylori* antigen *n* (%)	
	Negative	Positive
African	99 (27.2)	38 (39.6)
Middle Eastern	179 (49.2)	36 (37.5)
Burmese	26 (7.1)	11 (11.5)
Bhutanese	46 (12.6)	9 (9.4)
Others	14 (3.9)	2 (2.1)
Total	364 (100)	96 (100)

Table 2. Odds ratios of growth retardation in *Helicobacter pylori* (*H. pylori*) antigen-positive children

Multivariate analysis was adjusted for vitamin B12, iron, ethnicity, age, sex. *n* data for Multivariate analysis excludes those missing values of vitamin B12, iron and those with 'Other' ethnicity. OR, odds ratio; CI, confidence interval

Growth indicator	Bivariate analysis				Multivariate analysis			
	n	OR	95% CI	*P*	*n*	OR	95% CI	*P*
Stunting (ages 0 to 19)	460				428			
H. pylori negative		1.00				1.00		
H. pylori positive		1.98	0.82–4.77	0.13		2.09	0.81–5.42	0.13
Wasting (ages 0 to 9)	150				139			
H. pylori negative		1.00				1.00		
H. pylori positive		0.71	0.19–2.63	0.60		0.89	0.22–3.64	0.87
Thinness (ages 10 to 19)	310				302			
H. pylori negative		1.00				1.00		
H. pylori positive		2.97	1.22–7.25	0.02		4.28	1.48–12.40	0.01

Current Australian guidelines do not recommend 'test and treat' in newly arrived refugees for *H. pylori* unless they are symptomatic, and there are no recommendations for treatment based on growth parameters (Murray *et al*. 2009). Treatment must also be weighed against the potential negative side-effects, such as an allergic reaction or the development of antibiotic resistance. Prevalence of *H. pylori* in newly arrived refugees of all ages to developed countries ranges from 25.6 to 60% depending on country of origin and other social demographics (Cherian *et al*. 2008; Chaves *et al*. 2009; Gibney *et al*. 2009; Johnston *et al*. 2012; Mutch *et al*. 2012). Recent evidence has confirmed that testing with the stool antigen test and treating those in an adult migrant or refugee population with a prevalence of infection as low as 25% is cost-effective for the prevention of gastric cancer (Schulz *et al*. 2014).

The effects on growth may begin at a younger age, as seen by the lower centiles in the linear regression modelling in our study, but not reach statistical significance until after age 10 years, because of the increased duration of exposure to the bacteria (Kocaoglu *et al*. 2016). Thinness in children can further predict their cognitive ability, school performance, physical activity and endurance, which will influence their settlement in their new country (Sandjaja *et al*. 2013). Hence, screening a high-risk cohort may be warranted in order to protect children from the sequelae of growth retardation as well as the future risk of peptic ulcer and gastric carcinoma.

Limitations

As many newly arrived refugees are given a stat dose of albendazole before departure for Australia, there is likely to be a low prevalence of helminths found in the stools (Murray *et al*. 2009). It may be that those who are more likely to have *H. pylori* are also more likely to have had other parasites in the recent past, which have now been treated.

Other causes of anorexia and early satiety, such as psychological problems, might co-exist in those who come from low socioeconomic backgrounds and who also have an increased risk of *H. pylori*. Management and follow up were not part of this study and so we were not able to include height and weight after the initial screening or the number of children who were given treatment for *H. pylori* or determine whether their weight changed after treatment.

Symptoms, other signs and information about other co-morbidities were not collected as part of this research.

Conclusions

To the best of our knowledge, this is one of the first studies on the possible effect of *H. pylori* on the height or weight of refugee children. The hypothesis that refugee children with *H. pylori* were thinner than their non-infected counterparts is supported for those aged 10–19 years by the outcomes of this study. Due to the limitations of this study, we are unable to unequivocally determine the role of *H. pylori* in the aetiology of thinness.

It is recommended that newly arrived refugee children who are found to be thin (below the fifth centile for weight or who have a BMI <17) should be tested for *H. pylori* infection based on our findings. However, it is beyond the scope of this study as to whether all those who are *H. pylori* positive should be treated, or if only those who are symptomatic or who have a low weight or height should be treated. Currently, this would be a clinical decision based on individual cases.

Children who come to developed countries as refugees deserve the best possible start to their new life. Screening for health problems that may have little or no immediate symptoms, but possible long-term sequelae, is an important part of equity for these new citizens. Infection with *H. pylori* may appear to be asymptomatic, but an infected child might be at risk of decreased weight, peptic ulcer or gastric cancer. This study identifies a significant association between *H. pylori* and thinness in older children and adolescents who have recently arrived in Australia as refugees, and provides evidence to support screening for *H. pylori* in asymptomatic refugee children.

Conflicts of interest

None to declare.

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Discussion

Between 2010 and 2013, 927 patients across the spectrum of age and ethnicities had been seen at the Migrant Health Service; certainly a large enough data-set to answer my clinical questions. The data confirmed my interim findings that the overall prevalence of H.pylori is 21.5%, much less than previously reported (85). This adds valuable information to the national and international debate about whether H.pylori screening is pragmatic in newly-arrived refugees. Economic modeling by Schulz et al recently has shown that screening is cost-effective at this prevalence in newly-arrived refugees (97). The main difference in our research is that the prevalence in children is not significantly different from the prevalence in adults. This is a major variance from the rest of the population in a developed country where the prevalence increases with age. Dr Abdul Rahim presented the prevalence data at the International Conference on Migration Social Disadvantage and Health where Dr Cherian and Dr Schulz were part of a discussion about why our data might have been different to theirs.

The large data-set yielded 460 children, whose height, weight, ethnicity and H.pylori status could be analysed. This revealed that indeed, the children aged 10-19 years with H.pylori were significantly thinner than their non-infected counterparts (86). There is very limited literature on the height and weight of children infected with H.pylori, all from developing countries. This new research is very important, as low weight in refugee children with H. Pylori has not previously been recognised in a developed country. Thinness in children has been associated with decreased cognition and there is a medical imperative to treat these children so that their schooling and socialisation is not affected by this preventable cause, especially in the vulnerable early period of resettlement.

This exciting research will open up new opportunities for debate about the inclusion of screening for H.pylori Ag in newly-arrived refugees. Currently this is not one of the recommendations in any country but economic modeling would suggest that it should be seriously considered, even based solely on economic grounds.

The other challenge is regarding treatment. In Australia 'triple therapy' with esomeprazole, clarithromycin and amoxycillin is only Pharmaceutical Benefits Scheme (PBS) listed as a 'Restricted Benefit' for 'Eradication of Helicobacter pylori associated with peptic ulcer disease'. It otherwise would cost at least $37.70 for the week of treatment, beyond the budget for most newly-arrived refugees.

Management of H.pylori in children is even more problematic. There does not appear to be consensus on the most appropriate treatment for children and schedules range from monotherapy up to quadruple therapy for up to 6 weeks (98, 99). However, compliance with the complex medication schedule is a problem in children (100), reinfection in children is higher if their parents are also infected, and there appears to be a higher risk of antibiotic resistance (99). Treatment of H.pylori in children in Australia will also be expensive. There is no 'triple therapy pack' for children on the PBS and clinicians must write three separate scripts and calculate individual dosages per weight for each child.

Our research could also be used for the purpose of advocacy for the delisting of the triple therapy into the General Benefit without restriction. Consensus on a schedule for children and the development of a PBS listing so that the medication is affordable and easy to use is also an imperative. There are many other opportunities for future research that can springboard from these studies. In particular it would be important to know if the weight of children improved after treatment of their H.pylori.

These large cohort studies were well-powered to show significant outcomes for refugees which are at variance from the rest of the Australian population. Considering the well-established association of H.pylori with gastric ulcer and gastric cancer and the economic modelling that suggests that screening is cost-effective at the prevalence found in this study, it should be recommended that all newly-arrived refugees are screened for this bacteria. Similarly refugee children who are thin, especially those aged 10-19, should be screened for H.pylori.

These recommendations for newly-arrived refugees are different to those for the majority of the Australian population. Future research should clarify the

outcomes of treatment in decreasing the long-term risk for adults and in improving the weight of children after treatment.

Chapter 5. Age determination in Refugee Children

Background

In Australia we take it for granted that people know their age and date of birth. This is not so for many of those who arrive in Australia as refugees. There are many reasons why this is likely to be the case, but these have not been researched in the past. In most developed countries the Gregorian calendar is used but not in some of the source countries for refugees such as Afghanistan and Bhutan. For some refugees who were fleeing war and chaos, the date of a child's birth is unlikely to be remembered and there will be no paper-work available. Parents, government officials and immigration authorities will often estimate a date of birth, sometimes on the spur of the moment as they are filling in paperwork. Up to 25% of the refugees from some countries will have a date of birth of 31st December or 1st January.

In adults, not knowing an exact date of birth is likely to affect the Aged Pension and some medical screening such as for breast cancer or bowel cancer. However a more correct date of birth is more important for children. In order for newly-arrived refugee children to be given the appropriate vaccinations for their age as part of the catch-up immunisation schedule when they first arrive in Australia, and so that they are put in an age-appropriate class at school, it is important to ascertain a child's age as soon as possible after arrival in a new country.

The only previous method widely used to establish a child's age was a wrist X-ray and that developed by the Royal College of Paediatrics and Child Health in London (101). The Greulich and Pyle Bone Atlas was validated in the USA in the 1930s using the X-rays of 1000 children of European ethnicity and then reviewed in 2006 on 150 Italian children. It exposes children to non-therapeutic radiation and is unlikely to be able to be extrapolated for use across ethnicities or in different socio-economic groups. Most Australian and international health professionals and Colleges agree that for these reasons it is not the most appropriate way of determining the age of a child if they arrive in a developed country not knowing their date of birth, with an incorrect date of birth, or without the correct paperwork to confirm a date of birth.

