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Integrating HIV, hepatitis B and syphilis screening and treatment through the Maternal, Newborn and Child Health platform to reach global elimination targets

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Every year, an estimated 180 000 babies in the Western Pacific Region are infected by hepatitis B, 13 000 by syphilis and 1400 by HIV through mother-to-child transmission.[1] These infections can be largely prevented by antenatal screening, treatment and timely vaccination for newborns. Despite challenges in controlling each disease, major achievements have been made. National immunization programmes have reduced the regional hepatitis B prevalence from over 8% in 1990 to 0.93% among children born in 2012. In addition, HIV testing and treatment have helped keep the regional prevalence of HIV infections at 0.1%. In contrast, the number of maternal syphilis cases is still high in the Western Pacific Region, with an estimated 45 million cases in 2012. Elimination of mother-to-child transmission of these infections cannot be achieved through vertically applied programming and require using and augmenting to the shared Maternal, Newborn and Child Health platform to coordinate, integrate and enable cost efficiencies for these elimination efforts. The *Regional Framework for Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific 2018–2030* offers such a coordinated approach towards achieving the triple elimination of mother-to-child transmission of HIV, hepatitis B and syphilis and provides guidance for decision-makers, managers and health professionals working in programmes addressing maternal, newborn and child health, HIV, hepatitis, sexually transmitted infections and immunization.

The *Regional Framework for Triple Elimination of Mother-to-Child Transmission of HIV, Hepatitis B and Syphilis in Asia and the Pacific 2018–2030*[2] (Triple Elimination Framework) was endorsed by all Member States at the sixty-eighth session of the Regional Committee for the Western Pacific. It was developed to provide a coordinated approach to achieve and sustain elimination of these largely preventable infections using the shared Maternal, Newborn and Child Health (MNCH) platform for planning, service delivery, monitoring and evaluation. With nearly nine out of 10 mothers and children in this Region already receiving antenatal, perinatal, postnatal and well-baby care services, it is more efficient to build additional prevention services upon the shared platform than delivering them as single uncoordinated interventions solely through traditional, vertical, disease-specific control and surveillance programmes.

Endorsed by the World Health Assembly in 2016, the 2030 elimination targets for the *Global Health Sector Strategy on HIV 2016–2021*, the *Global Health Sector Strategy on Viral Hepatitis 2016–2021* and the *Global Health Sector Strategy on Sexually Transmitted Infections 2016–2021* include: 0.1% or lower hepatitis B surface antigen (HBsAg) prevalence among children and 50 or fewer cases per 100 000 live births for paediatric HIV infections and congenital syphilis.[3–5]

These three diseases have a significant burden in the Western Pacific Region: the Region alone accounts for 45% of all global hepatitis B infections;[2] an increasing trend of syphilis infections is observed among key populations including women of reproductive age;[6] and while HIV prevalence is low throughout the Region at 0.1%, the HIV mother-to-child transmission (MTCT) rate is high at 12%.[7]

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MNCH care has made significant progress in the Region. From 1990 through 2015, the maternal mortality ratio decreased by 64% from 114 to 41 maternal deaths per 100 000 live births,[8] in part due to the increases in antenatal care coverage and births attended by skilled birth attendants. Nearly nine in 10 pregnant women in the Region have attended at least one antenatal care visit and have delivered in a health facility, while provision of quality services and access to at least four antenatal visits still remain as challenges.[9] DTP3 vaccine coverage for children has remained over 95% since 2009 with 97.3% coverage in 2016.[10] These multiple entry points in receiving peripartum services provide a unique opportunity for coordination and integration of HIV, hepatitis B and syphilis interventions to move towards elimination of mother-to-child transmission (EMTCT) of these infections.

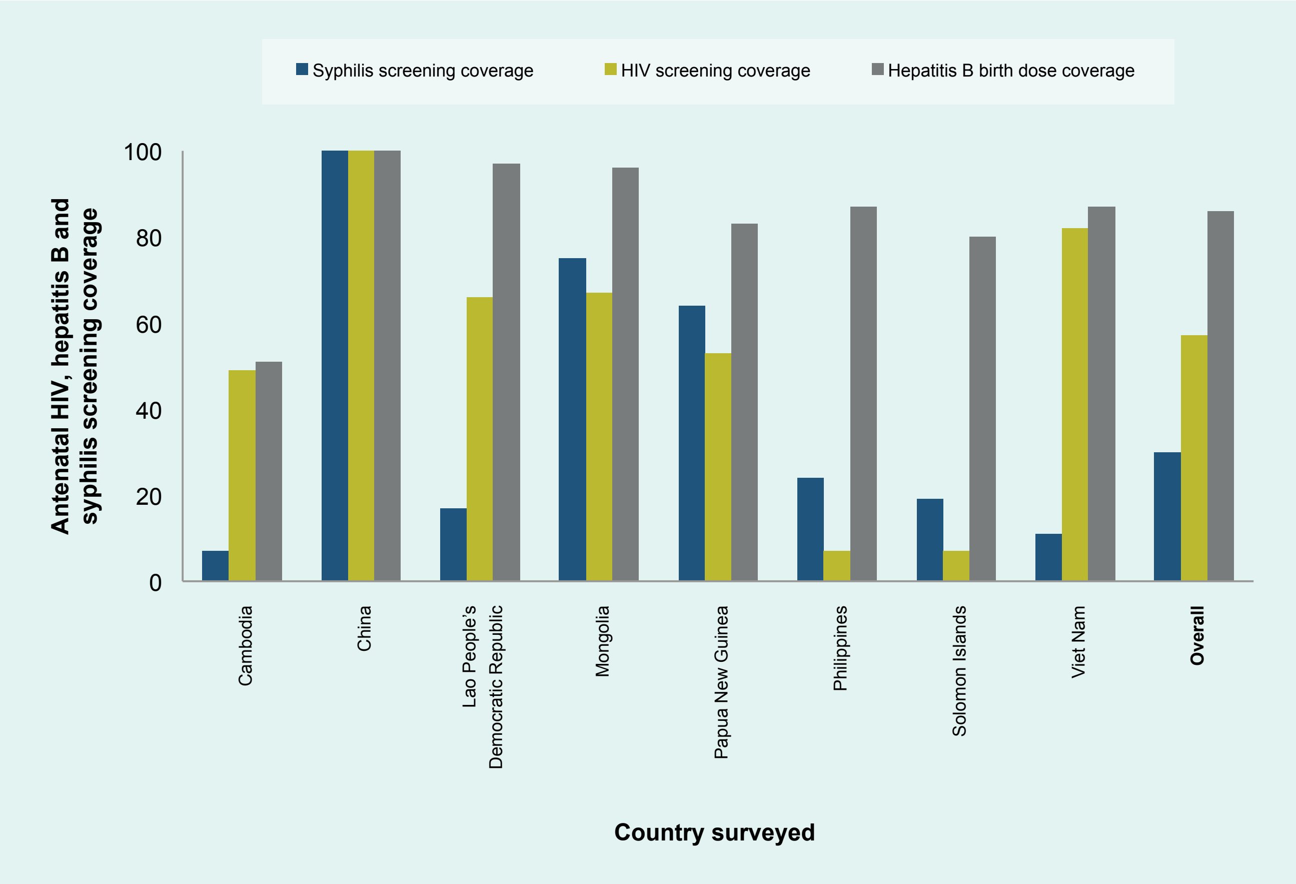
The Region has shown remarkable progress with national immunization programmes, reducing the regional HBsAg prevalence to less than 1% among children born in 2012. Not all countries met the 2012 or 2017 regional prevalence targets among 5-year-olds (less than 2% and less than 1%, respectively) or the regional 2017 milestones of 95% or higher hepatitis B birth dose and 95% or higher hepatitis B third-dose vaccine coverage.[11,12] Thirty countries had evidence of meeting the 2012 goal of less than 2%; as of November 2017, 18 countries have been verified as meeting the 2017 goal of less than 1%, with five additional countries having evidence of meeting this same goal. Introduction of additional interventions are likely to be required to reach the 0.1% HBsAg prevalence elimination target by 2030, including antenatal HBsAg screening, antiviral treatment of pregnant women with high viral loads and the use of hepatitis B immunoglobulin among infants born to HBsAg-positive mothers.[4] Modelling has shown that global elimination of hepatitis B as a major public health threat can only be achieved by scaling up hepatitis B vaccine third-dose coverage to 90% and birth-dose coverage to 80%, peripartum antivirals to 80% of hepatitis B e-antigen-positive mothers and increasing testing and treatment to 80% of those eligible.[13] To meet these suggested screening and treatment targets, immunizations programmes must work with MNCH and sexually transmitted infection programmes through an integrated effort to reach hepatitis B EMTCT.

In 2014, WHO established the global criteria for dual EMTCT of HIV and syphilis that were further updated in 2017.[14] Several countries were already validated as having achieved elimination. In this Region, EMTCT of HIV and syphilis has seen limited progress to date. With the target of a 90% reduction in new HIV infections among infants by 2015, actual reductions have only been 27%.[2] Maternal and congenital infections decreased by one-third from 2008 to 2012; however, coverage of antenatal syphilis screening and treatment remains low in several countries in the Region.[15]

Antenatal HIV and syphilis screening coverage and hepatitis B birth-dose coverage were assessed between October 2016 and June 2017 in 161 randomly selected health facilities that had introduced Early Essential Newborn Care (EENC) in Cambodia, China, the Lao People's Democratic Republic, Mongolia, Papua New Guinea, the Philippines, Solomon Islands and Viet Nam. Accounting for 97% of all neonatal deaths in the Region, these eight countries have been selected as priority countries since 2014 under the *Action Plan for Healthy Newborn Infants in the Western Pacific Region (2014–2020)*.[16] Hepatitis B birth-dose vaccination has been promoted through EENC coaching to health workers dealing with intrapartum and postnatal care.[17] **Fig. 1** shows that hepatitis B birth-dose coverage was higher than syphilis and HIV antenatal screening coverage in seven of eight countries, with China having 100% coverage for all three. This shows that coordination among the different programmes can improve access to essential services for both women and their babies, while lack of collaboration could result in limited access and inefficiencies.

