Systematic review of evidence on public health in the Democratic People's Republic of Korea

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ABSTRACT

Background Engaging in public health activities in the Democratic People's Republic of Korea (DPRK, also known as North Korea) offers a means to improve population health for its citizens and the wider region. Such an engagement requires an understanding of current and future needs.

Methods We conducted a systematic search of five English and eight Korean language databases to identify available literature published between 1988 and 2017. A narrative review of evidence was conducted for five major categories (health systems, communicable diseases (CDs), non-communicable diseases (NCDs), injuries, and reproductive, maternal, newborn and child health (RMNCH) and nutrition).

Findings We found 465 publications on the DPRK and public health. Of the 253 articles that addressed major disease categories, we found under-representation of publications relative to proportion of disease burden for the two most significant causes: NCDs (54.5% publications vs 72.6% disability adjusted life years (DALYs)) and injuries (0.4% publications vs 12.1% DALYs), in comparison to publications on the third and fourth largest disease burdens, RMNCH and nutrition (30.4% publications vs 8.6% DALYs) and CDs (14.6% publications vs 6.7% DALYs) which were over-represented. Although most disease category articles were on NCDs, the majority of NCD articles addressed mental health of refugees. Only 165 articles addressed populations within the DPRK and among these, we found publication gaps on social and environmental determinants of health, CDs, and NCDs.

Conclusion There are gaps in the public health literature on the DPRK. Future research should focus on under-studied, significant burdens of disease. Moreover, establishing more precise estimates of disease burden and their distribution, as well as analysis on health systems responses aimed at addressing them, can result in improvements in population health.

BACKGROUND

The continued division of the two Koreas is one of the greatest challenges for our generation, with major implications for population health for the two Koreas, the region and

Key messages

What is already known?

- ▶ The scope of published literature on public health in the Democratic People's Republic of Korea (DPRK) is currently unknown.

What are the new findings?

- ▶ There were 465 publications on the DPRK and public health.
- ▶ For articles addressing populations living inside the DPRK, we determined the proportion of papers by strategic policy area and found publication gaps on social and environmental determinants of health, communicable diseases (CDs) and non-communicable diseases (NCDs).
- ▶ For articles addressing major disease categories, relative to proportion of disease burden, we found under-representation of publications on NCDs and injuries, and over-representation of publications on reproductive, maternal, newborn and child health (RMNCH) and nutrition, and CDs.

What do the new findings imply?

- ▶ Future work should address evidence gaps, develop more accurate disease burden estimates, and analyse health systems.

globally.¹ Addressing evidence gaps in public health on the Democratic People's Republic of Korea (DPRK, also known as North Korea), presents an opportunity to address the health challenges faced by its citizens and the wider region.²

The DPRK is a signatory to the Sustainable Development Goals. However, monitoring progress presents a challenge due to data quality and availability.^{3 4} The Medium Term Strategic Plan (MTSP) for the Development of the Health Sector: DPR Korea 2016–2020, includes the DPRK Government's plans to strengthen research capacity and collaboration to improve population health and use resources more efficiently.⁴

Figure 1 The DPRK Medium Term Strategic Plan 2016–2020: eight strategic areas. DPRK, Democratic People's Republic of Korea.

To date, no published studies have systematically reviewed the public health literature on the DPRK or examined the gap between the existing evidence and need. The objective of this study is to review the evidence gaps in public health on the DPRK across the strategic policy areas of the MTSP to inform decision makers and research.

METHODS

Search strategy and selection criteria

Policy priorities: MTSP

The DPRK-UN multi-year health plan, *MTSP 2016–2020*, outlines eight strategic policy areas (figure 1) and 16 research priorities (box 1) in the DPRK.

Two researchers worked independently to identify studies that examined public health issues on DPRK populations. Due to the heterogeneity of articles (eg, topics, study design, variables and outcomes), we conducted a qualitative synthesis across the major MTSP topic areas to analyse the public health themes most relevant to policy-makers and researchers. Following selection of articles, two researchers independently classified and categorised articles, and assessed quality using Oxford Centre for Evidence Based Medicine Criteria—excluding level 5 articles (eg, viewpoints, perspectives, editorials, expert opinion and reports without empirical data).⁵ Following assessment of the articles, all empirical (including both qualitative and quantitative) articles were included due to the limited number of published studies on public health in the DPRK. DPRK or North Korean populations refer to those living within or outside the DPRK and we explored these separately. MTSP topic areas cover studies on populations living in the DPRK only, since the Government's health priorities focus on intra-DPRK health issues.