The Migrant Health Service runs a Newly Arrived Refugee Immunisation Clinic and is often asked by schools to help establish the age of a child so that they can be put in the appropriate class. The estimated age on the visa can be up to eight years different from the true age of the child. An appropriate and safe means for establishing a more realistic age needed to be found.

In order to address this need, I developed an 'Age Assessment Tool' (AAT) in association with Jan Williams, the nurse who is the Clinic Coodinator at the Migrant Health Service (26). This incorporated the narrative from the parents and other relatives and care-givers, taking into account the personal history of the child and family; the political and social events that occurred at the time of birth or other times in the child's life; timing of birth relative to other children in the family; height and weight plotted on the WHO centile charts; developmental assessment for age; other age-associated features such as appearance of teeth and toilet-training; and signs of puberty. Added to this was the 'gut reaction' of the nurse or doctor. This tool was successfully used at the Migrant Health Service for many years and, at the request of the other refugee health services in Australia I published it in the Australian Family Physician so that it was in the public domain.

An original literature review on the subject revealed no similar tools and I continued to search the literature over a decade to ascertain if a practical evidence-based tool had been developed. Because of the limited literature on this subject, the original paper was used for many other purposes, as well as for the determination of the age of refugee children. For instance, it was used by both sides of a discussion about the age of 'people smugglers' who were detained by the Australian government and whether they were over or under the age of 18. The AAT is not appropriate for this purpose but was quoted widely during this debate.

After we presented the AAT at the North American Refugee Health Conference in 2011, other international health professionals asked that I validate this tool so that they could justify using it in their health services, as there is nothing in the

international literature for them to use. Unknown age in children is very common as part of the refugee experience all over the world.

I discussed at length how the AAT might be validated with the other doctors, nurses, community health workers and the Paediatrician at the Migrant Health Service. There seemed to be two main arms to this question. The first was about the meaning of age and how it is measured and recalled in different cultures and the second arm was whether the AAT stood up to rigorous blinded investigation to validate the age of the child.

Both of these pieces of research would need extensive input of time in order to collect enough data to be meaningful. I did not personally have the time to do this and so looked around for someone who would.

Ashish Vaska, an Honours student I was supervising who was taking a year off from his medical studies, did the qualitative research for the first arm. As his supervisor, I had constant input into the project, reviewed his transcripts for coding purposes, and assisted with the writing up of the project. He performed semi-structured interviews at the Migrant Health Service with the aid of the community health workers (87).

The research for the second arm was led by Dr Scott Sypek, a Paediatric Registrar I co-supervised as part of his specialist qualifications. As well as assisting in the development of the protocol for the study, I was one of the researchers for this project, along with child health nurse, Kate Sparrow.

In order to validate the AAT, the team developed a more formal questionnaire and process based on the original AAT. This included a validated pubertal screening questionnaire. Jan Williams generated a list of children with documentation of a correct date of birth, and families were asked if they would like to be part of the study. Kate and I were blinded as to the dates of birth and used the AAT to make our own assessments of the age of the children (88).

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Benson J, Williams J. Age determination in refugee children. Aust Fam Physician 2008;37(10):821–24.

You can freely access the full text of this article at https://www.racgp.org.au/afp/200810/200810benson.pdf

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ORIGINAL ARTICLE

Age determination in refugee children: A narrative history tool for use in holistic age assessment

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Aim: To present the rationale for using a narrative history tool as part of a holistic age assessment of accompanied refugee children with age uncertainty by exploring cultural narratives of age.

Methods: Seven small group, semi-structured interviews with 24 humanitarian entrants (10 male, 14 female) recruited from Afghan, Bhutanese and Burundian communities in Adelaide, Australia were conducted. Interviews were performed with interpreters present, audio-recorded, transcribed verbatim and thematically analysed.

Results: Four themes emerged: the significance of age; ways of remembering age; the refugee experience and its effect on age recall; and the reliability and permissibility of documentation. Age was significant, but understood and remembered differently with knowledge of an exact date of birth not required for functioning in participants' home societies. Information regarding age was embedded in narrative accounts, related to events and other people. Birth was not always registered, with birth and age-containing documentation obtained later in life. These documents often reflected cultural ideas regarding age, rather than recording true chronological age. The refugee experience profoundly affected the ability of people to remember their age by disrupting methods used to recall specific events, including birth.

Conclusion: Narrative history provides valuable information regarding age in accompanied refugee children with age uncertainty, and allows for age to be located within a range that approximates true chronological age when age documentation is absent or clearly erroneous. The Age Assessment Tool questionnaire provides health professionals with a framework for conducting age assessment interviews.

Key words: age determination by skeleton; age determination by teeth; child; minors; refugees.

What is already known on this topic

1 Age uncertainty is an increasingly common problem faced by medical professionals when interacting with refugee and asylum seeking children and impacts on social and educational functioning and medical care.
2 There are numerous methodological and ethical issues associated with the most commonly used age assessment modalities, that is, medical assessment and bone age imaging.
3 National and international guidelines promote a holistic approach to age assessment including narrative history alongside medical and imaging techniques but the perceived subjectivity of interviews mean their findings are given less weight than those of medical and imaging approaches.

What this paper adds

1 Refugees and asylum seekers often utilise a different understanding of age, as existing within a time-span rather than focused on a particular date and remember age as part of narrative accounts, related to events and other people.
2 Interviews provide an opportunity to explore the narratives of age that refugees utilise, gathering information that facilitates approximation of true chronological age.
3 The narrative history component of the Age Assessment Tool questionnaire provides a framework for conducting age interviews for use in age assessment of accompanied refugee children and asylum seekers.

Age uncertainty is an increasingly common issue facing healthcare professionals when interacting with refugee and asylum seeking children.[1] Refugee children regularly arrive with incorrect or, less frequently, no age documentation due to loss or destruction of documents during flight, or administrative errors during processing, including the recording of generic '01/01/YY' or '31/12/YY' birthdates.[1–5] For others, lack of or erroneous documentation reflects the infrequency of birth registration globally,[6] a result of the absence of birth registration systems, societal unrest preventing recording of birth, or cultural lack of importance given to date of birth.[1,3,5,7]

In developed countries, knowledge of exact chronological age is vital and impacts on education, employment, socio-cultural rites of passage and legal and justice system interactions.[3,8] For children, knowledge of chronological age has medical

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implications, including: vaccination, assessment of growth and development and the provision of appropriate medical and dental care.[3,5]

The importance of chronological age to functioning in developed countries is closely linked to industrialisation in Europe and legislation regarding compulsory education and the workplace that aimed to distinguish between mature and immature persons, that is, children and adults, in a newly urbanised society.[9,10] However, there are ways of understanding age and its influence on social engagement that predate chronological age, namely the division of life into age-grades based on functional and physiological attributes.[4,6,11] These are still utilised in many developing countries and for refugee children, who often arrive from such countries, these contrasting conceptualisations of age must be bridged in order to facilitate their transition into a new society.

Currently, age assessment practices consist of one or more of: an interview, document review, medical assessment of development and anthropometric measurement, dental assessment and radiographic assessment of ossification, particularly the wrist.[1,3,12] Due to the perceived subjectivity of interviews and document checking, biomedical and radiographic assessments are commonly used, and their findings more heavily weighted.[5,6]

However, the literature discussing the ability of biomedical and radiographic assessments to determine age is contentious. Methodological issues noted include the large normal variation in physical development, use of outdated and inappropriately applied reference data for bone age assessment, and ethnic and socioeconomically influenced variations in development.[1,3,5,12] Ethical complexities around the nature of consent obtained, exposure of children to radiation for non-clinical purposes and the possible violation of the bioethical principles undergirding medical practice – patient autonomy, benevolence and non-maleficence, are also present.[1,12–14]

Accordingly, national and international guidelines emphasise the need for a holistic approach to age determination encompassing narrative history alongside psychosocial, medical, dental and radiological assessment.[1,6,8,12] This approach is thought to offer the best means of approximating true chronological age in the absence of accurate documentation.[6,12,15]

There is currently no standardised, evidence-based narrative history tool available for use in age assessment. It is thought that such a tool would mitigate concerns raised about narrative history assessments, namely inter-assessor variation and reliability of findings.[6,13,16] This study sought to explore narratives of age in three groups of humanitarian entrants in order to demonstrate that: (i) interviews are an important component of age assessment processes and (ii) the narrative history questionnaire component of the Age Assessment Tool questionnaire (AATq; Table 1) developed at the Migrant Health Service (MHS), Adelaide, provides a useful framework for conducting age assessment interviews (Table 2).

Table 1 The Age Assessment Tool questionnaire (AATq)

Questions to ask the parents/carers
1. Are you the parent of this child?
a. If not:
i. What is your relation to this child?
ii. How long has this child been with you?
iii. How old was this child when you started caring for them?
2. How old do you think this child is?
3. Are there records which may show the child's age?
a. Government documents – local or national identity documents
b. Hospital documents – birth certificates, Road to Health cards, immunisation records
c. Educational documents – school certificates, school registration
d. Refugee camp or agency documents
e. Other – family records, traditional documents
4. Do you think that the age recorded on these documents is accurate?
5. What can you remember about the time of their birth?
a. Political events – wars, death of a king/ruler
b. Cultural events – religious festivals
c. Catastrophic events – famines, earthquakes
d. Seasonal events – harvest time, summer/winter
6. Where were you when the child was born?
7. Did you conduct any ceremonies to celebrate the child reaching a particular age?
a. How old were they when you celebrated it?
b. How long ago did you celebrate it?
8. How long after you were married did you have this child?
9. What number child is this in your family?
a. How old does that make them?
10. Can you compare this child's age with a cousin or neighbour?
a. How old does that make them?
11. Pre-pubescent:
a. When did the child stop breastfeeding? How old were they?
b. When did they start walking (approx. 1 year)? How long ago was this?
c. Toilet trained i.e. dry in the day (approx. 3 years) – how long ago was this?