Some countries in the Region have already begun pioneering a coordinated approach to triple elimination. For example, China has an EMTCT strategy that integrates provision of the essential package of services for universal HIV, hepatitis B and syphilis screening where all three tests are offered concurrently and free of charge. Further interventions such as HIV and syphilis treatment, including hepatitis B prophylaxis and follow-up testing and care for mothers and their children are provided for free. As a result, MTCT of HIV decreased to 6.7% in 2013, and over 1200 paediatric HIV infections were averted in 2014.[18] Mongolia has developed national guidelines for HIV, syphilis and hepatitis B and C antenatal screening, recommending antiviral treatment of women with high viral loads and hepatitis B immunoglobulin to infants born to these mothers. These underpin the importance

Fig. 1. **Antenatal HIV and syphilis screening coverage and hepatitis B birth-dose coverage in eight countries in the Western Pacific Region**



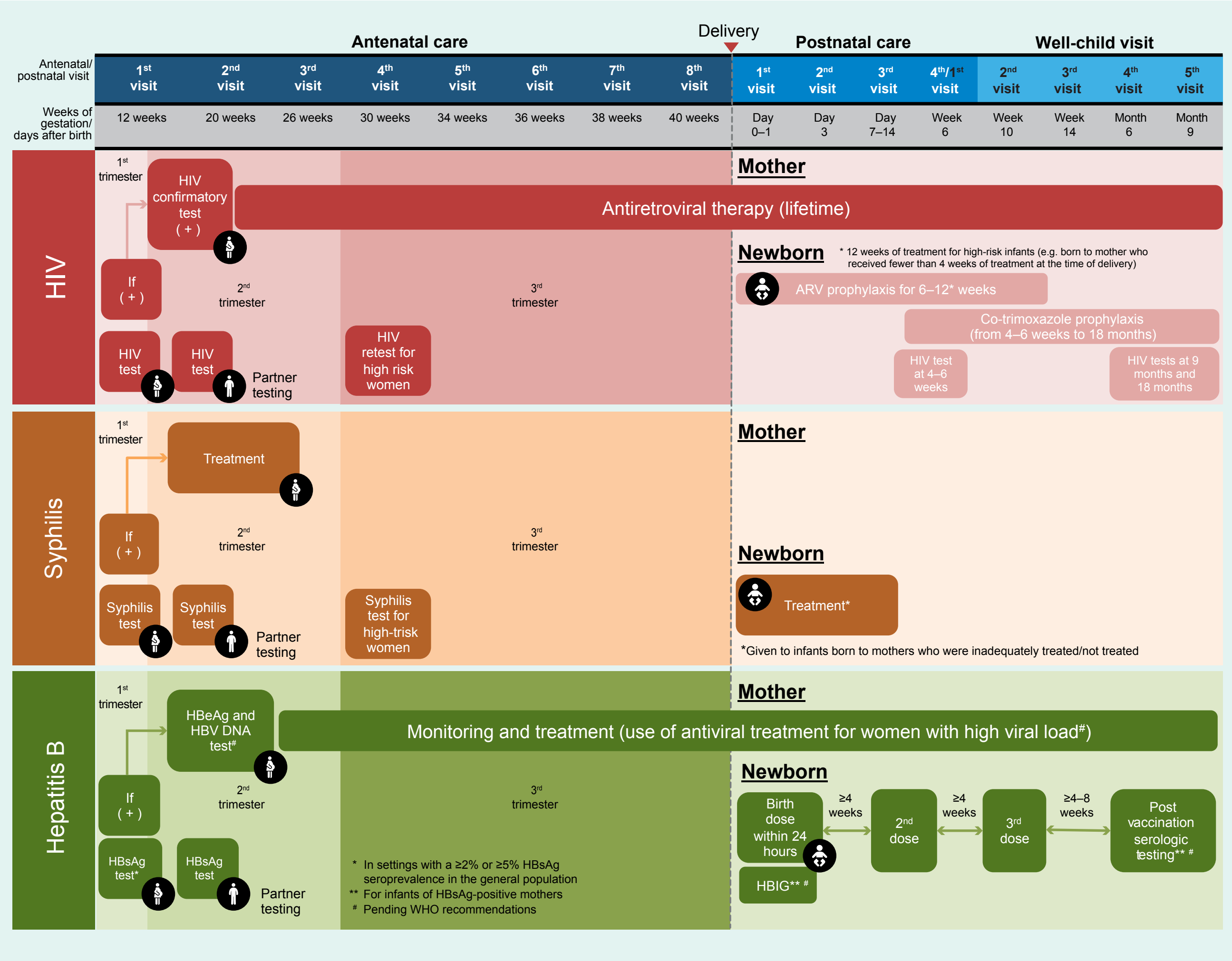
of coordination and collaboration among concerned programmes for better health outcomes for mother and child.[1]

Current interventions must be scaled up substantially, other interventions introduced and coordination among programmes improved to achieve the global EMTCT targets.[1,13] In response, the Triple Elimination Framework proposes a vision to provide every child the greatest chance to start a healthy life free of three preventable communicable diseases. By better coordinating service delivery among programmes and including the incorporation of hepatitis B screening into existing HIV and syphilis screening at antenatal clinic, the Triple Elimination Framework looks to integrate these programmes to enable pregnant women to know their own and their partners' infection status. It also allows pregnant mothers to understand and receive the necessary interventions for themselves and their baby during pregnancy, delivery and postnatally and to ensure that their babies receive these necessary interventions to prevent transmission of these infections (**Fig. 2**).

The Triple Elimination Framework suggests a set of key indicators under the headings of policy, impact and programme for monitoring and evaluating EMTCT. This includes eventually developing global guidance that incorporates hepatitis B into WHO established criteria for EMTCT of HIV and syphilis. The Triple Elimination Framework will also need to be supplemented by an economic analysis of the introduction of additional interventions for EMTCT of hepatitis B. This is particularly pertinent for countries with high hepatitis B vaccine birth-dose and third-dose coverage rates that are looking to expand their perinatal programmes.

Moving towards triple elimination should result in greater collaboration between programmes and thus improve accessibility, effectiveness, efficiency and sustainability of MNCH services for every woman, child and their family.

Fig. 2. **HIV, syphilis and hepatitis B screening, treatment and vaccination services offered during antenatal, delivery, postnatal care and well-child visits**



Ethics statement

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the World Health Organization (WHO) or the WHO regional offices.

Conflict of interest

None.

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Community-associated methicillin-resistant *Staphylococcus aureus* infections in Aboriginal children attending hospital emergency departments in a regional area of New South Wales, Australia: a seven-year descriptive study

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Objective: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) can cause bacterial skin infections that are common problems for Aboriginal children in New South Wales (NSW). MRSA is not notifiable in NSW and surveillance data describing incidence and prevalence are not routinely collected. The study aims to describe the epidemiology of CA-MRSA in Aboriginal children in the Hunter New England Local Health District (HNELHD).

Methods: We linked data from Pathology North Laboratory Management System (AUSLAB) and the HNELHD patient administration system from 33 hospital emergency departments. Data from 2008–2014 for CA-MRSA isolates were extracted. Demographic characteristics included age, gender, Aboriginality, rurality and seasonality.

Results: Of the 1222 individuals in this study, 408 (33.4%) were Aboriginal people. Aboriginal people were younger with 45.8% aged less than 10 years compared to 25.9% of non-Aboriginal people. Most isolates came from Aboriginal people who attended the regional Tamworth Hospital (193/511 isolates from 149 people). A larger proportion of Aboriginal people, compared to non-Aboriginal people, resided in outer regional (64.9% vs 37.2%) or remote/very remote areas (2.5% vs 0.5%). Most infections occurred in summer and early autumn. For Aboriginal patients, there was a downward trend through autumn, continuing through winter and spring.

Discussion: Aboriginal people at HNELHD emergency departments appear to represent a greater proportion of people with skin infections with CA-MRSA than non-Aboriginal people. CA-MRSA is not notifiable in NSW; however, pathology and hospital data are available and can provide valuable indicative data to health districts for planning and policy development.

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) can cause bacterial skin infections that are common health problems for many Australian Aboriginal and Torres Strait Islander (hereafter Aboriginal) children and families in rural areas in New South Wales (NSW).[1] The term CA-MRSA distinguishes the infection from MRSA acquired through health-care settings including hospitals.

Typical infections caused by CA-MRSA include skin and soft tissue infections, boils, impetigo, cellulitis and larger abscesses. CA-MRSA is contagious, transmitted by skin-to-skin contact from infected lesions, contact with contaminated objects or close contact with asymptomatic carriers.[2] Groups at higher risk of infection include children and young adults, Aboriginal people and people of lower socioeconomic status.[2] Indigenous populations in Canada, the United States of America and in Pacific island nations have also been associated with a high risk of infection with CA-MRSA attributed possibly to social and financial disadvantage.[3] Associated risk factors include crowded living conditions with poor housing infrastructure and lack of access to facilities for adequate personal cleansing, pre-existing skin

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conditions and previous antimicrobial drug treatment.[4] MRSA is not notifiable in NSW and hence, surveillance data describing its incidence and prevalence are not routinely collected. Such data would be invaluable in the planning, implementation and evaluation of public health programmes designed to prevent and control CA-MRSA.

Early diagnosis and treatment for CA-MRSA is recommended as delays may lead to serious complications including septicaemia.[4] Recommended treatment includes incision and drainage of wounds, cautious use of antibiotics (when indicated by pathology and/or when lesions are larger than 5 cm, with systemic sepsis or patients who are immunocompromised), personal cleansing measures (covering draining wounds, regular showering and handwashing and not sharing personal items such as linen, towels, razors), consideration of staphylococcal skin load reduction with bleach baths or formal decolonization for those with recurrent boils and/or household involvement and maintaining close follow-up by primary health care (PHC) services.[5] These guidelines may not adequately take into account important sociocultural factors or ways of living in Aboriginal communities where CA-MRSA infections can impact health, quality of life and contribute to poor school attendance.[1]

We used routinely collected pathology data from wound and/or skin swabs collected in emergency departments of hospitals in the Hunter New England Local Health District (HNELHD) to describe the epidemiology of CA-MRSA in Aboriginal children and young people. For the purpose of this study, we defined CA-MRSA as not 'hospital onset' or 'health-care-associated community origin'. This definition was taken from the study from where our data was collected.[6] It reflects both the Centers for Disease Control and Prevention (CDC) classification[7] and accommodates Australian practices and limitations of the data set (**Table 1**). Results will inform the development of health policy and community-based programmes to reduce the incidence and prevalence of the infection.

METHODS

The study setting was HNELHD, which covers a large regional area of northern NSW. The region is largely rural with one metropolitan centre in Newcastle (**Fig. 1**).[8] In 2011, the total population of HNELHD was 875 546 including 46 955 Aboriginal people (5.4%). Of the total Aboriginal population, almost half were aged under 20 years (23 207 or 49.4%) compared to just a quarter of the non-Aboriginal population (203 575 or 24.6%).[9]

We used routinely collected administrative data linked by laboratory number from a previous study examining the changing epidemiology of *Staphylococcus aureus* in HNELHD. This data set included pathology data from the Pathology North Laboratory Management System (AUSLAB) and patient characteristics and hospitalization data from the HNELHD patient administration system. The study period was 1 January 2008 to 31 December 2014. Five of the district's 38 hospitals were excluded as they did not use AUSLAB or data were not available for comparison.

From the complete data set of 81 133 positive *S. aureus* isolates, all those classified as CA-MRSA (n = 7789) were identified. Isolates from residents of residential aged-care facilities (n = 398), those not from skin or wound swabs (n = 768), those for which Aboriginal and/or Torres Strait Islander status was not recorded (n = 79) and those aged 20 years or older (n = 4335) were removed. Swabs collected within two days of an emergency department presentation were included. Those taken outside of the two-day period were considered to be from presentations to general practitioners (GP) and were excluded (n = 658). This left 1551 isolates for CA-MRSA from 1222 individuals.