Box 1: Research agenda in DPRK MTSP 2016 - 2020

1. Quality data assessment of immunisation coverage.
2. Tuberculosis: Research on the effectiveness on the current directly observed treatment, short-course (DOTS) medicine dose.
3. Community-based knowledge, attitudes and practices (KAP) survey on reasons of immunisations dropout.
4. Research to identify different types of adverse event following immunization (AEFI) and potential reasons.
5. Prevalence of hepatitis antigen carriers.
6. Operational research for elimination of malaria.
7. Survey to assess the prevalence of schistosomiasis.
8. Technical research on meridian.
9. Research to develop and introduce new types of traditional medicine.
10. Research on nutritional status.
11. National survey on quality of air.
12. A vulnerability assessment to consider the impacts of climate change on human health in the Democratic People's Republic of Korea (DPRK).
13. National survey on quality of water.
14. Assessment of the capacity of provincial and county hospitals for emergency response.
15. Risk assessment related to various kinds of hazards.
16. Assessment of mental health service needs.

Measuring the burden of disease

The Institute of Health Metrics and Evaluation's (IHME) estimates of disability adjusted life years (DALYs) was used to estimate the burden of disease in the DPRK for 2016. IHME collates data from 68 different data sources on the DPRK (eg, WHO STEPS survey data, Unicef and World Food Programme (WFP) nutrition assessments, Multiple Indicator Cluster Survey (MICS), World Drug Report, World Malaria Report and the DPRK Government including census data)⁶ and is a regularly used source of data on burden of disease. The four categories (NCDs, CDs, reproductive, maternal, newborn and child health (RMNCH) and nutrition, and injuries) were selected and adapted based on disease classifications used by IHME.

We used radar diagrams to visually illustrate the gap and compare research coverage, disease burdens and research and policy priorities.

This study was not funded and no ethics approval was needed as publicly available data and publications were used. JJP had access to all English language data. AYL had access to all Korean language data. JJP, AYL, KBP and HYS are responsible for the decision to submit the manuscript.

RESULTS

Description of dataset

The initial search identified 4654 publications in 1988 to 2017; applying our inclusion and exclusion criteria yielded 465 articles for analysis (see figure 2).

We identified 220 articles addressing diseases or conditions, 77 on health systems, 49 on both health systems and diseases or conditions, and 119 on other (ie, disasters, traditional medicine, environmental health and social and behavioural health) (table 1).

Figure 2 PRISMA flow diagram. CDs, communicable diseases; MTSP, Medium Term Strategic Plan; NCDs, non-communicable diseases.

Of these articles, 165 addressed populations living *inside* the DPRK (ie, not refugee populations), which we classified under the DPRK strategic policy areas (MTSP) (figure 3). We determined the proportion of papers by MTSP area and found publication gaps in social and environmental determinants of health (MTSP 8), communicable diseases (CDs) (MTSP 1) and non-communicable diseases (NCDs) (MTSP 2) (figure 3).

Of the 16 research priorities identified by the MTSP, seven related to CDs (MTSP 1) (43.8%), four on environment (MTSP 8) (25.0%), three on health systems, medicines, quality and medical science and technology (MTSP

4, 5, 6, 7) (18.8%), one on NCDs (MTSP 2) (6.3%) and one on RMNCH and nutrition (MTSP 3) (6.3%) (figure 3).

The eight categories used are based on the DPRK Government's strategic policy areas (MTSP). MTSP area 4, 5, 6 and 7 were grouped together, as most of these studies addressed health systems issues.

253 articles addressed NCDs, CDs, injuries, RMNCH and nutrition, inside and outside the DPRK (table 2). We compared the proportion of DALYs by disease or condition category with the proportion of publications (figure 4). We found that the proportion of publications was over-represented compared with their burden of disease for CDs (14.6% publications vs 6.7% DALYs) and RMNCH and nutrition (30.4% publications vs 8.6% DALYs) and under-represented for injuries (0.4% publications vs 12.1% DALYs) and NCDs (54.5% publications vs 72.6% DALYs) (table 2).