Methods

This study was approved by the SA Health Human Research Ethics Committee and the University of Adelaide Human Research Ethics Committee. Participant consent was obtained with the aid of interpreters.

Epistemologically, a critical realist approach was taken, acknowledging both the biological reality of ageing and its mediation through socially constructed understandings of age and childhood.[17]

Review of the literature informed the construction of the interview question guide which was piloted with the Primary Health Care Workers (PHCWs) of the MHS.

Sampling was purposive, including both genders, varying ages and urban and rural populations, based on literature review and discussion with MHS clinical staff and PHCWs. PHCWs directly approached and recruited participants, utilising their role as gatekeepers and community insiders.[18] Selection criteria were: Adult humanitarian entrants who were current or previous clients of the MHS, possession of a permanent protection visa (PPV) holder status and from the African, Middle Eastern or Bhutanese community. Exclusion criteria were: age less than 18 years, absence of PPV status, current personal or family involvement in age determination processes or proposed visa sponsors.

Table 2 Study findings and their influence on questions comprising the narrative history component of the Age Assessment Tool questionnaire (AATq)

Themes	Salient points	AATq
The importance of age	Knowledge of age important for community Knowledge of age considered holistically	How old do you think this child is?
Remembering age	In narrative accounts	Where were you when the child was born?
	Referencing events	How long after you were married was this child born?
	• Extrinsic	What can you remember about the time of their birth?
	• Intrinsic	Did you celebrate any ceremonies for the child's reaching a certain age?
	Referencing people	What number child is this in your family? Can you compare this child's age with a cousin or a neighbour?
	Referencing documents	Are there records which may show the child's age?
The reliability and permissibility of documents	Documentation meeting Australian Government standards rare	Do you think that the age recorded on these documents is accurate?
	Informal records can be reliable	Subquestion regarding "other" documents – family records, traditional documents

Seven semi-structured mixed gender group interviews with 24 participants (14 male, 10 female, ages 24–78) were conducted with the PHCWs acting as interpreters. Interview sizes ranged between 2–6 participants and duration between 50–74 minutes. Interviews were audio-recorded, with the "live" translation of the interpreter transcribed verbatim and de-identified. Data analysis was concurrent with collection and a theoretical thematic analysis performed using the six-stage approach outlined by Braun and Clark.[19] Transcript coding was reviewed by JE and JB, and initial themes iteratively reviewed and refined in light of the entire dataset and deviant cases until the themes satisfactorily represented the data. Triangulation with the existing literature was performed.

Quotes were selected to illustrate points of analysis and participants' perspectives. Minor editing of speech, specifically addressing grammar, was made to clarify meaning.

Results

Four themes emerged: The significance of age, ways of remembering age, the effect of the refugee experience on age recall and the reliability and permissibility of documentation (Table 2).

The significance of age

In participants' countries of origin, knowledge of age and attaining particular ages was important for functioning, impacting on work life, education and social activity. However, the legal and bureaucratic importance of age was secondary to its social value and ability to bring the community together:

> Seven days after a child is born, there is a celebration. The parents call their extended family for a celebration to present the baby to the community.
>
> Burundi Group 1, M

Chronological age was understood within a holistic framework that considered functioning and physical development as equally important, and more practically relevant for day to day activities such as schooling and work:

> It [exact date of birth] doesn't have any usage in daily life.
>
> Afghanistan Group 2, F

Remembering age

Age was remembered through events, people and records. The weight given to a particular means of remembering age was dependent on socio-cultural factors, such as how a culture marked time. In general, participants oriented to the absence of celebration of date-based events as being indicative of the lack of importance given to remembering age:

> People don't celebrate their birthday, or anniversary - it's not important to remember.
>
> Afghanistan Group 1, M

Events used to remember age were classified as intrinsic, that is, 'transition ceremonies' directly linked to attaining a particular age; or extrinsic, that is, community or population level events otherwise unlinked to age.

Intrinsic events played a dual role, marking age and serving as a point of social gathering. These were clustered around the time of birth, early years and the time of puberty.[20–22] While they assisted in recalling age, intrinsic events were celebrated at the instigation of the parents of the child, and therefore not always performed:

> When a son is 3 years old, the parents perform chawar [ceremonial head shaving] and they can calculate age from that. If such an event is performed, it's easier to remember age.
>
> Bhutan Group 1, group discussion summarised by interpreter

Extrinsic events provided a more objective reference point and included catastrophic events such as 'earthquakes', plagues of 'crickets' and 'famine'; political events, such as 'the death of a king' and 'war'; religious 'festivals'; 'seasons'; and the lunar cycle. Interestingly, these were embedded in narrative accounts, as parts of stories told to children about their age. It was the story that assisted in age recollection, rather than the event itself:

> I can remember my father saying, in the year of famine, you were 2 years old and it was a very hard time for us, because we could not feed you.
>
> Afghanistan Group 2, M

Age was remembered in relation to other people, such as siblings or extended family and through the memory of parents and community elders. Appraisement of physical appearance and development to estimate age was common. While it was acknowledged by participants that physical development did not always align with chronological age, this was considered a valid approach, as an approximation of age was sufficient for functioning:

> We observe their body. Sometimes they are older but are very weak, so we don't ask them to work or we don't know whether they are able to go to school.
>
> Bhutan Group 1, F

Documents and records assisted in remembering age. In the absence of universal birth registration, documents were sourced from hospitals, refugee camps and agencies, educational institutions, and the government. Age documentation was often obtained later in life, either through self-reporting of age or through the visual assessment of age by government officials, impacting on its accuracy:

> In earlier times, whatever date we said was recorded. I had four or five dates of birth recorded in Bhutan.
>
> Bhutan Group 3, M

> There is an experienced officer who looks at the person and determines the age of the person based on the condition of the skin and body. The officer writes down: 'The person looks like they are 25 years old in 2013'.
>
> Afghanistan Group 2, F

Informal records, kept by literate family members or community leaders, were another source of documentation and could be more accurate and detailed than official documents:

> When the baby is born, the parents immediately go and tell the priest what time, day, date and how the baby was born - where the head is faced, everything. The priest will write this down.
>
> Bhutan Group 1, F

The refugee experience and its effect on age recall

Longstanding societal turmoil diminished the importance of knowing and accurately recalling age. Loss of documents and separation of families during flight further damaged ability to remember age. This was especially so for children, who often fled with extended family who did not know their correct age.

> People are displaced from one area to another, families are separated, houses are destroyed, burnt down and even those very little memories are destroyed.
>
> Afghanistan Group 1, M

Initial registration at refugee camps was a key source of erroneously documented age. Participants highlighted fatigue and the role of officials, who would ask 'what is your age' or request they 'find an easy date to remember' rather than documenting exact date of birth, in the recording of generic '01/01' or '31/12' birth dates.

> You are already so stressed out, sometimes you cannot even tell your own age, and that [incorrect] age is registered.
>
> Bhutan Group 1, F

The reliability and permissibility of documents

Participants affirmed 'refugee camp' and 'hospital' birth certificates as the most reliable, that is, accurately recording chronological age, followed by refugee agency, educational institution and military documents. These documents typically met criteria for permissibility, and were thus usable for official and legal purposes in Australia. Overseas government documents were permissible for use but were not thought to be as reliable. Informal records, such as family or village registries, were considered reliable due to their contemporaneous construction but were not permissible. However, even relatively reliable sources of documentation such as school certificates were not without error, as in the absence of universal birth registration, they too were based on self-reported age:

> When children are admitted in school, parents have to give one tentative kind of dates – maybe this one or that one.
>
> Bhutan Group 3, M

Pragmatically, participants maintained that whatever documentation people had with them should be permitted for use as a "very low percentage of people" would have documentation meeting Australian immigration authority standards.

Discussion

Participants utilised a construction of age that was founded on communal and shared memories, and referenced events and other people. This socio-relational construction was embedded into narrative accounts told to children about their age.[4,6] Age

was spoken of and understood as an approximation, with knowledge of exact date of birth having little relevance to daily life in their home countries. Physical characteristics and level of function were commonly used to determine engagement with society.[4,6] This approximate understanding of an age echoes the more formal structuring of age-grades, where people of similar age were allocated to an age bracket, to perform particular roles, relying on pre-recording means of knowing age.[4,6,11] This is a fundamentally different means of conceptualising age to the chronological construction prevalent in developed countries such as Australia.

The use of events as reference points for age did have limitations. Unless birth aligned with an extremely significant date such as the coronation of a king, an exact date of birth was not identifiable. Furthermore, events used by participants to assist in remembering age were not always easily verifiable, as local political events and natural disasters did not always register on national or global scales and were often unrecorded. These limitations were acknowledged by participants and it was apparent that, at best, age was able to be located within a range, using a combination of significant extrinsic events and more local extrinsic events such as seasons.

The socio-relational construction of age described increasingly existed alongside, and was supplanted by a chronological construction of age predicated on knowledge of age through records. In a best-case scenario, exact date of birth was recorded. More often, in the absence of universal birth registration, documentation often reflected existing understandings of age as a span, and physical appearance and level of function as proxies for chronological age. Participants' comments reflected the tension existing in this period of transition, confirming estimation of age based on appearance by government officials as a source of erroneous documentation while simultaneously affirming functional assessment based on appearance as an accepted approach to guiding employment and educational engagement.

The experience of flight from turbulent socio-political contexts had a clearly negative impact on participants' ability to recall age. The breakdown of structures such as education, healthcare, and employment, diminished the, at times, tenuous importance of remembering age. This was further compounded by the disruption of families and communities, and the destruction of memories and records[16] effectively, leaving participants with neither a socio-relational nor records-based means of recalling age.