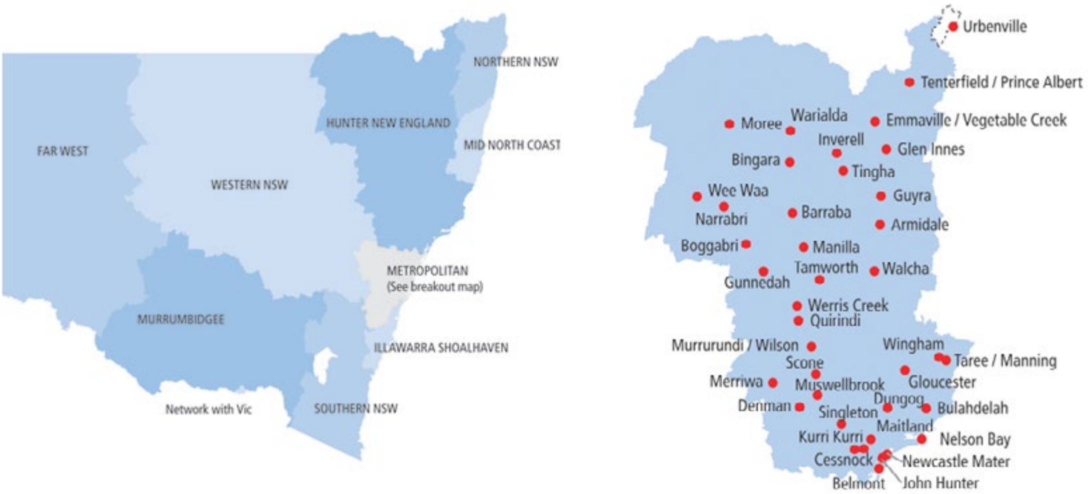
The number of isolates by hospital emergency department was used as a measure of burden of disease. From the 1222 individuals with a first isolate of CA-MRSA (as opposed to isolates of repeated testing), demographic characteristics including age, gender and Aboriginality were described. Street addresses were used to assign a Statistical Area Level 2 (SA2) location to each individual and to classify rurality. Seasonality of infection was described using date of first isolate.

Proportions and counts were analysed using Stata 14® and Excel 2010®. The Australian Statistical Geography Standard (ASGC) Remoteness Structure 2011 was used to classify metropolitan, regional and remote/very remote settings. The ASGC: Volume 1, 2011 population counts were used to calculate rates within SA2 areas.[10] Geocoding was conducted using the Geocoder Optimised for Population Health Epidemiology and Research from NSW Ministry of Health.

Table 1. **Comparison of study definitions of hospital origin (HO) and health-care-associated community onset (HACO) methicillin-resistant *Staphylococcal aureus* (MRSA) with the Centers for Disease Control and Prevention (CDC) definitions**

MRSA category	Study definition	CDC definition[8]	Rationale for difference
HO MRSA	Culture obtained within 48 hours following admission or 48 hours following discharge	Culture obtained within 96 hours of admission	Study definition reflects Australian definition of hospital-associated infection as used in National Health Performance Authority reports
HACO MRSA	Not HO MRSA, and culture was obtained within 365 days of a previous hospital admission or within 365 days of receiving dialysis	Includes patients with a central vascular catheter (CVC). Includes residence in a long-term care facility.	Unable to determine presence of CVC from collected data. In line with Australian conventions, long-term care facilities (residential aged-care facilities) should not be classified as health-care facilities.

Fig. 1. **Map of Hunter New England Local Health District and hospitals, NSW, 2017**



Source: http://www.health.nsw.gov.au/lhd/Pages/hnelhd.aspx

RESULTS

Of the 1222 individuals in this study, 408 (33.4%) were Aboriginal people and 814 (66.6%) were non-Aboriginal people (**Table 2**). Overall, Aboriginal people were younger with 45.8% aged less than 10 years compared to 25.9% of non-Aboriginal people. There was a higher proportion of males than females (ratio 1.3/1.0).

Of the 1551 isolates, 511 (32.9%) were from Aboriginal people. The highest number of isolates from Aboriginal people came from those who attended the regional hospital in Tamworth (193/511 isolates from 149 people) and John Hunter Hospital in Newcastle (69/511 isolates from 55 people). For non-Aboriginal people, most isolates came from people who attended John Hunter Hospital (256/1040 isolates from 196 people) and Maitland Hospital (176/1040 isolates from 139 people), which lies within close proximity to Newcastle (data not shown).

The proportion of Aboriginal people residing in outer regional and remote areas (64.9% and 2.5%, respectively) was higher compared to that of non-Aboriginal people (37.2% and 0.5%, respectively) (**Table 3**).

Aboriginal people resided largely in the SA2 locations of the regional centre of Tamworth (n = 146, 36.0%) and in Armidale (n = 34, 8.4%) (**Table 4**).

Seasonal analysis of CA-MRSA isolates in the study period showed most cases occurred in summer and early autumn. For Aboriginal patients, there was a downward trend through autumn, continuing through winter and

Table 2. **Number and proportion of individuals aged under 20 years with hospital emergency department wound/skin swabs with CA-MRSA, by age and Aboriginality, Hunter New England Local Health District, 2008–2014**

Age (years)	Aboriginal		non-Aboriginal	
	n	%	n	%
0–4	87	21.3	91	11.2
5–9	100	24.5	120	14.7
10–14	108	26.5	209	25.7
15–19	113	27.7	394	48.4
Total	**408**	**100.0**	**814**	**100.0**

Table 3. **Number and proportion of individuals aged under 20 years with hospital emergency department wound/skin swabs with CA-MRSA by region, Hunter New England Local Health District, 2008–2014***

Region	Aboriginal		non-Aboriginal	
	n	%	n	%
Major city	78	19.3	249	30.9
Inner regional	54	13.3	254	31.5
Outer regional	263	64.9	300	37.2
Remote/very remote	10	2.5	4	0.5
Total	**405**	**100.0**	**807**	**100.0**

* Australian Standard Geographical Classification (ASGC)

Some missing data and individuals residing outside HNELHD account for totals less than full data set in **Table 2**.

spring. Apart from a peak in early autumn for non-Aboriginal patients, the trend was similar for both groups (**Fig. 2**).

Ethics

Ethics approval was obtained for this study by HNELHD Human Research Ethics Committee (12/12/12/5.08).

DISCUSSION

Overall, Aboriginal people accounted for 33.4% of CA-MRSA first isolates in the study period while accounting for just 10.2% of the total population aged under 20 years in the wider HNELHD population.[9] Aboriginal people in this study tended to live in outer regional, rural or remote areas, especially in the north-west of the state of NSW including Tamworth, Armidale and Inverell. The emergency department at the regional centre of Tamworth had the highest number of CA-MRSA isolates identified in Aboriginal people. An important and less described finding was that most isolates were from summer months and early autumn when it is warmer, more humid and when children are more likely to be playing outdoors. A similar trend was reported for paediatric patients in Rhode Island, USA, where approximately 1.85 times as many CA-MRSA infections per emergency department visit occurred in summer and autumn.[11]

Published data describing the local epidemiology of CA-MRSA are limited, impeding informed policy development and health service planning that can address the burden of skin infection experienced by Aboriginal families. This study provides new information that can be used to direct health resources to areas within HNELHD where needs are higher and when the number of CA-MRSA infections are high, such as summer and early autumn. There are advantages in using readily available administrative data as a source of surveillance information to inform practice. Data are readily available for timely analysis, collected routinely and are easily linked for analysis of trends and patient characteristics. These methods can be reproduced by other local health districts that have access to linked pathology and hospital data. In this way, more information about CA-MRSA infections in NSW can be uncovered.

It is known that Aboriginal people are more likely to attend hospital emergency departments if access to community-based, culturally safe and appropriate PHC is limited. This may occur more often in rural and remote areas.[12] It is important to ensure that staff working in emergency departments provide a culturally safe place for Aboriginal people to seek care about skin infections. Currently the NSW treatment guidelines for skin infections may not incorporate the consideration of important, associated and interwoven contributors such as social, economic, housing and environmental factors in the management of infections.[1] Tailoring treatment guidelines to respond to these social determinants of health for Aboriginal people in rural areas, who access PHC in acute settings, may be an effective step to reducing recurrence of disease.[1] The emergency department could be an important setting for improving skin health through sharing of health information, initiating referrals and arranging for follow-up of children with skin diseases.

Fig. 2. **Individuals aged under 20 years with hospital emergency department wound/skin swabs with CA-MRSA, by season, Hunter New England Local Health District, 2008–2014**

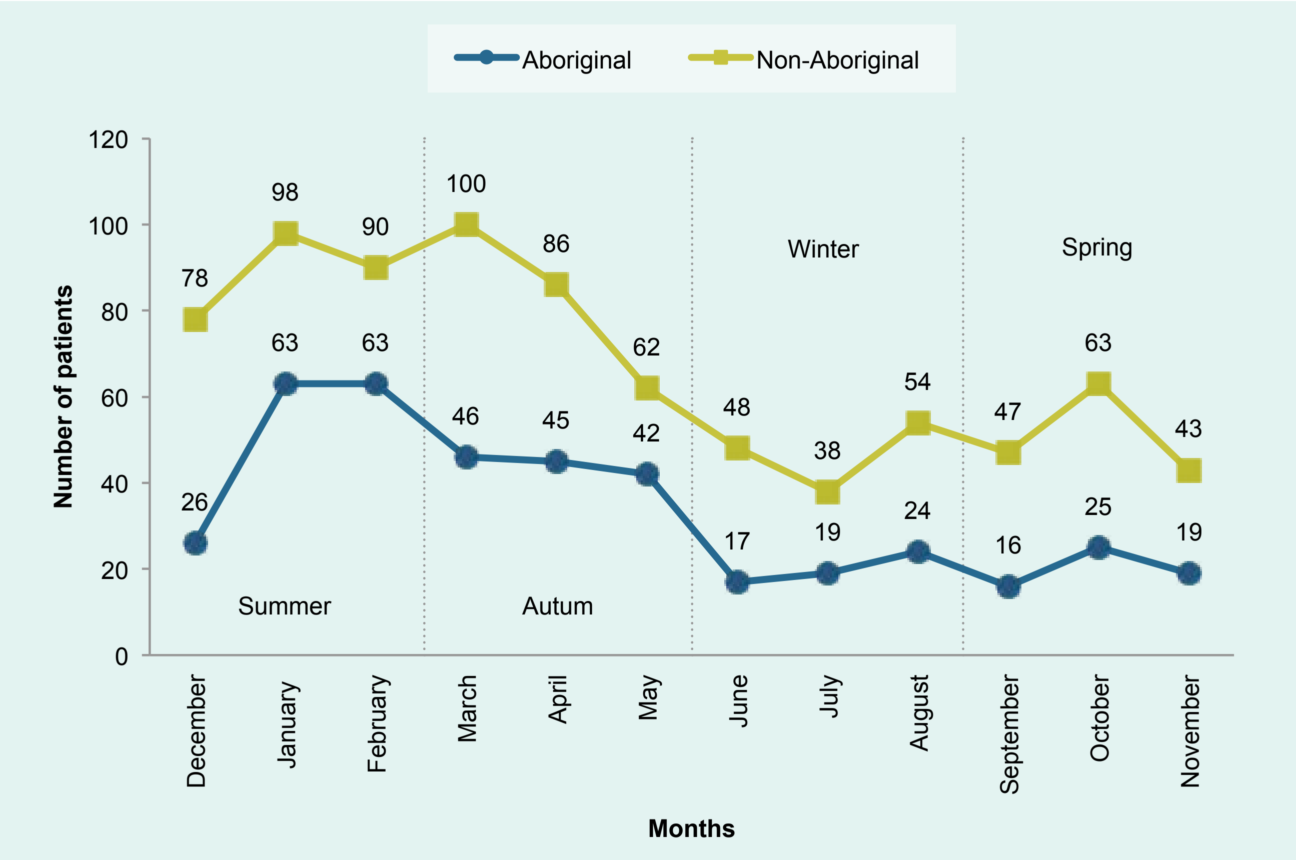


Table 4. **Number and proportion of individuals aged under 20 years with hospital emergency department wound/skin swabs with CA-MRSA by top 12 geographic locations, Hunter New England Local Health District, 2008–2014**