A narrative review of evidence was conducted for five major categories: CDs, NCDs, injuries, RMNCH and nutrition, and health systems.

Communicable diseases (CDs)

The published literature on CDs focused on tuberculosis (TB), hepatitis B and helminths.

Table 1 Categories of selected publications

Article category	Publications n (%)
Health systems	77 (16.6)
Diseases or conditions	220 (47.3)
Both health systems and diseases or conditions	49 (10.5)
Other	119 (25.6)
Total	465 (100)

Figure 3 Distribution of publications and research priorities by the DPRK strategic policy areas. CDs, communicable diseases; NCDs, non-communicable diseases; RMNCH, reproductive, maternal, newborn and child health.

TB

One set of studies on TB relates to work of the Eugene Bell Foundation (EBF), which has supported the DPRK multidrug-resistant tuberculosis (MDR-TB) treatment programme, including providing equipment, anti-TB medications and clinical training for DPRK medical staff.⁷ EBF analysis of 1 year treatment outcomes for 353 patients with rifampicin resistance showed that 250 (71%) were treated successfully.⁸ Examination of 947 sputum samples from 667 patients between 2007 and 2009 from multiple TB sanatoria across the DPRK demonstrated high rates of resistance to first-line drugs, including isoniazid (94.7%, n=463) and rifampicin (77.7%, n=380) from 489 culture positive patients.⁹ EBF data has given an insight into the resistance patterns from multiple regions and regional variations including greater prevalence in

larger cities compared with sites in smaller regions.⁹ EBF has combined effective clinical treatment for MDR-TB with public health research to advocate for scale up of treatment and care.⁸

Figure 4 Distribution of publications by major disease category. CDs, communicable diseases; NCDs, non-communicable diseases; RMNCH, reproductive, maternal, newborn and child health; DALYs, disability adjusted life years.

Table 2 Publications by four major disease categories which account for the largest disease burden as measured by disability adjusted life years

Disease-specific category	Publications n (%)	DALYs (%) [*]
NCDs [†]	138 (54.5)	72.6
RMNCH and nutrition	77 (30.4)	8.6
CDs	37 (14.6)	6.7
Injuries	1 (0.4)	12.1
Total	253 (100)	100

^{*}Disability adjusted life years for DPRK in 2016

[†]NCDs include dental health and mental health, as per IHME. CDs, communicable diseases; NCDs, non-communicable diseases; RMNCH, reproductive, maternal, newborn and child health.

Two publications have described collaboration among Stanford University, Christian Friends of Korea and the DPRK Ministry of Public Health (MOPH) to develop the first TB reference laboratory in the DPRK in 2010, including delivery of equipment, training, and managing practical operational issues, such as problems with central power and extremes of weather.^{10 11}

Two small-scale TB studies on DPRK refugees in South Korea found high prevalence of pulmonary TB and 'severe' forms of TB¹² and low levels of TB knowledge.¹³

Hepatitis B

A study by Unnewehr and Stich highlight the results of a nation-wide hepatitis B programme implemented by Caritas Germany and MOPH, which enabled vaccination of 3.7 million children aged 6 to 16 years old, between 2010 and 2012, achieving a coverage rate of 99.2% (3.7 million out of 3.75 million). It described collaboration on clinical training and activities to develop hepatitis B virus (HBV) prevention strategies in the DPRK.¹⁴

Lee and Park used a Markov model to establish cost effectiveness of different vaccination strategies for the prevention of perinatal HBV transmission in the DPRK and showed that selective vaccination may be more cost-effective than universal vaccination.¹⁵

One study examined 78 refugees and showed an HBsAg positive rate of 15.4% (n=12) and anti-HBs positive rate of 33.3% (n=26),¹⁶ and another showed low knowledge of hepatitis B among 198 refugees on a hepatitis B knowledge questionnaire.¹⁷

Helminths

Intestinal parasitic infections were examined for 236 residents and soldiers in a town bordering China and the DPRK in Hamgyeongbukdo and 46 refugees in China in 2003. It found high helminth egg positive rates among residents (64.7%; 123 out of 190), while relatively lower rates were found for soldiers (28.3%; 13 out of 46) and refugees in China (41.3%; 19 out of 46).¹⁸ A team led by Seoul National University visited the DPRK over a 3-year period to promote education and knowledge transfer on diagnostics, provision of diagnostic kits and antihelminth medicines for 10 000 people and treatment of 894 residents, although data was not released under a confidentiality agreement.¹⁹