Conclusion

Age assessment is a challenging problem facing medical professionals. Due to the relative lack of importance given to remembering exact date of birth, difficulties with obtaining and retaining reliable age documentation and a considerably different conceptualisation of age, it may not be possible to identify exact chronological age for many refugee and asylum seeking children. Nevertheless, the socio-relational construction of age and the narrative accounts told to children about their age contain valuable information that can assist in age determination. This can only be ascertained through interviews, supporting the use of narrative history interviews as a routine component of the holistic approach to age assessment promoted in the literature.[1,6,8,12] The narrative history component of the AATq developed by the MHS provides a useful framework for health professionals to conduct interviews, and is a step towards the development of a standardised questionnaire that can offset inter-assessor variability.[6,16–23]

The similarities in conceptualising age across the three diverse cultural groups involved suggest these findings may be applied to humanitarian entrants more generally. While issues with utilising narratives of age and documentation reliability remain, by taking time to work through the narrative of age elicited[4] and reviewing all documentation available, including informal records,[1,6,12] the age of children may be more closely approximated to their true chronological age. This will mitigate the far-reaching effects of grossly erroneous age documentation and ensure that refugee children with age uncertainty receive holistic, best practice care.

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ORIGINAL ARTICLE

A holistic approach to age estimation in refugee children

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Aim: Many refugee children arriving in Australia have an inaccurately documented date of birth (DOB). A medical assessment of a child's age is often requested when there is a concern that their documented DOB is incorrect. This study's aim was to assess the accuracy a holistic age assessment tool (AAT) in estimating the age of refugee children newly settled in Australia.

Methods: A holistic AAT that combines medical and non-medical approaches was used to estimate the ages of 60 refugee children with a known DOB. The tool used four components to assess age: an oral narrative, developmental assessment, anthropometric measures and pubertal assessment. Assessors were blinded to the true age of the child. Correlation coefficients for the actual and estimated age were calculated for the tool overall and individual components.

Results: The correlation coefficient between the actual and estimated age from the AAT was very strong at 0.9802 (boys 0.9748, girls 0.9876). The oral narrative component of the tool performed best ($R = 0.9603$). Overall, 86.7% of age estimates were within 1 year of the true age. The range of differences was −1.43 to 3.92 years with a standard deviation of 0.77 years (9.24 months).

Conclusions: The AAT is a holistic, simple and safe instrument that can be used to estimate age in refugee children with results comparable with radiological methods currently used.

Key words: adolescent; child; paediatric; refugee.

What is already known on this topic

1 Refugee children arriving in Australia often have an inaccurately documented date of birth.
2 An accurate age is an important criterion for accessing many services in Australia as well as in the assessment of a number of paediatric conditions.
3 There is no consensus on methods to use to estimate age, and often, requests are made for radiological imaging.

What this paper adds

1 A holistic age assessment tool based on the basic tenets of medicine (a thorough history and examination) is as at least as accurate as radiological investigation in this population.
2 This study provides the foundation for further development of the age assessment tool and testing extended to a larger number of ethnic groups.
3 Immigration and education authorities should be made aware of the value of clinical assessment when writing policies regarding children whose age is in dispute.

Each year, 40% of Australia's refugee intake are children.[1] Many of these children have inaccurate documentation of their date of birth (DOB) or no documentation at all. Medical services receive requests to assist in assessing the age of these children.

Inaccurately documented age occurs for a variety of reasons. Many refugees come from countries with low rates of birth registration. The United Nations Convention on the Rights of the Child includes the right to birth registration in article 7.[2] However, approximately one-third of the global population under 5 years have not had their births registered.[3]

In the chaos of fleeing conflict, documents that do exist can be lost and children are often assigned a DOB when entering a refugee camp.[4] A DOB of 01/01/YEAR or 31/12//YEAR is often used when an actual DOB is unknown, which can lead to inaccuracies in age and difficulties in proving identity during the settlement process.[5]

An accurate age is taken for granted in developed countries, where it has medical, socio-cultural and legal significance. The assessment of a number paediatric conditions (e.g. short stature, precocious and delayed puberty and developmental delay) relies on knowing the age of a child. A child's age also guides placement in the appropriate grade at school, the timing of vaccinations and the dosage of some medications. Being a child entitles a person to specific protections in guidelines from the United Nations High

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Commissioner for Refugees (UNHCR), that are not necessarily applied to adults.[6] Age is also a determinant of criminal responsibility and governs where a person may be held in detention. Later in life, age is major component of eligibility criteria for driving, marriage, voting and various welfare entitlements.[4]

While guidelines exist on the age assessment of children, there is no international consensus on methods.[7] Non-medical (documentation, interview) and medical (examination by a doctor, radiological imaging) are used. Across Europe, there is a reliance on skeletal and dental assessment using X-ray.[8] However, the imaging of bones and teeth has been shown to be an imprecise way to assess chronological age.[9] The reference standards used in radiological assessment may not be suitable for children of many ethnic backgrounds.[10] There are also ethical concerns about exposing children to ionising radiation for an administrative purpose.[11,12]

A holistic approach (combination of non-medical and medical methods) has been advocated.[9,13] At the Migrant Health Service in Adelaide, South Australia, a multifactorial age assessment tool (AAT) has evolved in response to an increasing number of requests to provide a medical assessment of age. It was unclear whether these assessments provided an accurate age assessment for these children.

This pilot study tested the AAT on a group of refugee children. The aims of this study were to evaluate the accuracy of the AAT in estimating the true age of refugee children and to determine which components of the AAT were the most useful in assessing age.

Methods

The study assessed 60 children with a known age using a holistic AAT between August 2013 and March 2014. The subjects were refugee children aged 5–17 years interviewed with a parent/guardian familiar with the child's history by an assessor blinded to the child's actual age. A list of potential subjects was generated from the client database selecting those aged 5 to 17 years. We excluded children with a DOB listed as 1 January or 31 December (20% of clients in the Migrant Health Service database) as these dates are often ascribed to people with an unknown DOB. If families believed that the child's documented DOB was inaccurate, they were excluded. We also excluded children whose visa status was not finalised because of the potential concerns from families that involvement in the study may influence their visa outcome. Children known to the assessors were also excluded.

Children who met inclusion criteria were invited to participate in the study. Non-random convenience sampling was used to suit subject availability and in an attempt to assess a broad mix of ethnic backgrounds. An information sheet in English was provided and explained to potential subjects using an interpreter. Written consent was obtained from parents for young children and directly from adolescent subjects themselves. This study was approved by the South Australian Health Human Research Ethics Committee.

Two assessors used the AAT to conduct interviews. The first assessor is a child health nurse who has school-aged children and 25 years of experience working in paediatric nursing, including 5 years in refugee health. The second assessor is a general practitioner with adult children and over 30 years experience in general practice and 13 years in refugee health. These assessors were chosen to test the validity of the AAT in the hands of different professional groups and individuals with different direct personal experience of children in the age groups being assessed. Assessors were blinded to the subjects' DOB. The assessments were undertaken with the assistance of an interpreter, and subjects were instructed to answer all questions honestly but not to reveal their true age or DOB.

The AAT consisted of four main components and took approximately 30 min to complete. These four main components are the oral narrative, anthropometric measures, developmental assessment and pubertal assessment.

Oral narrative

Through an interpreter, the parent's story of the circumstances of their child's birth was documented. Directed and open questions are used related to the child's history: place of birth, birth order in family, timing around significant world events/festivals at that time, details of achieving developmental milestones (walking, toilet training, etc.). The assessor used this narrative to estimate the age of the child. These questions (Appendix I) were derived from focus groups and interviews with refugee families from several ethnic backgrounds conducted as part of a separate study (Ashish Vaska, 2013, data unpublished).

Developmental assessment

An informal assessment was performed observing the child's interactions and asking parents and children about tasks they perform, developmental milestones, their role in the household and comparison with peers. Assessors were asked to list a 'developmental' age based on the child's physical and cognitive milestones as well as 'maturity' age based on observation of relationships with others.

Anthropometric measures

The subject's height and weight were plotted at the 50th centile on World Health Organization growth charts. When available, midparental height (MPH) was used to predict adult height in children, and this centile used to estimate their age at their current measured height.

Pubertal assessment

The Puberty Development Scale (PDS)[14] was used to assess subjects who appeared to be adolescents. Five questions were asked through an interpreter about pubertal changes and provided a score that was converted to one of five stages of pubertal development. The PDS correlates well to self-reported and physician-rated Tanner staging.[15,16]

The assessor then considered the information gathered from the interview and the four components of the AAT, and using their individual clinical judgement, documented a final overall age estimate for the child (in years plus months). Data analysis was performed using stata software package (stata Corporation, College Station, TX, USA). The strength of association between subjects' actual age and the estimated age using the AAT (and each of its components) was described using the Pearson correlation coefficient (R). Lin's concordance correlation coefficient was used to explain the precision and accuracy of the AAT.[17] The mean difference (and standard deviation) between actual and

estimated age was calculated to facilitate comparison with studies using other age assessment techniques.

Results

A total of 60 children (32 boys) were assessed using the AAT. The nurse assessor interviewed 43 children. The mean actual age was 12.5 years (5.08 to 17.83 years).

Table 1 lists the correlation coefficients for each item of the AAT. The number of subjects varies as assessors did not accurately document an age for every item for every subject. For the whole study sample, the correlation coefficient for estimated age and actual age was 0.9802 (boys 0.9748, girls 0.9876). The oral narrative component correlated strongly ($R = 0.9603$). The weight, height and pubertal assessments showed the weakest correlation ($R = 0.8425$, 0.8484, 0.8219, respectively).

While the Pearson correlation coefficient measures strength of association, the concordance correlation coefficient measures the accuracy and precision of agreement between actual and estimated age. For the AAT as a whole, this was 0.975 and is demonstrated in Figure 1.

There were four main ethnic groups across the study population (Table 2). The number of subjects in each group was too small for meaningful analysis.

Assessments by the nurse assessor appeared to be more accurate than for the doctor assessor both overall ($R = 0.9897$ vs. 0.9405) and for the oral narrative component ($R = 0.9810$ vs. 0.8402) (Table 3). However, the number of subjects assessed by the doctor was comparatively small, meaning that a significant outlier heavily influenced the results. This likely reflects the fact that the nurse was more familiar with using the AAT and highlights the need for standardised training for those using the tool.