Location (SA2)	Aboriginal		non-Aboriginal	
	n	%	*n*	%
Tamworth – West	66	16.3	25	3.1
Tamworth – East	40	9.9	46	5.7
Armidale	34	8.4	22	2.7
Tamworth – North	25	6.2	20	2.5
Maitland – East	16	4.0	31	3.8
Tamworth Region	15	3.7	39	4.8
Raymond Terrace	11	2.7	47	5.8
Muswellbrook	11	2.7	10	1.2
Kurri Kurri – Abermain	10	2.5	27	3.3
Inverell	9	2.2	12	1.5
Tenterfield	9	2.2	4	0.5
Cessnock	9	2.2	25	3.1
Total top 12 sites	**255**	**63**	**308**	**38**

CA-MRSA surveillance models, coordinating both hospital and community activities at the local and state level have been proposed as a way of providing a more comprehensive epidemiological assessment.[13] Local hospitals, general practitioners and other health facilities would be required to collect data from patients and contacts while state authorities would aggregate and disseminate surveillance reports. The resources required to implement such a system would be significant (personnel, materials, time, storage and transportation) and underreporting may be another limitation.[13] A five-year incidence study of CA-MRSA in remote communities in Canada found high rates of infection with 25% of infections being re-infection. The study concluded that surveillance was important in understanding antibiotic resistance and the changing profile of CA-MRSA.[14] While this debate continues, the surveillance of CA-MRSA in NSW could be improved by adopting a uniform surveillance definition for community association. Surveillance alone will not solve the problem of bacterial skin infections caused by CA-MRSA. Health and other services need to address the contextual factors which cause persistent infection, especially the social determinants,[15] normalization of the problem of bacterial skin infections, transgenerational trauma and access to culturally safe and appropriate PHC.[1]

This study has some limitations. Using passive surveillance through administrative hospital data has not captured all cases. Many people with CA-MRSA use PHC, including Aboriginal Community Controlled Health Services, community health centres and GPs, from which data were not available for inclusion. Data from some hospitals were not included as they did not use AUSLAB or data were not available due to changes in information systems. These limitations imply that the number of people experiencing CA-MRSA is higher than reported here. As our numerators were uncertain, we were unable to either calculate population rates or use statistical methods to compare results between groups or locations that would have provided additional useful data.

CA-MRSA is not notifiable in NSW; however, pathology and hospital administration data can be linked to assist in the estimation of the magnitude and scope of the problem. Implementing routine surveillance requires further consideration in light of the costs and limitations of notification of CA-MRSA. Timely dissemination of these data can assist in service planning, policy development and evaluation. Targeted prevention activities can be designed in collaboration with Aboriginal health services for rural hospital emergency departments before and during peak seasons. This would be particularly valuable in rural and remote areas where, in the absence of adequate, culturally safe PHC, many Aboriginal people utilize hospital emergency departments for management of bacterial skin infections caused by CA-MRSA. Further research using administrative pathology data can be undertaken to better understand the phenotypes and antibiotic sensitivity of CA-MRSA affecting Aboriginal children in NSW. Due to changing patterns of antibiotic resistance, genotyping of regular samples from hospital and community settings would be valuable.

Conflict of Interest

None declared.

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Pulmonary tuberculosis and non-recent immigrants in Japan – some issues for post-entry interventions

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Foreign-born persons are considered one of the high-risk populations for tuberculosis (TB), and numerous studies have discussed the potential role of pre-entry TB screening for immigrants. However, rates of TB disease among immigrants can remain high several years after entry. In Japan, approximately 50% of TB among foreign-born persons occurs among those who have entered Japan more than five years before being diagnosed, i.e. non-recent immigrants. However, little attention has been paid so far to the issue of TB control among the non-recent immigrants. A detailed analysis of the Japan Tuberculosis Surveillance data was therefore conducted to describe the characteristics of TB among non-recent immigrants and discuss policy implications in terms of post-entry interventions in Japan. The main findings were as follows: 1) the proportion of pulmonary TB cases aged 65 years and older was higher among non-recent than recent immigrants (9.8% vs 1.2%); 2) the proportion of those with social risk factors including homelessness and and being on social welfare assistance was higher among non-recent than recent immigrants; and 3) the proportion of those detected via routine screening at school or workplace was significantly lower among non-recent immigrants aged between 25 and 64 than among recent immigrants in the same age group (15.4% vs 28.7%). Our results suggested the need to increase the opportunities for and simultaneously improve the take-up rate of community-based screening for non-recent immigrants.

BACKGROUND

The proportion of tuberculosis (TB) borne by foreign-born persons, especially in low-incidence countries, has been increasing.[1] Several of these countries have adopted screening programmes for immigrants that may take place either before entering the destination country, at entry or post entry.[1] The effectiveness of these programmes has been discussed elsewhere;[2] however, rates of TB disease among immigrants can remain high several years after entry,[3,4] and return and repeated visits to their country of origin may be a significant risk factor for immigrants as well.[5,6] Post-entry intervention is, therefore, also potentially important in considering TB control among foreign-born populations.

Japan is a TB medium-burden country with a notification rate of 14.4 per 100 000 population in 2015.[7] Although the proportion of foreign-born persons among the total cases is relatively small compared to similarly industrialized countries, between 2005 and 2014, it steadily increased by approximately 1.7 times (from 3.5% to 5.8%) and among those aged 20 to 29 by 2.5 times (from 17.8% to 44.1%).[7] It has also been estimated that the TB notification rate per 100 000 population among foreign-born persons increased from 40.7 in 2007 to 56.2 in 2016, in contrast to the decreasing notification rate among the general population.[8] Furthermore, data from the Japan TB Surveillance (JTBS) indicate that approximately 50% of TB among foreign-born persons occurs among those who entered Japan more than five years before being diagnosed.[9] Although discussions have begun regarding the possible impact of pre-entry TB screening if it were introduced in Japan, little attention has been paid so far to the issue of TB control among these non-recent immigrants. Our objective, therefore, was to describe and analyse the characteristics of TB among non-recent immigrants compared with recent immigrants who had entered Japan within five years of being diagnosed and to discuss policy implications in terms of post-entry interventions in Japan.

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Japan Tuberculosis Surveillance

Japan introduced the first nationwide computerized TB surveillance system, the JTBS, in 1987. TB is a notifiable disease, and public health centres (PHCs) are responsible for collecting and entering the data of notified patients to the system. The data are summarized every month and annually and are made available online. Mechanisms to ensure data quality include the system's automatic verification programme as well as regular meetings attended by local staff from hospitals and PHCs. Periodic refresher trainings on data entry are also provided to PHC staff across the nation.[9]

Data regarding the nationality of patients (either Japanese or non-Japanese) were added to the JTBS in 1998. The country name and the timing of entry (either within five years, more than five years or unknown) were added in 2007. In 2012, the category of nationality was changed to country of birth (either Japan-born or foreign-born); for the foreign-born persons, the name of the country and the year of entry are simultaneously collected.

METHODS

We conducted a cross-sectional study whereby aggregated cohort data of pulmonary TB (PTB) cases newly notified to the JTBS between 1 January 2007 and 31 December 2014 were analysed. A TB case was defined as either a person whose biological specimen was positive by smear, culture or other examinations or a person without bacteriological confirmation but active TB was diagnosed by a clinician. A PTB case includes both those exclusively with pulmonary or bronchial infection and those with concomitant extrapulmonary disease. Immigrants were defined as either those patients whose nationality has been recorded as non-Japanese before 2012 or those whose county of birth was foreign-born after 2012. Those whose nationality or country of birth was recorded as unknown were excluded from the analysis (n = 3830, 2007–2014). Non-recent immigrants were defined as those who had entered Japan more than five years before being diagnosed or whose timing of entry was unknown; recent immigrants were those who had entered Japan within five years of being diagnosed. Characteristics of PTB among non-recent immigrants were analysed and compared with the recent immigrants in terms of sex, age groups, countries of birth, job categories, modes of case detection and treatment outcomes. Standardized death rates were calculated using the Japanese population of 1985 as reference. χ^2 tests or Fisher's exact tests were conducted to compare proportions, and Bonferrni correction was applied for multiple comparisons. R version 3.1.3 (R Development Core Team, Vienna, Austria) was used for all statistical analyses.

Ethics

Ethical clearance was deemed not necessary, as the electronic JTBS data do not include case identifiers per the Ethical Guidelines for Epidemiological Research established by the Ministry of Education, Culture, Sports, Science and Technology and Ministry of Health, Labour and Welfare of Japan.

RESULTS

General characteristics

Between 2007 and 2014, a cumulative total of 6211 foreign-born PTB cases were notified; 46.8% (n = 2908) were non-recent and 53.2% (n = 3303) were recent immigrants. General characteristics of the two groups are summarized in **Table 1**. The age distribution was significantly different with a higher proportion of those aged 65 and above among the non-recent than among the recent immigrants (9.8% versus 1.2%). The proportion of females among the non-recent immigrants was significantly greater than that among the recent immigrants (58.0% versus 49.9%, P < 0.001). The overall distribution of cases by country of birth was also significantly different. Furthermore, looking at the country of birth by age groups, the recent immigrants from the People's Republic of China (China) and the Philippines combined contributed approximately 50% of all recent immigrants for all age groups; among the non-recent immigrants, the proportion of those from the Republic of Korea increased with increasing age group. Among those aged 65 and above, those from the Republic of Korea and China contributed approximately 66% of the non-recent immigrants (**Fig. 1**).

Job categories of those aged between 25 and 64 years old were also compared. There was a significant difference in the overall distribution of job categories with a higher proportion of those with no regular income, i.e. unemployed and homemaker, and a lower proportion of high-school, university and college students among the non-recent compared with the recent immigrants (33.0% vs 22.0%, 6.1% vs 21.7%) (**Table 1**).

Table 1. **General characteristics of non-recent and recent immigrants with pulmonary TB, newly notified, 2007–2014**

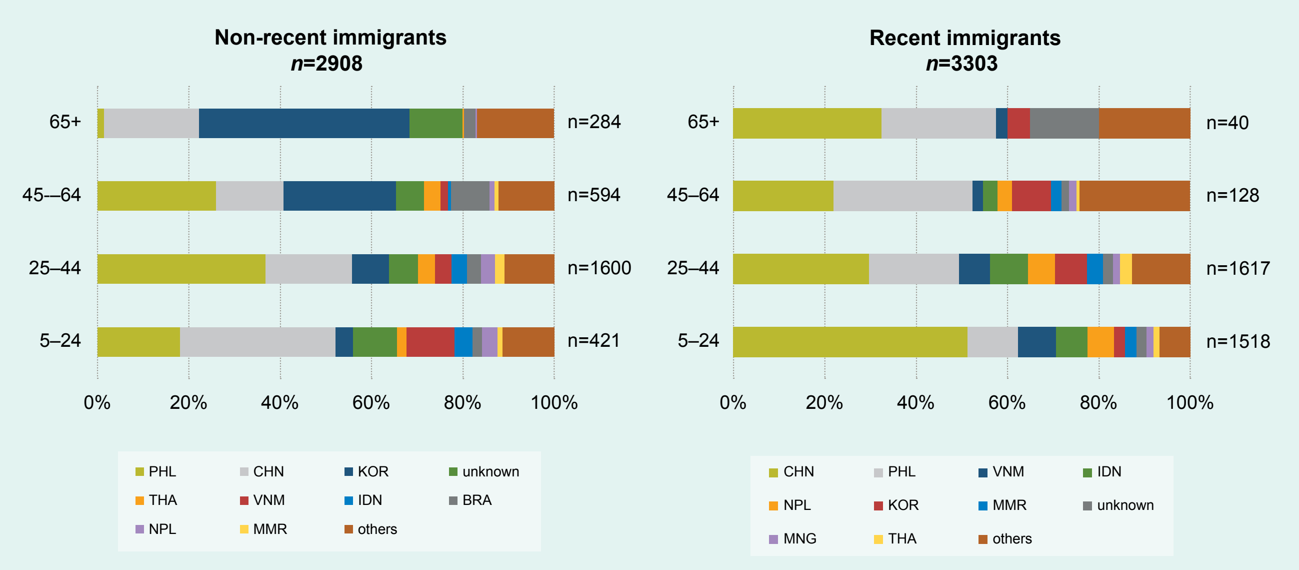
		Non-recent immigrants n	Non-recent immigrants %	Recent immigrants n	Recent immigrants %	p-value
	Total	**2908**	**100.0**	**3303**	**100.0**	
Age group						< 0.001
	5–14	9	0.3	25	0.8	
	15–24	421	14.5	1493	45.2	
	25–44	1600	55.0	1617	49.0	
	45–64	594	20.4	128	3.9	
	65+	284	9.8	40	1.2	
Sex						< 0.001
	Male	1221	42.0	1654	50.1	
	Female	1687	58.0	1649	49.9	
Country of birth						< 0.001
	China	598	20.6	1301	39.4	
	Philippines	827	28.4	544	16.5	
	Republic of Korea	424	14.6	165	5.0	
	Indonesia	76	2.6	247	7.5	
	Viet Nam	113	3.9	241	7.3	
	Nepal	69	2.4	189	5.7	
	Others	801	27.5	616	18.6	
	Total*	**2194**	**100.0**	**1745**	**100.0**	
Job category						< 0.001
	Full-time workers#	829	37.8	631	36.2	
	Unemployed	497	22.7	293	16.8	
	Temporary	297	13.5	256	14.7	
	High-school & university/ college students	134	6.1	379	21.7	
	Homemakers	228	10.4	91	5.2	
	Unknown	115	5.2	44	2.5	
	Self-employed	65	3.0	26	1.5	
	Others	23	1.0	10	0.6	
	Health-care professionals	6	0.3	15	0.9	

Non-recent immigrants: immigrants who had entered Japan more than five years before being diagnosed with TB or whose timing of entry was unknown. Recent immigrants: immigrants who had entered Japan within five years before being diagnosed with TB.

* Total number of immigrants with PTB aged 25 to 64 years old

\# Full-time employed workers, excluding health-care professionals

Fig. 1. **Countries of birth among non-recent and recent immigrants with pulmonary TB, newly notified, by age groups, 2007–2014**



Non-recent immigrants: immigrants who had entered Japan more than five years before being diagnosed with TB or whose timing of entry was unknown. Recent immigrants: immigrants who had entered Japan within five years before being diagnosed with TB.

PHL: Philippines, CHN: China, KOR: Republic of Korea, THA: Thailand, VNM: Viet Nam, IDN: Indonesia, BRA: Brazil, MNG: Mongolia, NPL: Nepal, MMR: Myanmar

Case detection of PTB among non-recent immigrants

Table 2 summarizes the modes of detection of non-recent immigrants with PTB compared with that of recent immigrants among the working-age group (aged 25 to 64) and the elderly (aged 65 and above). In the working-age group, there was a significant difference in the overall distribution of the modes of detection with the proportion of those with TB symptoms detected at medical institutions (64.7% vs 56.2%, $P < 0.001$, with Bonferroni correction) and via health checks as outpatients or inpatients for other diseases (7.6% vs 2.3%, $P < 0.001$, with Bonferroni correction) significantly greater; those detected via routine screening, either at workplace or school, were significantly smaller (15.4% vs 28.7%, $P < 0.001$, with Bonferroni correction) among non-recent than recent immigrants. The odds ratios of non-recent migrants being detected at medical institutions with TB symptoms and via health checks were 1.48 and 3.50, respectively, while the odds ratio of being detected via routine screening was 0.45. No significant difference in the distribution of modes of case detection between non-recent and recent immigrants was observed among those age 65 and above.

Social risk factors of PTB among non-recent immigrants

Table 3 summarizes the social risk factors besides unemployment of non-recent immigrants with PTB compared with that of recent immigrants among the working-age group and the elderly. The proportions of those with a history of homelessness (2.1% vs 0.9%, $P = 0.02$) and those receiving social welfare benefits (8.2% vs 1.3%, $P < 0.001$) were significantly greater among non-recent than recent immigrants with PTB; the same tendency was observed for both age categories.

Treatment outcome of PTB among non-recent immigrants

Table 4 summarizes the treatment outcomes at the end of 12 months of non-recent immigrants with PTB compared with those of recent immigrants. The proportion of those who had died was significantly higher among the non-recent immigrants (3.2% vs 0.3%, $P < 0.001$, with Bonferroni correction); after adjusting for age, the standardized mortality rate ratio was 2.3.

DISCUSSION

Two distinctive issues in TB among the non-recent immigrants were identified in our study: a larger proportion of those aged 65 and above and a smaller proportion of those being detected via routine school and workplace screening among those aged between 25 and 64.

For the first issue, a significantly greater proportion of non-recent than recent immigrants were aged 65 and above (9.8% vs 1.2%), 66% of whom were from the Republic of Korea and China. Several studies have raised the issue of poor socioeconomic and health status of older foreign-born residents in Japan, especially those from Asia, including higher smoking and drinking rates.[10,11] It has also been suggested that higher morbidity and mortality among the older foreign-born residents may to a certain extent be attributable to long years of poor working and living conditions in Japan.[11]

We also found the proportion of those with social risk factors, such as a history of homelessness and those receiving social welfare benefits, were significantly higher among non-recent than recent immigrants. Among those aged 65 and above, the difference was even more evident with the proportion of those with a homeless history being 4.2% and 0.0% and of those receiving social welfare benefits being 26.3% and 2.6% among the non-recent and recent immigrants, respectively. These socioeconomic factors have been reported to be associated with poor treatment outcomes, including death and prolonged treatment.[12]

The second issue concerned the proportion of those detected via routine screening at school or workplace, which was significantly smaller among non-recent than recent immigrants aged between 25 and 64 (15.4% vs 28.7%). In Japan, under the Infectious Diseases Control Law, routine TB screening is mandatory for school students, teachers and employees of selected institutions including hospitals, social welfare facilities and nursing homes for the elderly. For full-time employees aged 40 and above in other industries, chest X-rays are included in the annual workplace health check per the Industrial Safety and Health Law. From the job categories of the JTBS, it is reasonable to assume that that full-time workers; health-care professionals; and high-school, university and college students are eligible for those routine screening. According to our results, of the 2194

Table 2. **Modes of detection among non-recent and recent immigrants with pulmonary TB, newly notified, by age group, 2007–2014**

Mode of detection	Aged 25–64					Aged 65+				
	Non-recent immigrants		Recent immigrants			Non-recent immigrants		Recent immigrants		
	n	%	n	%	p-value	n	%	n	%	p-value
Total	**2194**	**100.0**	**1745**	**100.0**	< 0.001	**284**	**100.0**	**40**	**100.0**	0.860
Routine school and workplace screening	338	15.4	503	28.7		3	1.1	1	2.5	
Routine community-based screening	37	1.7	18	1.0		4	1.4	1	2.5	
Individual health check	56	2.6	60	3.4		3	1.1	1	2.5	
Contact investigation	109	5.0	79	4.5		3	1.1	0	0.0	
Other mass investigation	18	0.8	35	2.0		1	0.4	0	0.0	
Hospital visit with TB symptoms	1420	64.7	981	56.2		178	62.7	29	72.5	
Health check as out- or inpatient	166	7.6	40	2.3		86	30.3	8	20.0	
Others	17	0.8	13	0.7		5	1.8	0	0.0	
Unknown	21	1.0	13	0.7		1	0.4	0	0.0	
During TB follow-up	12	0.5	3	0.2		0	0.0	0	0.0	

Non-recent immigrants: those who had entered Japan more than five years before being diagnosed with TB or whose timing of entry was unknown. Recent immigrants: those who had entered Japan within five years before being diagnosed with TB.

Table 3. **Social risk factors of non-recent and recent immigrants with pulmonary TB, newly notified, 2007–2014**

		Non-recent immigrants		Recent immigrants		
		n	%	n	%	p-value
All ages	History of homelessness*	24/1170	2.1	6/869	0.9	0.020
	Receiving social welfare benefit*	193/2361	8.2	23/1723	1.3	<0.001
Aged 25–64	History of homelessness*	18/1028	1.8	6/855	0.7	0.070
	Receiving social welfare benefit*	120/2083	5.8	22/1685	1.3	<0.001
Aged 65+	History of homelessness*	6/142	4.2	0/14	0.0	NA
	Receiving social welfare benefit*	73/278	26.3	1/38	2.6	0.001

Non-recent immigrants: those who had entered Japan more than five years before being diagnosed with TB or whose timing of entry was unknown. Recent immigrants: those who had entered Japan within five years before being diagnosed with TB.

* The denominators do not necessarily equal to the total number of non-recent and recent immigrants due to missing data.

Table 4. **Treatment outcomes of non-recent and recent immigrants with pulmonary TB, newly notified, 2007–2014**

	Non-recent immigrants		Recent immigrants	
	n	%	n	%
Total	**2908**	**100.0**	**3303**	**100.0**
Success	1743	59.9	1857	56.2
Died	93	3.2	10	0.3
Lost to follow-up	215	7.4	242	7.3
Treatment failed	16	0.6	17	0.5
Still on treatment	198	6.8	185	5.6
Unevaluated	366	12.6	404	12.2
Transferred out	277	9.5	588	17.8

Non-recent immigrants: those who had entered Japan more than five years before being diagnosed with TB or whose timing of entry was unknown. Recent immigrants: those who had entered Japan within five years before being diagnosed with TB.

non-recent immigrants aged between 25 and 64, the proportion of those who belonged to these job categories was lower at 44.2% (969/2194) as compared with 58.7% (1025/1745) among the recent immigrants.