The limits of agreement plot (Fig. 2) demonstrates the mean difference between actual and estimated age (0.3 years or 3.6 months) and the range of differences (−1.43 to 3.92 years). The standard deviation was 0.77 years (9.24 months). The majority (86.7%) of age estimates were within 1 year of the true age, with a slight trend to underestimating actual age.

Discussion

Guidelines from the UNHCR on dealing with children seeking asylum recommend that age assessment practices take into account physical appearance as well as psychological maturity, respect a child's dignity and give them the benefit of any doubt and accept there is a margin of error in such assessments.[7] The AAT evaluated in this study aims to follow these guidelines.

Oral narrative

As is the case in seeking a medical diagnosis, the most useful tool in assessing age is a thorough history. There was a strong correlation between the estimated age using the oral narrative and the child's actual age ($R = 0.9603$). There are some limitations with this method. It relies on the child being accompanied by a guardian who is familiar with the child's history, and for many refugee children separated from their parents, this is not possible. In this population, there is the potential for past trauma to influence the recall of past events. Inconsistent history from different family members led to a 17-year-old Bhutanese boy being estimated to be 13 years old. Also, where a child or family has a potential secondary gain in being a certain age (qualifying for age-dependent welfare payments, the treatment of minors vs. adults in detention), the oral narrative component is open to misrepresentation.

Developmental and maturity assessment

Developmental assessment in the AAT is informal and not standardised between assessors. A broad guideline of typical

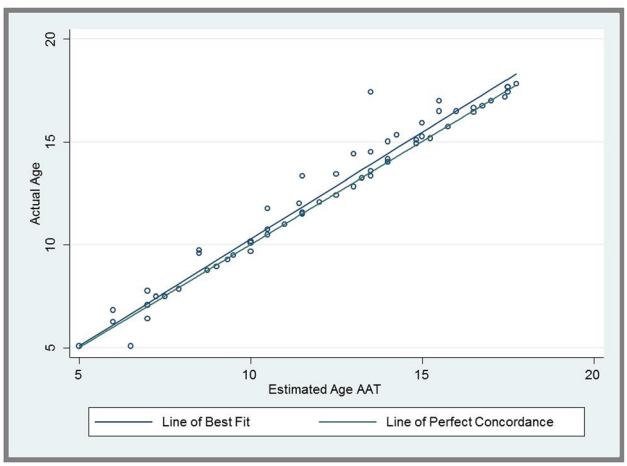

Fig. 1 Scatter plot of actual and estimated age (years).

Table 1 Pearson correlation coefficients for estimated age versus actual age

	Actual age (correlation coefficient)			Number of subjects
	Total	Males	Females	
Overall estimated age	0.9802	0.9748	0.9876	60
Age for weight (50th centile)	0.8425	0.8371	0.8544	60
Age for height (50th centile)	0.8484	0.8858	0.8257	60
Age from oral narrative	0.9603	0.9375	0.9854	51
Age from developmental assessment	0.9770	0.9654	0.9906	28
Age from pubertal assessment	0.8219	0.8680	0.8502	60
Age from maturity assessment	0.9651	0.9490	0.9813	45
Age from plotted midparental height	0.9253	0.9672	0.8830	41

Table 2 Pearson correlation coefficients for estimated age versus actual age by ethnic group

	Actual age (correlation coefficient)			
Ethnicity	Afghan (9)	African (12)	Bhutan (32)	Burmese (6)
Overall estimated age	0.9955	0.9768	0.9687	0.9991
Age for weight (50%)	0.8987	0.7970	0.8297	0.9111
Age for height (50%)	0.9180	0.8393	0.8203	0.9666
Age from oral narrative	0.9885	0.9697	0.9264	0.9967
Age from developmental assessment	0.9994	Nil	0.9672	0.9967
Age from pubertal assessment	0.7764	0.7679	0.8160	0.8414
Age from maturity assessment	0.9963	0.9528	0.9569	0.9958
Age from plotted midparental height	0.9877	0.9185	0.9244	0.9445

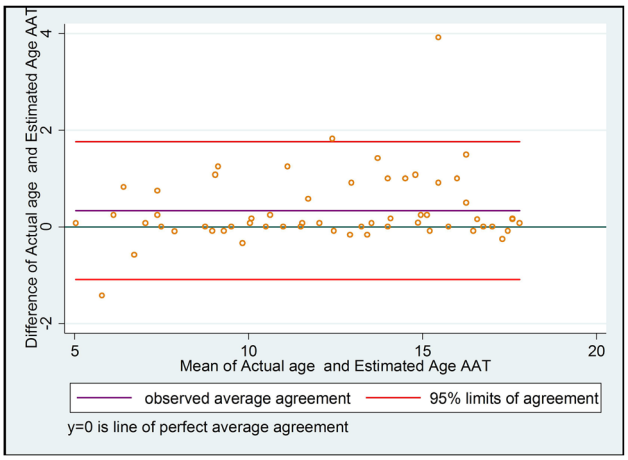

Fig. 2 Limits of agreement plot for actual and estimated age (years).

social and motor milestones in Australian children is provided for the assessor's reference and is not relevant for all cultural groups. Although the developmental and maturity assessments appear to have a stronger correlation, this is likely an effect of bias. The assessors did not record an estimated age for every child using the developmental and maturity assessments (28 and 45 subjects, respectively, with none recorded for African children). On a review of data midway through the study, we found that the assessors were only committing to record an age when they felt confident about the accuracy of that age. We corrected this for the continuation of the study; however, this likely has biased the result to indicate a stronger correlation.

Developmental assessment in this population is complex. Formal developmental tools often assume access to education and western cultural norms. Exposure to trauma and malnutrition will also influence developmental progress.[18] Formal developmental assessment has a limited role in age assessment as results provide a developmental age that may not equate to a chronological age.

Anthropometric measures

Height and weight are not reliable predictors of age. We used the World Health Organization standard growth charts for 5–19 years (2007 revision) in a manner opposite to their conventional use,[19] for example, a boy who is 130 cm is plotted on the 50th centile at an age of 8 years and 6 months; 95% of boys of height 130 cm are aged between 6 years and 9 months and 11 years. The wide range can only provide a guide in estimating age. There are many factors that determine a person's height including race, nutrition, environmental and genetic influences.[13] Using MPH to estimate age ($R = 0.9253$) was more accurate than an individual height alone ($R = 0.8484$). Many adolescents were already achieving their predicted adult heights probably because of improved nutrition compared with their parents.

Pubertal assessment

Pubertal progress is often measured using the Tanner sexual maturation scale. We used the PDS, a series of questions that allow an adolescent to self-assess their pubertal status.[14] The PDS has been shown to be more acceptable to adolescents (than examination or pictures) and have moderate to high correlation with Tanner staging as assessed by a paediatrician.[15,16]

The timing of pubertal events is influenced by genetic and environmental factors. Studies formulating the PDS used predominantly Caucasian populations.[14,16] There is variation in the onset of pubertal stages between ethnic groups.[20] A Bhutanese boy when presented with the questions said, 'My father does not even have body hair'. The correlation between pubertal age and actual age was not strong ($R = 0.8219$), so we would not recommend using pubertal stage alone to estimate age.

Comparison with other techniques

Radiological techniques are recommended in some guidelines[21] and criticised by others.[11,12] Bone age is typically assessed using the Greulich and Pyle Bone Atlas[22] that was originally based on the X-rays of Caucasian, middle class, American children in the 1930s. Dental age assessment commonly uses the scoring system for dental maturation described by Demirjian[23] formulated on data from a French Canadian population. There are fundamental limitations to the use of both methods.[9] These include the wide range of normal variation and the influence of ethnicity, socioeconomic status and environmental factors such as nutrition and disease not considered in the standard assessment systems.[24]

A sample of studies using these methods to estimate chronological age is presented in Table 4. The mean difference and standard deviation between estimated and chronological age

Table 3 Correlation coefficients for estimated age versus actual age for each assessor

	Actual age (correlation coefficient)		Number of subjects	
Assessor	Doctor	Nurse	Doctor	Nurse
Overall estimated age	0.9405	0.9897	17	43
Age for weight (50%)	0.8516	0.8512	17	43
Age for height (50%)	0.8689	0.8486	17	43
Age from oral narrative	0.8402	0.9810	12	39
Age from developmental assessment	0.9328	0.9924	13	15
Age from pubertal assessment	0.7732	0.8391	17	43
Age from maturity assessment	0.9312	0.9807	17	28
Age from plotted midparental height	0.9684	0.9171	14	27

Table 4 Comparison of a sample of published studies using different age assessment methods

			Mean difference (SD) (years)	
Study	Assessment method	Population (no. and ethnicity)	Males	Females
Our study	Holistic age assessment tool	60 multiethnic	0.31 (0.84)	0.36 (0.60)
Mughal (2014)[25]	GP bone age	220 Pakistani	1.32 (1.07)	0.55 (1.12)
Moradi (2012)[26]	GP bone age	425 Iranian	0.37 (0.98)	0.04 (0.78)
Prabhakar *et al.* (2002)[27]	Demirjian dental age	151 Indian	1.2 (1.02)	0.9 (0.87)
	GP bone age		1.24 (0.9)	0.27 (1.03)
Maber *et al.* (2006)[28]	Demirjian dental age	946 Bangladeshi and British Caucasian	0.25 (0.84)	0.23 (0.84)

GP, Gruelich and Pyle; SD, standard deviation.

for the radiological techniques are comparable with a holistic approach without X-ray.

In our study, the overall estimated age from the AAT had a stronger correlation with actual age than any individual component of the tool. This supports recommendation that a multifactorial, holistic assessment is most useful in assessing age.[13]

Limitations

The sample size and convenience sampling did not provide adequately sized subgroups to meaningfully compare the use of the AAT in different ethnic groups. Future research should ensure a recruiting method to achieve this. Combining the many components of the AAT to reach a final estimated age relies heavily on the clinical judgement of the individual assessor. The inter-rater reliability and the validity of the tool in the hands of different assessors should be further assessed.