On the other hand, screening opportunities for working-age immigrants who are unemployed, self-employed or homeworkers, including 36% (790/2194) of non-recent immigrants aged between 25 and 64, are limited to ad hoc TB screening campaigns organized by local authorities and nongovernmental organizations for the general community and some specifically targeting foreign residents. Although reports are limited, the take-up of community-based screenings by foreign residents appears to be low due to various barriers including language, geographical distance, lack of information and economic difficulties.[13]

Analysis of the TB surveillance data indicates that the proportion of sputum smear-positive PTB cases detected via routine screening has constantly been smaller than that of those detected in hospitals while being hospitalized for other diseases or while seeing a doctor for other diseases (25.6% vs 62.1% in 2015).[14] Another study has similarly reported smaller proportions of positive sputum smears and cavity disease among those patients with professions that are more likely to be detected via routine workplace screening.[15] This suggests the possibility that non-recent immigrants, who have fewer opportunities for routine school and workplace screening, are more likely to be detected with a progressed disease and thereby are at a higher risk of infecting others.

Increasing the opportunities for and improving the take-up rate of community-based screenings for non-recent immigrants may not only contribute to early detection of TB, prevention of secondary infection and better treatment outcome but also may provide improved general health, especially for the elderly immigrants. Further studies are needed to assess the cost–effectiveness of possible different routine screening programmes for those who are not eligible for workplace and school-based screenings.

Limitations

The study is not without limitations. First, as this was a cross-sectional study in design, we merely compared the characteristics between non-recent and recent immigrants, and we could not determine whether the status of being a non-recent immigrant was a risk factor for TB. Second, the timing of entry was only dichotomized in our analysis – within five years and more than five years. This was due to the fact that the year of entry was collected only after 2012; before that, the timing of entry to Japan had only been collected as within five years, more than five years or year of entry unknown. As we had placed a greater emphasis on increasing the number of cases for analysis, the study period was set from 2007. Nonetheless, a recently published report suggests that of the non-recent immigrants approximately 40% entered between five and nine years and 60% more than 10 years before being diagnosed with TB.[8] Third, the general TB screening policy has undergone some changes in the recent years – for example, since 2010, a chest X-ray is no longer mandatory in the annual routine workplace screening for those aged 40 and below. The extent to which such a change affects the epidemiology of foreign-born TB remains to be investigated.

CONCLUSIONS

The demographic and socioeconomic background of pulmonary TB among non-recent immigrants are distinctively different from that of recent immigrants. The former, being more integrated into the Japanese society, may be more invisible and hard to reach than recent immigrants. Despite being integrated, they often fail to benefit from TB programmes targeting the obvious foreign-born population in Japan such as workplace and school-based TB screening. An integrated approach, including a community-based comprehensive health check, may be necessary as part of the greater effort to control TB among the foreign-born population in Japan.

Conflicts of interest

None declared.

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Trends in adult chlamydia and gonorrhoea prevalence, incidence and urethral discharge case reporting in Mongolia from 1995 to 2016 – estimates using the Spectrum-STI model

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Objective: To estimate Mongolia's prevalence and incidence trends of gonorrhoea and chlamydia in women and men 15–49 years old to inform control of STIs and HIV, a national health sector priority.

Methods: We applied the Spectrum-STI estimation model, fitting data from two national population surveys (2001 and 2008) and from routine gonorrhoea screening of pregnant women in antenatal care (1997 to 2016) adjusted for diagnostic test performance, male/female differences and missing high-risk populations. Prevalence and incidence estimates were then used to assess completeness of national case reporting.

Results: Gonorrhoea prevalence was estimated at 3.3% (95% confidence interval, 1.6–3.9%) in women and 2.9% (1.6–4.1%) in men in 2016; chlamydia prevalence levels were 19.5% (17.3–21.9%) and 15.6% (10.0–21.2%), respectively. Corresponding new incident cases in women and men in 2016 totalled 60 334 (36 147 to 121 933) and 76 893 (35 639 to 254 913) for gonorrhoea and 131 306 (84 232 to 254 316) and 148 162 (71 885 to 462 588) for chlamydia. Gonorrhoea and chlamydia prevalence declined by an estimated 33% and 11%, respectively from 2001 to 2016.

Comparing numbers of symptomatic and treated cases estimated by Spectrum with gonorrhoea case reports suggests that 15% of symptomatic treated gonorrhoea cases were reported in 2016; only a minority of chlamydia episodes were reported as male urethral discharge cases.

Discussion: Gonorrhoea and chlamydia prevalence are estimated to have declined in Mongolia during the early 2000s, possibly associated with syndromic management in primary care facilities and improving treatment coverage since 2001 and scale up of HIV/STI prevention interventions since 2003. However, prevalence remains high with most gonorrhoea and chlamydia cases not treated or recorded in the public health system.

Control of sexually transmitted infections (STIs) and HIV is a health sector priority in Mongolia. Since 2001, syndromic case management is implemented in primary care facilities that lack capacity for laboratory diagnosis. Prevention services targeted at high-risk groups have been intensified since 2003 with support from the Global Fund to Fight AIDS, Tuberculosis and Malaria.[1] In Mongolia, laboratory-diagnosed syphilis, gonorrhoea and trichomoniasis, as well as syndromically diagnosed male urethral discharge (UD) and genital ulcer disease from health facilities not doing laboratory diagnosis, are reportable; approximately 15 000 new STI cases are registered annually.[2–5] However, the true burden is believed to be higher due to undiagnosed and untreated cases, cases treated but not reported through private-sector facilities and those self-treated through pharmacies.[6–8]

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Syphilis surveillance draws on periodic serological surveys and routine, near-universal screening among pregnant women attending antenatal care (ANC). For gonorrhoea and chlamydia, however, no such systematic measurement is in place.

In 2017 Mongolia, with support from the World Health Organization (WHO) and Avenir Health, estimated its adult prevalence trends for chlamydia and gonorrhoea using the Spectrum-STI model[9] to inform strategic planning for its STI response and strengthen its STI surveillance system.

The Spectrum-STI tool estimates trends in adult prevalence and incidence of STIs at the national level using data from routine STI surveillance and population-based surveys.[9]

This article presents Spectrum estimates of adult prevalence and incidence of gonorrhoea and chlamydia in Mongolia from 1995 to 2016 using prevalence survey data. Estimated male gonorrhoea and chlamydia case numbers were compared to UD case reports to estimate treatment coverage and reporting completeness. This study represents the first national-level STI trend estimation in an Asian country using an internationally agreed approach and assumptions.

METHODS

Overview

The Spectrum-STI tool (http://avenirhealth.org/software-spectrum.php)[9] estimated prevalence and incidence of gonorrhoea and chlamydia in adults aged 15–49 years. Data and assumptions were reviewed at a three-day technical workshop held in Mongolia in February 2017. Participants included representatives of the Ministry of Health, HIV/AIDS and Maternal and Child Health programmes, the central reference laboratory and partners supporting or implementing the national HIV/STI response. Mongolia-specific parameter values and results from the base-case analysis were agreed at the workshop and are summarized here. Spectrum default parameter values have been described elsewhere.[9]

Prevalence estimation

National prevalence levels for adult women were estimated over time as a moving average through all data points.

For both STIs, prevalence data were identified from studies conducted between 1995 and 2016 in representative general adult populations. For Mongolia, this included pregnant women attending ANC; no prevalence data were identified from any other low-risk populations.

Prevalence data from each study were adjusted for sensitivity and specificity of diagnostic tests used[10–12] (Supplemental Digital Content (SDC) 1). For gonorrhoea the national data from routine screening of women attending ANC (SDC2) used culture or Gram stain on cervical or vaginal swabs; sensitivity of these tests was set at 35% to reflect challenges in testing in routine care settings.

Each prevalence data point was adjusted upward by 10% to account for the contribution of higher-risk populations.[10]

National sample surveys were assigned a weight of 100% (the maximum, given that these should be nationally representative). Routine screening data were assigned a 40% weight, as agreed at the national workshop, as these were not nationwide or systematically sampled. Since the 40% value was somewhat arbitrary, we present estimates using different weights as sensitivity analysis.

Since no prevalence data were available for men, male prevalence was inferred from female estimates by applying a time-constant male-to-female prevalence ratio of 0.86 (range 0.58–1.15) for gonorrhoea and 0.80 (range 0.53–1.07) for chlamydia with uncertainty bounds incorporating both uncertainty in female prevalence and in the male-to-female ratio.[10]

The 95% uncertainty or confidence intervals were generated to account for binomial sampling variability in prevalence observed in the data and modelling error.[9] Test-adjusted prevalence rates were simulated (in 10 000 replications) following β distributions to which we added random terms in the logit scale; the random terms were sampled from a uniform distribution on residuals obtained after fitting the original data set.

Incidence estimation and STI episode durations

Incidence was estimated by dividing estimated prevalence by an assumed average duration of infection.[13] The 95% confidence intervals on incidence reflect uncertainty in both the underlying prevalence (estimated by bootstrap) and in the duration of infection set at ± 50%.

STI episode durations were as assumed in the WHO 2012 global and regional estimates.[10] In the WHO estimates, the region that Mongolia is a member of was assumed to have intermediate treatment coverage.[10] However, following discussions at the national workshop, and lacking national population-based data about STI treatment coverage, we decided to use longer STI durations, reflecting low treatment coverage.

Assuming 35% treatment coverage of symptomatic gonorrhoea and chlamydia episodes in men and 22.5% in women,[10,14] we calculated average durations of gonorrhoea and chlamydia episodes weighted between the fractions treated and untreated (SDC3). The average duration in men was 0.32 years for gonorrhoea and 0.86 years for chlamydia and 0.47 years for gonorrhoea and 1.22 years for chlamydia in women (SDC3).

STI case reporting completeness

An expected case load for UD was estimated from Spectrum-estimated case incidence, assuming that 64% of gonorrhoea cases and 14% of chlamydia cases are symptomatic and 35% of these are treated[10] (SDC3). The Spectrum estimates of symptomatic gonorrhoea cases and UD cases were then compared to national-level case reports for laboratory-diagnosed gonorrhoea and UD (a non-overlapping set of cases without laboratory diagnosis) from 1995 to 2016 collected by the National Center for Communicable Diseases[15,16] (SDC4) to estimate reporting completeness.

Sensitivity analysis

Univariate sensitivity analyses assessed the sensitivity of 2016 estimates to key assumptions and Mongolia-specific input data and assumptions: the weight of routine ANC screening data points; gonorrhoea relative to national ANC surveys; the sensitivity of culture and wet-mount in routine ANC gonorrhoea screening; the gonorrhoea prevalence data used; the decline rate in chlamydia (based on few data points) relative to that in gonorrhoea (based on a longer and more continuous time series); and (as determinant of reporting completeness) the gonorrhoea incidence rate in men 50–64 years. More general and global assumptions of the Spectrum methodology were addressed elsewhere.[9]

RESULTS

Gonorrhoea and chlamydia prevalence

Two national surveys were identified from the general population; both measured gonorrhoea and chlamydia in pregnant women attending ANC in 2001[17] and 2008[18] (SDC2, **Fig. 1A & B**). For gonorrhoea, national prevalence data were also available for 1997 to 2016 from routine screening of women attending ANC.