We aimed to assess refugee children with a known DOB. Although we eliminated children with a DOB 1/1/year and 31/12/year, it is possible that some children in our study had an inaccurate DOB that would affect the validity of our results.

Conclusion

Age estimation is a challenge, and many of the current methods in use are imprecise. This pilot study shows that the AAT can achieve age estimation accuracy comparable with other medically based methods. Refining components of the AAT and retesting them on different ethnic populations would serve to improve overall accuracy and usefulness of this tool.

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Appendix 1

Observation and assessment guidelines determining for age of child:

Observations and initial impressions

(gut feelings)

- Physical appearance including voice tone and posture.
- Attitude and level of engagement.
- Self-sufficiency. Do they carry their own documents, bus tickets, interact independently?
- Degree of comfort/confidence in speaking to an adult.
- Ability to sit for time period, concentration.
- Interaction with assessor and others – parents/carer, siblings.

Questions to ask the parents/carers

- Are you happy with your child's recorded date of birth?
- Are there any other records which may show child's age?
- What can you remember about their birth?
- Birth order in family?
- What season was it? Was the weather hot or cold?
- How long after marriage did the pregnancy occur?
- Where were you when the child was born? What was happening there? Who was with you?
- If not birth parents – how long has the child been with you? How old were they when you started to care for them?
- Pre-pubescent: When did the child stop breastfeeding? Walking (approximately 1 year) – how long ago? Toilet trained, that is, dry in the day (approximately 3 years) – how long ago?

Questions to ask the child

- Are you satisfied that your age is correct?
- Have you been to school? How long for? Any gaps in schooling?
- Have you started school in Australia?
- Do you feel the same age as the kids in your class?
- How old are the kids you like to be with?
- What do you like to do in you spare time?
- What sports do you play?
- Have you ever lived independently or have you always been with adults? Level of independence, that is, cooking for self, buying food.

Self-portrait by Dylan Chapman (5), from Operation Art 2015.

Discussion

The outcomes of Ashish's research generated some very interesting and new information about how age is remembered and celebrated very differently across the cultures investigated. The use of narrative history was confirmed as an important constituent of the AAT (87).

The data from Scott's research show that the AAT is as good as or better than any other method for assessing the dates of birth of newly-arrived refugee children. It studied the oral narrative, developmental and maturity assessment, anthropometric measures and pubertal assessment (88).

There were many difficulties involved in these projects despite the excellent outcomes. As well as the ethnic and cultural differences in height, weight, pubertal development and maturity, many families remembered important dates very differently. For instance, negotiating the exact date of a historical event such as the death of a king was much became problematic than would be expected, and the age when children started school seemed to vary enormously.

In June 2015, Ashish, Scott and Kate presented the findings of our research at a workshop at the North American Refugee Health Conference. The organisers were very excited about this outcome and internationally others are keen for the AAT to be published. It is expected that once it is published it is likely to become an established tool in many refugee health services.

We have already had requests from teachers and social workers in Adelaide for training in how to use the AAT. This opens up the issue of whether it is appropriate for non-health professionals to use the tool. Some of the questions about child development assessment and pubertal changes need some level of health training. Currently we have declined training but once the tool is in the public domain, others will be free to use it as they see fit.

This novel research supplies a pragmatic and safe solution to a problem experienced all over the world. It is hoped that others will continue to validate and even refine the AAT so that it becomes an international gold standard for age determination in children of unknown age. Knowing the correct age of a child is

not a problem for the majority population in Australia, however for newly-arrived refugees this problem can cause many problems if not resolved as soon as possible after arrival.

Chapter 6. Discussion and Conclusion

Background to the Discussion

The social determinants of health have been a constant theme since about 1948 as practitioners and policy-makers throughout the globe grapple with the 'social roots of disease and health inequities' (102). Their importance was recognised as far back as Virchow in 1848, and then 'crystallized' with the primary health care movement at Alma-Ata in 1978 (102). The impact of the social determinants of health are more obvious in developing countries, however it is really only since the 1980s that those such as Michael Marmot began to alert practitioners and policy-makers to the importance of the social determinants of health in the more vulnerable people in our Western societies (103). A differential in these determinants is now well-recognised as a cause of increased morbidity and mortality and include the well-known parameters of income, education, employment, childhood development, food insecurity, housing, social exclusion, social safety, access to health, gender, race and disability (27). The detection of health inequities due to avoidable differences in health status has become an important goal throughout the world (27). In developed countries such as Australia, which pride themselves on their equitable and accessible health system, such differences have the political, economic and structural potential to be addressed when they are recognised (104).

Throughout history there has always been movement of people from one country to another due to wars, persecution and the safety of minority groups. However it has only really been since World War 2 and the Refugee Convention in 1951 that countries have begun to recognise refugees as a group needing special consideration (34). The fact that their health issues are likely to need specialized care is an even more recent development and it is only in the last 20 years that specific refugee health services, guidelines and protocols have begun to develop. Governments and health systems in the developed world are now struggling to adjust to the increased influx of refugees and asylum seekers (105).

Despite the fact that the concepts and importance of public health and primary health are rooted in antiquity, the fields of 'Public Health' and 'General Practice'

are new additions to the list of medical specialties in Australia (106, 107) and in many areas of the world are still not recognised as medical specialties (108). More specifically, the concept that GPs need dedicated training in their field has only emerged in the last 30 years and that GPs should be taught and encouraged to do research in their field is even more recent (107).

It has been suggested that there should be three levels of Evidence-Based Medicine (EBM) and research in General Practice (20). The first is about using the current evidence-based guidelines in a clinical situation and developing skills and knowledge about when such guidelines might not be valid. The second is about examining the scientific literature in a critical way in order to ascertain if there is good supporting evidence for the particular population or situation, where the guidelines might not be appropriate or if a different protocol might be more relevant. The third is researching the population or situation in order to build a new evidence base that is more applicable (20).

Spending the last 15 years of my career working in refugee health as a GP with an interest in research has given me a unique opportunity to watch and be part of the expertise and evidence in this field. I have endeavoured to encompass EBM principles and research into my everyday practice and out of this has come the publications that make up this thesis. I found that the guidelines were not always applicable to the refugee population, that there was not enough literature to inform me about what I should be doing and so I began to research the issues myself.

The Social Determinants of health and the significance of this thesis

All health practitioners need to be aware of how the health of newly-arrived refugees is different to the majority population. This research has highlighted some of these differences.

The importance of asking about the past social determinants of health such as the country of origin, refugee status, previous living situation, access to food and

trauma history, are not usually elements in a doctor's history-taking. There is an assumption that the 'evidence' and 'guidelines' used for the majority population will be applicable to newly-arrived refugees after they have settled in a new country. However this body of work has affirmed that at least those issues I have researched have a different prevalence, presentation and need for follow-up to 'usual' practice. Vitamin B12 deficiency, chronic suppurative otitis media, cholesteatoma, H.pylori causing thinness in children and the need to determine the age of a child, are not part of the everyday practice of most doctors.

There is quite an extensive body of research in vegans and those with pernicious anaemia outlining the morbidity and mortality of Vitamin B12 deficiency (9). Much of this is very old literature, as the importance of this vitamin has been known for a long time. There is a small body of research from middle-income countries such as Mexico, Kenya and Iran highlighting the increased prevalence of Vitamin B12 deficiency in these countries with suggestions that the parameters for detection might be different (109-111). It was not until my first publication in 2010 that there was any published literature to alert clinicians to the importance of Vitamin B12 deficiency in refugees (24). With the inclusion of Vitamin B12 as a new section in the 2016 ASID guidelines (19) based on our research, its detection and management should now be considered when screening in refugee health clinics. The Australian national study (11) has also paved the way for further research in this important area. There has been a very limited amount of research looking at ethnicity and Vitamin B12 deficiency and there are many opportunities for future research in this area, but the most likely reason for the increased burden of Vitamin B12 deficiency in newly-arrived refugees is the differential in social determinants of health.

The detection and treatment of chronic suppurative otitis media is well-established in the literature in those populations who have lower socio-economic status, overcrowding and poor nutrition (112-114). It is known to be responsible for about 80% of the hearing impairment worldwide, the majority in the developing world (115). Australian Aboriginal people are acknowledged as having one of the highest rates of CSOM in the world (116), and it was my experience of working in remote Aboriginal communities that I brought to my

refugee work. Most Australian and other health professionals in developed countries would not have seen CSOM, particularly if they are not looking for it, and would not be aware of the international literature on this subject. Even though the numbers are small in our study, the research showed that the prevalence was significantly higher than in the general population. More importantly its publication has led to the inclusion of CSOM in the new ASID guidelines (19).

Helicobacter pylori (H.pylori) has only been recognised as an important pathogen since 1984 (117). The full extent of its effects on morbidity and mortality are still being explored. There is quite an extensive literature on the importance of the social determinants of health on the prevalence of H.pylori and a small body of research on its prevalence in refugees (118-123). One of the difficulties in this field has been that of detection of active infection. With the recent use of stool antigen our studies were more valid and useful than many previous studies that used serum H.pylori antibodies. The publication of our large prevalence article in 'Helicobacter' is the first time an article specifically on refugee health has been published in this journal. The increased prevalence of thinness in adolescents with H.pylori has only previously been found in a few studies, none of them in refugees (96, 124). It is hoped that when these articles are published, other researchers and policy-makers will begin to look more closely at the morbidity and mortality in refugees and grapple with the difficulties of developing screening and treatment protocols.