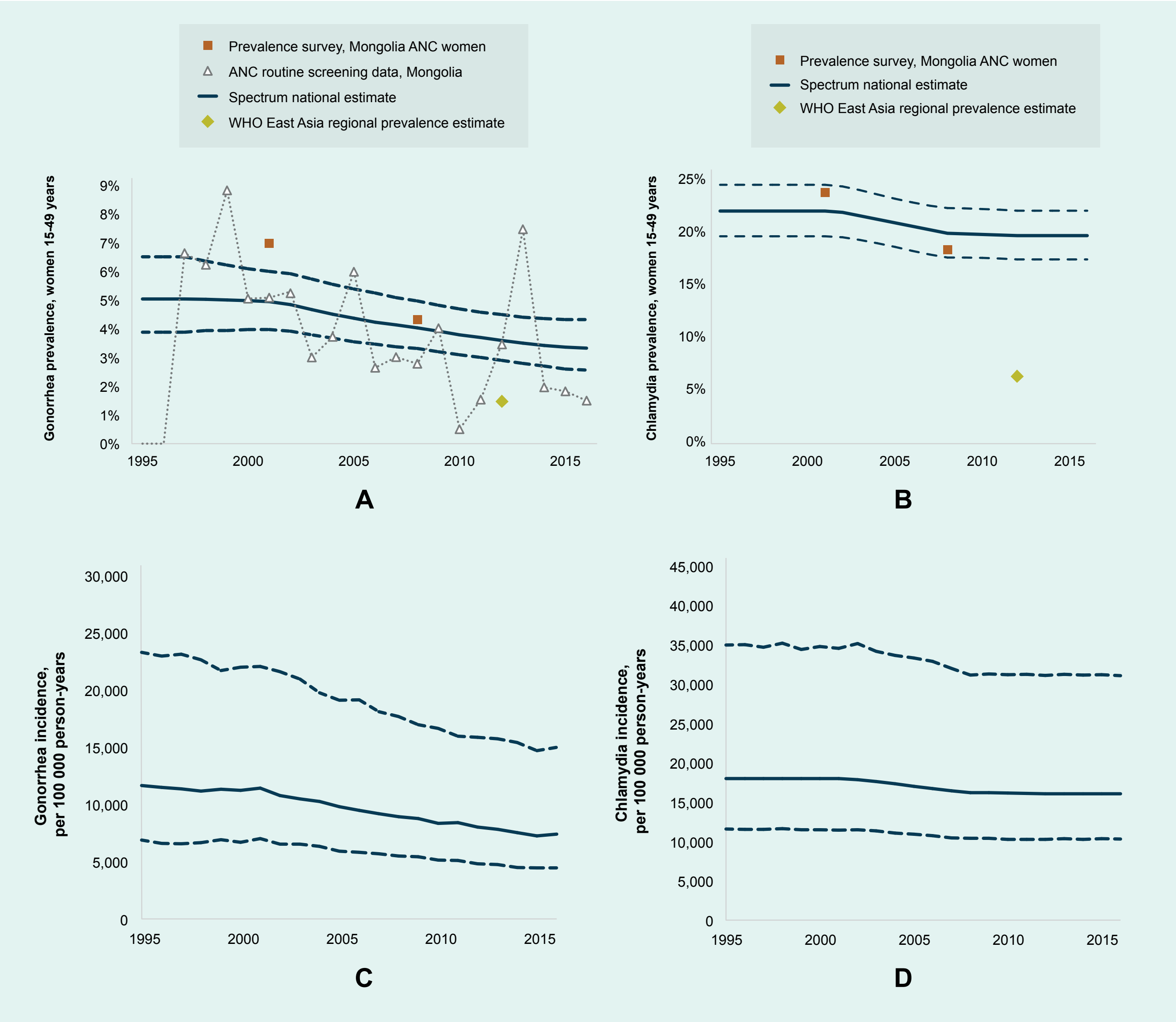
For gonorrhoea in women, Spectrum estimated a stable 5.0% prevalence from 1995 to 2001 followed by a decline to 3.3% (95% confidence interval, 1.6–3.9%) in 2016 (**Fig. 1A**). For chlamydia, estimated prevalence fell from 2001 (the year of the first survey) and 2008 (the year of the second and final survey), and the model thereafter assumed stable prevalence. In 2000–2001 chlamydia prevalence was 21.9% (19.5–24.4%) and in 2016 19.6% (17.3–21.9%, **Fig. 1B**). From 2001 to 2016, gonorrhoea and chlamydia prevalence declined by 33% and 11%, respectively.

No data were identified for men; therefore, male gonorrhoea and chlamydia estimates were based on female estimates (see Methods). In men, gonorrhoea prevalence was estimated at 4.3% between 1995 and 2001 and falling to 2.9% (1.6–4.1%) by 2016. For chlamydia, prevalence was estimated at 17.5% (15.6–19.5%) in 2000 and 15.6% (10.0–21.2%) in 2016.

Gonorrhoea and chlamydia incidence

Fig. 1C & D show estimated trends in gonorrhoea and chlamydia incidence. In 2016, Spectrum estimated 60 334 (36 147–121 933) and 76 893 (35 639 to 254 913) new gonorrhoea cases in women and men aged 15–49 years, respectively and 131 306 (84 232 to 254 316) new cases of chlamydia in women and 148 162 (71 885 to 462 588) in men (**Table 1**). For both STIs, incidence was higher in men than in women despite higher prevalence in women, reflecting longer average duration of both infections in women than in men.

Fig. 1. **Prevalence of (A) gonorrhoea and (B) chlamydia and incidence rate of (C) gonorrhoea and (D) chlamydia in women 15–49 years in Mongolia**



Prevalence data are shown after adjustments for diagnostic test performance (including routine ANC screening-based gonorrhoea prevalence levels adjusted for 35% estimated sensitivity of culture and wet-mount, see SDC1), and missing high-risk populations (SDC2), as described in Methods. WHO regional prevalence estimates for East Asia in 2012[10] are shown for comparison, but were not used in statistical estimation for Mongolia. Solid lines are best estimates: dotted lines are 95% Confidence Intervals. Data and prevalence estimates shown are for women 15–49 years.

Gonorrhoea's estimated case incidence rate declined in women from 11 650/100 000 in 1995 to 7409 in 2016 and in men from 13 991 to 9316 (**Fig. 1C**). Over this period, chlamydia incidence fell from 17 953 to 16 023/100 000 in women and from 20 374 to 18 184/100 000 in men (**Fig. 1D**). For chlamydia, annual incident case numbers increased slightly from 1995 to 2002, a period when prevalence (**Fig. 1B**) and incidence rates (**Fig. 1D**) were estimated to have been stable; population growth implied slightly increasing annual case numbers (**Fig. 2B**). From 2002 to 2016, annual chlamydia cases were stable (**Fig. 2B**), reflecting the counterbalancing effects of declining prevalence and incidence rates (**Fig. 1B and 1D**) and population growth.

Gonorrhoea reporting completeness and treatment coverage

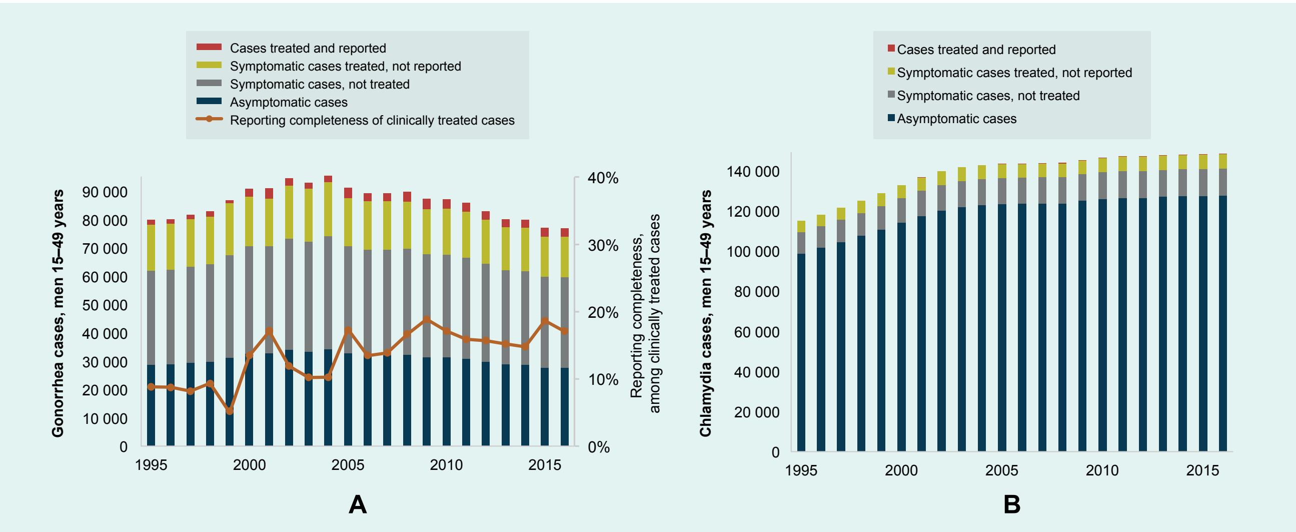
Fig. 2A shows Spectrum-estimated incident gonorrhoea cases in men from 1995 to 2016 split into episodes symptomatic and asymptomatic, treated and untreated and reported and unreported. Comparing national gonorrhoea case reports (SDC4) with Spectrum estimates of the number of men who were symptomatic and

Table 1. **Spectrum-estimated prevalence and incidence rate (per 100 000 person-years) of gonorrhoea and chlamydia in women and men 15–49 years, Mongolia in 2016**

STI	Metric	Women		Men	
		Point estimate	95% CI	Point estimate	95% CI
Gonorrhoea	Prevalence	3.3%	1.6–3.9%	2.9%	1.6–4.1%
	Incidence rate per 100 000 total adult population	7409	4439–14 974	9316	4318–14,314
	New incident cases, 15–49 years	60 334	36 147–121 933	76 893	35 639–254 913
Chlamydia	Prevalence	19.5%	17.3–21.9%	15.6%	10.0–21.2%
	Incidence rate per 100 000 total adult population	16 023	10 279–31 034	18 184	8823–27 546
	New incident cases, 15–49 years	131 306	84 232–254 316	148 162	71 885–462 588

95% CI = 95% confidence interval

Fig. 2. **Spectrum-estimated incident gonorrhoea and chlamydia cases in men 15–49 years by treatment and reporting status, Mongolia**



Reporting completeness is expressed as the reported gonorrhoea plus urethral discharge cases, relative to estimated incident gonorrhoea, chlamydia and other UD cases treated in clinics for which the calculation is detailed for year 2016 in **Table 2**.

treated, reporting completeness for gonorrhoea cases treated in clinics improved from 8% in 1997 to 15% in 2016 (**Table 2**).

Chlamydia treatment and reporting coverage, 1995–2016

Of the Spectrum-estimated 148 162 chlamydia cases in men aged 15–49 years in 2016, some 20 743 were expected to be symptomatic of which 7260 would have been treated (**Table 2** and **Fig. 2B**).

Laboratory diagnosis is not commonly practiced for chlamydia and chlamydia is not reportable; chlamydia cases in men should instead be reported as UD cases per the syndromic management policy. However, reported UD cases ranged between just 342 and 1648 in 2001 and in 2005 to 2015; years 2002 to 2004 were missing.

In 2016, of population-level estimated incident gonorrhoea plus chlamydia cases (76 893 gonorrhoea plus 148 162 chlamydia; total 225 055), the reported 2625 gonorrhoea cases plus 606 UD cases covered only 1.4 %. This calculation assumed all UD cases were due to gonorrhoea and/or chlamydia; in reality, not all UD cases are caused by gonorrhoea or chlamydia (SDC5), thus these reporting completeness estimates are optimistic. Most unreported chlamydia cases were asymptomatic

Table 2. **Incident cases of gonorrhoea, chlamydia and urethral discharge and the subset who are treated and reported in men 15–49 years in Mongolia, 2016**

	Gonorrhoea	Chlamydia	Comment & source
New incident cases (Spectrum estimate)	76 893	148 162	Spectrum-STI estimate
Gonorrhoea or chlamydia cases developing UD/ symptoms (Spectrum estimate)	49 212	20 743	Assuming 64% of male gonorrhoea[10] and 14% of male chlamydia cases develop symptoms[13,19] & SDC3
UD cases due to gonorrhoea or chlamydia treated in a clinic (Spectrum estimate)	17 224	7260	Assuming 35% of gonorrhoeal & chlamydial UD cases seek and get treatment[10] & SDC3
Actual case reports	Gonorrhoea: 2625; UD (unknown etiology): 606		Mongolia National Center for Communicable Diseases
Gonorrhoea reporting completeness among gonorrhoea cases treated in clinics	15%		= 2625/17 224
Reported cases relative to population-level incidence – gonorrhoea and chlamydia	1.4%		= (2625 + 606)/(76 893 + 148 162)

UD = urethral discharge

(69% in 2016, **Fig. 2B**), symptomatic but not treated (20% at 2016) or treated but not reported (10% in 2016).

Sensitivity analysis

Excluding routine ANC data from estimations, increased estimated gonorrhoea rates in 2016 (4.2% instead of 2.9% in men) and reporting completeness of male gonorrhoea cases was correspondingly lower. Conversely, when ANC routine data points were given an increased weight, namely the same weight as each ANC survey, the estimated gonorrhoea prevalence and incidence fell slightly (male prevalence 2.7% instead of 2.9%) and gonorrhoea reporting completeness increased.

Gonorrhoea results were also very responsive to the assumed sensitivity of culture in routine ANC-based screening: when varying the sensitivity between 25–75.7%[9] male prevalence in 2016 varied from 1.5–3.9% and gonorrhoea reporting completeness from 11–29%.

Had gonorrhoea prevalence in Mongolian men in 2016 been as low as 1.28% (the WHO 2012 estimate for men in East Asia) instead of our national estimate of 2.9%, then gonorrhoea reporting completeness would have been 34% instead of 15% completeness.

Our analysis assumed that national case report was for men 15–49 years old. In fact, some reported cases will have been from older men. Estimated gonorrhoea reporting completeness would be 13% instead of the best estimate of 15% if we assume additional gonorrhoea and chlamydia cases to occur in men above 49 years at a rate equal to men 15–49 years.

Finally, Spectrum estimates for chlamydia were based on two national surveys (2001 and 2008) and it was assumed that prevalence was constant after 2008. If chlamydia prevalence, however, fell between 2008 and 2016 at the same rate as gonorrhoea prevalence fell, the chlamydia prevalence in 2016 would have been 13% rather than 15.6%.

DISCUSSION

Prevalence trend estimations for Mongolia generated using the Spectrum-STI model and data from ANC-based surveys and routine screening indicate that prevalence of both chlamydia and gonorrhoea fell from 2001 to 2016. However, prevalence levels remained extremely high: for both STIs, Mongolia's estimated prevalence in 2012 was considerably above WHO estimates for the East Asia and central Asia regions[10] (**Fig. 1A & B**).

Chlamydia was estimated five times more prevalent than gonorrhoea as shown in the WHO 2012 estimates globally and for Asia.[10] From 2001 to 2016, the estimated decline was stronger for gonorrhoea than for chlamydia, reflecting the gonorrhoea decline observed in ANC routine testing. We cannot exclude that for chlamydia the decline from 2001 to 2008 also continued after 2008 (see **Table 3**); however, there are no data

Table 3. **Sensitivity analysis – effect of varying (selected) assumptions and values on national estimates of gonorrhoea and chlamydia prevalence and incidence and the estimated reporting completeness for symptomatic treated gonorrhoea in Mongolian men 15–49 years, in 2016**

Parameter	Default assumption	Alternative assumption		Prevalence		Incidence per 100 000		Gonorrhea case reporting completeness
		Lower	Upper	Gonorrhoea	Chlamydia	Gonorrhoea	Chlamydia	
Best/default estimate				**2.9%**	**15.6%**	**9316**	**18 184**	**15.2%**
Weight of routine ANC screening data points, gonorrhoea, relative to national ANC surveys	40%	0%		4.2%	As default	13 735	As default	10%
			100%	2.7%	As default	8724	As default	16%
Sensitivity of culture and wet-mount, in routine ANC gonorrhoea screening	35%	25%		3.9%	As default	12 622	As default	11%
			75.7%[9]	1.5%	As default	4841	As default	29%
Gonorrhoea prevalence as WHO's East Asia regional estimate of 2012[10]	Fitted to Mongolia data			1.28%	As default	4172	As default	34%
Chlamydia prevalence: decline from 2008–2016 proportional to the estimated prevalence decline over 2008–2016 in gonorrhoea	Constant from 2008–2016			As default	13.0%	As default	15 138	As default
Gonorrhoea incidence rate in men 50–64 years	0		Same as at 15–49 years	As default	As default	As default	As default	13%[1]

post-2008 to establish this. Conversely, the estimated chlamydia decline from 2001 to 2008, based on two surveys, is our best estimate but is not as robust as a trend estimate based on multiple data points might have been. Estimates of chlamydia rates and especially their time trend are therefore less certain than for gonorrhoea.

The declines in gonorrhoea and chlamydia prevalence are attributable to several factors including the expanded HIV/STI response and scale-up of (Global Fund-supported) HIV/STI prevention interventions including outreach services with communication, counselling and HIV and STI testing for key groups since 2003.[1] The declines are in line with Spectrum estimations for syphilis in ANC women.[20]

Declining prevalence of both gonorrhoea and chlamydia based on ANC data contrasts with stable or possibly increasing gonorrhoea and chlamydia prevalence in female sex workers (FSW) in Ulaanbaatar sampled through Integrated Bio-Behavioural Surveillance; FSW gonorrhoea prevalence increased from 13.6% in 2002[21,22] to 15.6% in 2009[23] and from 19.3% to 24.5% for chlamydia. This trend may be a true increase or reflect that in 2009 a higher-risk FSW population was sampled.

While gonorrhoea is the predominant cause of UD cases seen in clinics,[15,16] at the population level the prevalence, incidence and case numbers are much higher for chlamydia. Still large numbers of gonorrhoea and especially chlamydia cases are not treated because many infections in both men and women do not cause symptoms and because over half of symptomatic chlamydia-infected adults do not access treatment.

Comparison of reported male gonorrhoea case numbers with Spectrum-estimated incident cases suggests that in 2016 15% of male symptomatic gonorrhoea cases were treated and reported through public sector providers. Estimated reporting completeness improved after 2001 (8%), coinciding with Mongolia's phased roll-out of syndromic STI treatment from a WHO-supported pilot in 2001[1] to nationwide implementation in 2005.[24,25] In Spectrum simulations, treatment rates were assumed constant over time. If, however, treatment coverage improved then annual numbers of new cases (for a given prevalence) may have been higher and reporting completeness lower. The low reporting completeness highlights the need to strengthen Mongolia's national reporting system and ensure it covers both public and private providers.[8] National surveys in 2010 and 2014 found that up to half of self-reported STI treatments were in the private sector (including purchases from pharmacies),[14,26] yet only 9% of reported cases were from private clinics in 2015.[24]

Despite recent declines, Mongolia has STI rates higher than neighbouring countries. This probably reflects persistent poor coverage of effective STI treatment by qualified providers. The high STI rates constitute a persistent risk factor for the possible future spread of HIV.[27]

Limitations

The estimations are limited by the quality and quantity of prevalence data, modelling assumptions and assumptions made when data was lacking.[9] For prevalence estimation, uncertain assumptions include that all prevalence data were from ANC women who may (as for HIV) not be representative for non-ANC non-pregnant women.[28] Uncertainties particularly affected results for men (based on female estimates, applying a global fixed male-to-female prevalence ratio) and results for chlamydia (with less national data than gonorrhoea).

Incidence estimates depended on treatment coverage and assumed durations of treated and untreated infections for which longitudinal data are lacking. Assumed proportions of episodes that become symptomatic were calibrated on WHO estimates for the East Asia region[10] not on Mongolia-specific data. Proportions of symptomatic episodes that get treated were also taken from regional-level WHO assumptions[10] where we situated Mongolia as a country with low treatment coverage, an assumption we could not validate against population-based local data.

Finally, the assessment of gonorrhoea and UD case reporting completeness required additional assumptions, most of which were global rather than Mongolia-specific.

Implications for surveillance and programmatic response

The last national STI survey in Mongolia was conducted in 2008 in ANC women, and as of 2017 no survey has measured STI prevalence levels in low-risk men. Mongolia would benefit from regular population-based prevalence measurements looking at multiple STIs in low-risk men and women. These do not need to be large surveys but should be carefully designed to identify trends over time. Opportunities may be developed for tagging affordable sentinel STI screening onto existing data collection platforms. For example, screening and treatment for chlamydia in adolescents, as recommended in the WHO global STI strategy 2016–2021,[29] may yield useful data but is as yet not implemented in Mongolia. Reliable monitoring of both STIs would, furthermore, benefit from strengthening the national reporting system and expanding it to track cases treated in private-sector services, including self-treatment with drugs dispensed by pharmacies.

Our analyses confirm challenges Mongolia faces with STI case reporting; with access to laboratory facilities for diagnosis, which is largely limited to Ulaanbaatar serving just half of the national population;[3,7,8] and with adherence to syndrome-based case reporting. At present, Mongolia reports negligible numbers of UD cases because most providers do not follow the syndromic approach by which STI patients would get recorded by syndrome whether or not subsequently an etiological diagnosis is established. More consistent implementation of the syndromic approach for both treatment and reporting may improve completeness of treatment (avoiding loss of patients between initial syndromic diagnoses, referral to the laboratory, and waiting time for diagnosis and referral for treatment) as well as case reporting to become more usable for surveillance and planning. Additionally, reporting from pharmacies of clients presenting with UD symptoms might support surveillance. However, self-treatment with over-the-counter drugs should not be encouraged as a treatment policy due to risks of spreading antimicrobial resistance among gonococcal isolates.[30]

In conclusion, model-based estimations based on prevalence surveys suggest that gonorrhoea and chlamydia have declined in Mongolia but remain high. The high STI rates, much of which remains undiagnosed and untreated, bring a substantial burden of sequelae including infertility, pelvic inflammatory disease and ectopic pregnancy; they are a behavioural marker and biomedical cofactor for HIV transmission.

These results, and the wide confidence intervals around most estimates, argue for improved data input though periodic prevalence surveys beyond key populations. Our findings also highlight a largely hidden burden of untreated chlamydia that merits intensification of control efforts beyond routine clinical services.

Screening should be intensified in primary care settings, among key populations, within antenatal care and for youth, e.g. via school-based clinics. New diagnostic and delivery approaches and affordable point-of-care tests[29] should facilitate clinic-based and non-clinic-based screening thus improving treatment coverage and surveillance and reducing disease burden.

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