Knowing your own age is something we take for granted in the developed world. Measurement of age is culturally based but also, for many refugees, not knowing their age is due to the chaos and lack of infrastructure inherent in their plight as a displaced person or in a country in turmoil. The determination of age has rested with the medical profession in the past as it has relied on wrist X-rays (125). The development of a validated non-invasive tool that is easy to use will ensure that children will be given the correct medication, vaccines and that the expectations from the school and government will be age-appropriate (26). It is hoped that when the evidence surrounding this tool is published that it will be used instead of the other less reliable, more costly and more dangerous options.

It is imperative when doing research with vulnerable populations that the communities are part of every step of the research process and that the findings and their implications are communicated back to them. This has been a firm principal in all of this research. In the final phase of the Vitamin B12 research recently completed by my Honours student, the community health workers and the participants in that study were all very well aware of the importance of Vitamin B12 deficiency. Similarly, the importance of ear health and the possibility of a 'bacteria in the stomach' are also discussed more openly by refugee patients. Teachers and social workers are also keen to start using the Age Assessment Tool.

Limitations and Future Directions

This body of research is small compared with the overall burden of illness in the enormous number of asylum seekers, refugees and internally displaced people in the world. It is a snapshot of the refugees in Adelaide over the 15 years I worked at the Migrant Health Service in Adelaide. However the aim of bringing the past social determinants of health into present consultations in developed countries so that vulnerable people are given an opportunity to have equitable health-care is a universal one.

All of the research making up this thesis used a similar methodology, that of a clinical audit of the data from the Migrant Health Service. They were all studied after I identified a need for audit from my clinical experience, so the option for other methodologies was not available. The interpretation of the results is based on the limited cohort of patients and experience at the Migrant Health Service during the time that I worked there. The findings may not be able to be extrapolated to other populations, health services, or countries of settlement. Hence they are all really 'pilot' studies identifying a need for further investigation.

Because the issues researched were all 'gaps' in the literature with very few or no previous studies on the topics, they should be validated with further research using larger populations. This will be difficult given the ever-changing

environment of refugee health, the clinical nature of the workforce and the small numbers settled in each place. Bringing together the five refugee health centres for the national Vitamin B12 study was extremely complex. It was only possible because we were all part of the Refugee Health Network of Australia and knew each other well. Gathering enough data for statistical significance would be impossible without such collaboration.

Screening newly-arrived refugees for Vitamin B12 deficiency, chronic suppurative otitis media and cholesteatoma had not been considered before I began researching these problems. Since presenting my findings at conferences and publishing the articles, refugee health services in Australia and overseas have begun to screen and similarly find a high prevalence. Some of the other health services had already begun to question the same issues, but in many cases, mine was the first publication identifying the problem. This can be seen from the number of times that the research has been cited in a relatively short period of time. The morbidity and economic cost of missing these diagnoses is high. H.pylori screening and Vitamin B12 deficiency are controversial subjects and my research will add to the debate about whether this should be part of the screening protocol for newly-arrived refugee adults or children or both.

The research on Vitamin B12 deficiency continues to leave openings for future research. The population I studied may not have had the statistical power to show changes in mental health parameters with treatment of Vitamin B12 deficiency. Considering the high burden of mental health issues in refugees, and the morbidity associated with mental health, there is a need to further study this issue in order to ascertain if there might be such an association. Whether the high rate of deficiency is due to inadequate animal source food or for some other reason remains unknown. Finding an answer to this question would also assist in working out a protocol for how long follow-up of Vitamin B12 should continue. If there is an assumption that adequate supplies of animal source foods is enough to solve the problem, without research to back up this claim, there may be people whose Vitamin B12 deficiency is undetected and untreated with consequent high morbidity. Newer blood tests such as ‘Active B12’ (holotranscobalamin) have not been validated on different ethnicities or on

those who have been exposed to general food insecurity over a long period of time. As pathology laboratories begin to report on holotranscobalamin as well as serum Vitamin B12, new studies will need to be done in order to validate this test across different ethnicities and in people who possibly may have other nutritional deficiencies.

The research on chronic suppurative otitis media and cholesteatoma was done on recent arrivals. Future research might look at whether the rate of CSOM decreases as the immune system of refugees improves with better nutrition and other social determinants of health. My small study on cholesteatoma did not differentiate those who had previously had CSOM as compared to those who had head trauma. Numbers were small in my study and a much larger cohort would be needed in order to find statistically significant evidence for these issues.

The research on Helicobacter pylori also leads to many avenues for future research. Important areas to look at are whether an improvement in the social determinants of health such as better housing, hygiene and safer water decreases the incidence, prevalence, morbidity and mortality associated with H. pylori. There has also been limited research on whether the weight of children improves in those who have been treated for Helicobacter pylori and this has not been done on a refugee population. Future incidence of stomach cancer in people of refugee background in developed countries will need to be audited, in order to guide protocols for screening those at high risk.

Finding the correct age of refugees has been a contentious issue ethically and politically for many decades. It is imperative that the politics make way for an ethical and clinically sound means to find a realistic age for those who lack documentation. The Age Assessment Tool has been shown to be at least as good as and probably superior to other methods for determining age. Other research continues to look at a physical means for assessing age such as ultrasound. However these will always be more expensive than our well-validated tool. Changing policy to accept the Age Assessment Tool as a valid instrument is likely to be slow.

The main problem with all research in the refugee health arena is the changing population and the constant need to reassess for new and emerging issues. Clinical researchers are few in this space and the literature will always lag behind the experiential evidence, clinical knowledge and practice. As the world and the populations change, so will the prevalence of Vitamin B12 deficiency, CSOM, H.pylori and the need for age assessment.

I have made a significant contribution to the international peer-reviewed literature in refugee health over the last fifteen years. However, the work will never be complete. There will always be many unanswered questions in the refugee population and the scope for future research is endless.

Conclusion - New Evidence in this thesis regarding the health of newly-arrived refugees and its application to guidelines and policy

The research that makes up this thesis has grappled with two of the main issues leading to the lack of evidence needed to inform care of newly-arrived refugees in developed countries - the paucity of published peer-reviewed audits from refugee health services and the lack of research to clarify new and emerging issues in refugee health. There is a gap between the knowledge and practice of health practitioners who work with newly-arrived refugees and the peer-reviewed literature. Evidence such as the research contained in this work is needed to guide clinical practice, teaching, guidelines, advocacy and policy.

During the period of time this research was being undertaken, I discussed my finding at clinical meetings of the other doctors and health practitioners at the Migrant Health Service. On some occasions this alerted them to a disease they may not have otherwise been aware of, such as CSOM. The research identified the increase in the diagnosis of CSOM after we began discussing it at our clinical meeting. Similarly, it was from discussions about the Age Determination Tool at medical updates, that the two students became interested in being part of the research team in order

to validate the Tool. As I identified each issue, before the publications were written up, I updated the Migrant Health Service guidelines. As well as being used by the doctors at the Migrant Health Services, these guidelines were used by many of the other GPs in Adelaide.

Screening guidelines for clinical practice, such as those published by ASID and reviewed by RHeaNA need evidence on which to base their recommendations. The original guidelines were written at a time when 60% of the refugees were from sub-Saharan Africa and the most pressing issue was the burden of infectious diseases not usually seen in Australia (16, 19). The necessity for rewriting these guidelines encapsulates the rapidly changing environment of refugee health. Not only have the source countries changed dramatically so that the majority of people currently come from the Middle East and Asia, the UNHCR protocols have changed and so the majority of people are now investigated and treated for many of the infectious diseases we saw previously, including helminths, malaria and TB (105). Since the first Refugee Health Guidelines were written in 2008, more evidence has come to light about issues that were not included in the original document. Many of the clinicians working in refugee health have recognised, as have I, the importance of research in building an evidence-base for refugee guidelines and policy. In the eight years since the original publication, new evidence from national and international research has highlighted the importance of nutritional deficiencies, non-communicable diseases and a 'risk-based' protocol for many other diseases (19).

The new ASID guidelines published in 2016 have changed their recommendations based on my research into Vitamin B12 deficiency and chronic suppurative otitis media (19). A committee compiled the guidelines after a literature review, focusing on research published since the previous guidelines were written. The research on H.pylori and age determination had not yet been published when the new guidelines were being formulated. Citing my research they recommend in Chapter 13 that health professionals should 'consider screening for vitamin B12 deficiency if arrival <6months with a history of at least several years of significantly restricted food access e.g. patients from Bhutan, Afghanistan, Iran or the Horn of Africa' (19). In Chapter 16 there is a new

recommendation about checking for Chronic Suppurative Otitis Media that cites my research findings (19). The ASID guidelines will continue to be used in the future by health practitioners throughout Australia, who will now consider whether the newly-arrived refugees they are assessing might be at risk of Vitamin B12 deficiency and CSOM. Future research is likely to identify whether these new guidelines have changed the clinical behaviour of practitioners.

Advocacy for equity of health-care for newly-arrived refugees must also be based on evidence, and organisations such as RheaNA have been instrumental in changing the PBS schedule for diseases such as malaria and schistosomiasis in the recent past (45). Evidence such as that from the research making up this thesis is needed in order to advocate for such changes. For instance, it may be that in the future health practitioners will utilize this research to advocate for a PBS-listed treatment regime for children with H.pylori. I also hope it will assist in decreasing the use of X-rays for the assessment of age in refugee children.

The purpose of a recent document from the Australian Government Department of Health was to 'determine whether vitamin B12 testing is appropriate for MBS reimbursement' and acknowledged that 'there are no Australian clinical guidelines that either advocate or recommend against routine testing for vitamin B12'. They have recommended that serum vitamin B12 can only attract a Medicare rebate once in a 12-month period (126). They do not mention the increased risk of Vitamin B12 deficiency in refugees. However their literature review and stakeholder consultation were conducted in 2013 and it may be that it was done before our article was published. This omission highlights the importance of published evidence to inform such policy. If the Medicare rebates tighten even more, and our evidence is not taken into account, it may be that in the future newly-arrived refugees will not be eligible for screening for Vitamin B12 deficiency based on their refugee status.

The new ASID guidelines do not recommend screening all refugees for H.pylori but only those with symptoms or a family history of gastric cancer. Our H.pylori studies were not published at the time the new guidelines were written, but will add to the debate on this topic and hopefully trigger more research in refugees in

order to ascertain their risk of gastric cancer and other morbidities. The H.pylori research will also be of use to those who are advocating for screening underweight children and for a change in the PBS schedule to include an easy-to-use and affordable therapy for children. The new ASID guidelines include a regime for children but it is not available as a single prescription 'combination pack' and so is complex and expensive (19).

Similarly the Ciprofloxacin drops needed to treat Chronic Suppurative Otitis Media are only available on the PBS for children under the age of 18 and for Aboriginal people (127). In our audit 80% of those with CSOM were adults (10). Advocacy using the evidence from our study is needed for the Department of Health to recognise that adult refugees are also a high-risk population.

It is interesting to note that many of the peer-reviewed journals on the topic of age determination of children have been in the legal field (128, 129). This research is also important outside the field of medicine and the range of publications citing the original article shows how many others have struggled with this concept. With the recent publication of our validating studies it is expected that teachers, lawyers and government bodies will be interested in using the Age Assessment Tool to determine the age of refugee children.

To date I have published 31 articles in peer-reviewed journals, with over 200 citations. My H-index is 11. My series of articles in the Australian Family Physician has been the basis for learning and teaching about refugee health in many forums throughout Australia. The citations for the articles making up this thesis are in the Appendix.

I am extremely gratified to know that the information from these articles has been used by GPs and other health professionals to manage refugees in their practices and that, without these articles, they would not have had access to this information. It is also very gratifying to see that my research has changed the new Australian Refugee health guidelines. I look forward to watching for future protocols, advocacy and research that may be influenced by the research in this thesis in order to improve the care we give to our refugee clientele.

Appendix 1.

Citations as of July 2016

Low vitamin B12 levels among newly-arrived refugees from Bhutan, Iran and Afghanistan: a multicentre Australian study (2013)– 13 citations

Article	Authors	Journal	Year
1. Nutrition for refugee children: risks, screening, and treatment	M Fabio	Current problems in pediatric and adolescent health	2014
2. The resettlement of refugees in Australia: a bibliography	K Neumann	Book	2013
3. A safe and healthy future? Epidemiological studies on the health of asylum seekers and refugees in the Netherlands	ESM Goosen	Book	2014
4. Prevalence of dyslipidaemia and micronutrient deficiencies among newly arrived Afghan refugees in rural Australia: a cross-sectional study	MS Pour, S Kumble, S Hanieh, B Biggs	BMC Public Health	2014
5. Health Profiles of Newly Arrived Refugee Children in the United States, 2006–2012	K Yun, J Matheson, C Payton et al	American journal of public health	2016
6. The Status of Vitamin B12 and Folate among Chinese Women: A Population-Based Cross-Sectional Study in Northwest China	S Dang, H Yan, L Zeng, Q Wang, Q Li, S Xiao, X Fan	PloS one	2014
7. Cognitive assessment of refugee children: Effects of trauma and new language acquisition	I Kaplan, Y Stolk, M Valibhoy, A Tucker, Baker J	Transcultural Psychiatry	2016
8. Adaptation to extreme heat and climate change in culturally and linguistically diverse communities	A Hansen, M Nitschke, P Bi	Applied Studies in Climate Adaptation	2014
9. Hepatitis B Screening and Prevalence Among Resettled Refugees—United States, 2006–	KC Scott, EM Taylor, B Mamo,	MMWR	2015

2011	ND Herr et al		
10. Myanmarese Neuropathy: Clinical Description of Acute Peripheral Neuropathy Detected among Myanmarese Refugees in Malaysia	H Fu Liong, DP Santhi, V Shanthi, Mohd Hanip R	International Scholarly Research Notices	2014
11. Highly Heterogeneous Probiotic Lactobacillus Species in Healthy Iranians with Low Functional Activities	Rohani M, Noohi N, Talebi M, Pourshafie M	PloS one	2015
12. Food Insecurity and Risk of Depression Among Refugees and Immigrants in South Africa	Maharaj M, Tomita A, Thela L, Mhlongo M	Journal of Immigrant and Minority Health	2016
13. Low levels of vitamin B12 can persist in the early settlement of refugees; Symptoms, screening and monitoring	Benson J, Phillips C, Kay M, Hanifia H, Giri G, Leahy C, Lorimer M	Australian Family Physician	2015

Age determination in refugee children (2008) - 14 citations

Article	Authors	Journal	Year
1. Age assessment of young asylum seekers	A Hjern, M Brendler-Lindqvist, M Norredam	Acta paediatrica	2012
2. Age determination of unaccompanied asylum seeking minors in the European Union: a health law perspective	HDCR Abbing	European journal of health law	2011
3. Accuracy of three age determination X-ray methods on the left hand-wrist: a systematic review and meta-analysis	S Serinelli, V Panetta, P Pasqualetti, D Marchetti	Legal Medicine	2011

4. Age and bone age determinations-inaccurate methods at their best	Z Zadik	Journal of Pediatric Endocrinology and Metabolism	2009
5. Clinical and legal requirements for age determination in the living.	P Beh, J Payne-James	Age Estimation in the Living - Chapter 3	2010
6. Age evaluation and odontology in the living.	J Taylor, M Blenkin	Age Estimation in the Living - Chapter 10	2010
7. Refugee children: Rights and wrongs	K Zwi, G Chaney	Journal of paediatrics and child health	2013
8. Gaps in smiles and services: a cross-sectional study of dental caries in refugee-background children	A Quach, IL Laemmle-Ruff, T Polizzi, Paxton G	BMC oral health	2015
9. Proof of age required: estimating age in adults without birth records	C Phillips, S Narayanasamy	Australian Family Physician	2010
10. Age Determination at Tikur Anbessa Specialized Hospital, Addis Ababa University.	S Hailu, R Fikre, H Yohannes, A Daniel, L Biruk	East and Central African Journal of Surgery	2011
11. Accuracy of MRI skeletal age estimation for subjects 12-19. Potential use for subjects of unknown age	S Serinelli, Paneblanco V, Martino M, Battisti S et al	International Journal of Legal Medicine	2015
12. Moving the Virtual Border to the Cellular Level: Mandatory DNA Testing and the US Refugee Family Reunification	E Holland	California Law Review	2011
13. Age determination in refugee children: A narrative history tool for use in holistic age assessment	Vaska A, Benson J, Eliott J, Williams J	Journal of Paediatrics and Child Health	2016
14. The Health of Resettled Refugee Children: a Modified Systematic Review 2001-2009	Beauchamp JR	Masters Thesis Victoria University of Wellington	2010

Vitamin B12 deficiency: why refugee patients are at high risk – 8 citations

Article	Authors	Journal	Year
1. Low vitamin B12 levels among newly-arrived refugees from Bhutan, Iran and Afghanistan: a multicentre Australian study	J Benson, C Phillips, M Kay, MT Webber, AJ Ratcliff et al	PloS one	2013
2. Nutrition for refugee children: risks, screening, and treatment	M Fabio	Current problems in pediatric and adolescent health	2014
3. Prevalence of dyslipidaemia and micronutrient deficiencies among newly arrived Afghan refugees in rural Australia: a cross-sectional study	MS Pour, S Kumble, S Hanieh, B Biggs	BMC Public Health	2014
4. Health issues in refugee children	S Shah, M Siddharth, K Yun	Refugee health care	2014
5. HIV and Other Sexually Transmitted Infections: Testing and Treatment Considerations for Refugees	S Jain, J Adelson-Mitty	Refugee health care	2014
6. Chronic Disease Management in Refugees	P Cronkright, AK Ramaiya	Refugee health care	2014
7. Beware of the Ailments of Vitamin B12 Deficiency	AS Manolis, TA Manolis, E Poulidakis	Hospital Chronicles	2013
8. The effect of Vitamin B12 supplemention on fatigue in hemodialysis patients	A Tayyebi, S Savari, B Nehrir, A Rahimi, B Eynollahi	Iran J Crit Care Nurs	2013

Chronic suppurative otitis media and cholesteatoma in Australia's refugee population (2012) – 3 citations

Article	Authors	Journal	Year
1. A prospective study of seven patients with chronic mastoiditis	HAL Mousa	JMM Case Reports	2015
2. End wall mastoidectomy treatment of cholesteatoma. Clinical Effect	Guo Xin, Chen Fu Hua, Ma Ning	Sichuan Medical Journal	2013
3. Efficacy of microsurgical treatment of 40 cases of cholesteatoma with facial nerve canal injury	Chun , the Xuqiu Fen	China Clinical Research	2013

Impact Factors of Journals in which the articles are published

Australian Family Physician - Impact Factor 0.7

1. **Benson J**, Maldari T, Turnbull T (2010) Vitamin B12 deficiency – why refugee patients are at high risk.
2. **Benson J**, Phillips C, Kay M, Hanifi H, Giri G, Leahy C, Lorimer M (2015). Low levels of Vitamin B12 can persist in the early resettlement of refugees: symptoms, screening and monitoring.
3. **Benson J,** Williams J (2008) Age Determination in Refugee Children. *Australian Family Physician , 37(10), 821-824*
4. **Benson J**, Mwanri L. Chronic suppurative otitis media and cholesteatoma in Australia's refugee population (2012). *Australian Family Physician*; 41(12):978-80.

PLoS One – Impact Factor 3.234

1. **Benson J**, Phillips C, Kay M, Webber M, Ratcliff A, Correa-Velez I, Lorimer M (2013) Low Vitamin B12 levels in newly-arrived refugees from Bhutan, Iran and Afghanistan; a multicentre Australian study

Journal of Paediatrics and Child Health – Impact Factor – 1.0

1. Vaska AI, **Benson J**, Eliott JA, Williams J. Age determination in refugee children: A narrative history tool for use in holistic age assessment. *Journal of paediatrics and child health*. 2016 May;52(5):523-8.
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