Non-communicable disease

NCD is the leading burden of disease in the DPRK (72.6% DALYs in 2016).⁶

Prevention of NCDs

A DPRK Government-WHO policy paper published rates for tobacco and alcohol use, elevated blood pressure (BP) and body mass index (BMI) in Pyongyang in 2005.²⁰ Of the 2920 individuals aged 15–64 initially chosen for survey, 2655 responded (response rate 90.9%; male: n=1316 and female: n=1339). Among men, 55.8% (n=734) were smokers and 20.9% (n=275) were heavy drinkers (more than five drinks a day); no women reported smoking or

heavy drinking. Smoking and heavy drinking prevalence rose with age. Mean BP was 131/89 for males and 129/87 for females, with a hypertension (systolic BP≥140 mm Hg and/or diastolic BP≥90 mm Hg) prevalence of 19.4% (n=255) for males and 18.0% (n=241) for females. The mean BMI for males was 22.5 and 22.3 for females.

A 2013 national survey, reported in the UN-DPRK MTSP, indicate a smoking prevalence of 43.9% (adult males)—a reduction from 52.3% in 2009.⁴

Smoking and alcohol usage rates examined among DPRK refugees indicate similarly high rates to the South.^{21 22} To deliver better prevention of NCDs, authors from the DPRK Government and WHO published a paper demonstrating the efficacy of the WHO Package of Essential Non-Communicable Disease (PEN) protocol pilot study in improving risk management of cardiovascular disease and recommended its expansion to provinces.²³

On cancer prevention, four studies explored cervical and breast neoplasms. Only one study was conducted within the DPRK, covering six provinces and purposively sampling 200 women. It showed good knowledge of cervical cancer with non-significant differences between rural (63%, n=62) and urban women (60%, n=61). However, significant gaps were identified in the usage of services, with only 6% (n=12) reporting to have had previous cervical cytology smear test. Significantly more rural women (62%, n=61) than urban women (0%, n=0) (p<0.001) stated long travel distances were a barrier to accessing service facilities.²⁴

Refugee studies based in South Korea examined the facilitators and barriers of accessing cervical cancer screening for DPRK women through qualitative interviews,²⁵ education on breast cancer screening and rates of self-examination by surveys,²⁶ and cervical screening rates.²⁷

Dental health

There are 10 studies on dental health. Four papers in English examine oral health of children in Wonsan,²⁸ knowledge of healthy oral habits in Pyongyang,²⁹ prevalence of dental caries³⁰ and dental caries prevention and oral health habits in Pyongyang.³¹ Six studies published in the Korean language examine North Korean dental terminology,³² systems,³³ research trends,^{34 35} education³⁶ and dental health exchanges between the South and North.³⁷

Mental health

The majority of NCD papers (n=138) examine mental health issues (n=110) on refugee populations. Most studies were conducted in South Korea, although a few studies were based in China^{38 39} and Japan.⁴⁰ Post-traumatic stress disorder or trauma (n=20) and depression (n=15) were studied most frequently. Survey respondents were usually recruited from South Korean government facilities, used databases held under the Ministry of Unification and tended to study females populations

aged 30–50 years old—reflecting the demographics of refugees.⁴¹

Reproductive, maternal, newborn and child health (RMNCH) and nutrition

Refugee studies in South Korea have examined reproductive, maternal, newborn and child health (RMNCH) service access using surveys^{42 43} and qualitative interviews.⁴⁴ Although the DPRK has conducted Reproductive Health Surveys (RHS) in 1997, 2002, 2010, these were not publicly available, and there were no published studies using data from these surveys.

Nutrition has been an area of substantive research as a result of National Nutrition Surveys (NNS), led by WFP and Unicef in 1997, 1998, 2002, 2004 and 2012.^{6 45} In contrast to RHS, NNS have been subject to in-depth secondary analysis including 1997,⁴⁶ 2002⁴⁷ and 2012 surveys.⁴⁸ Regional variations are measured through NNS, and in 2012, stunting prevalence remained highest in Ryanggangdo (39.6%) compared with Pyongyang (19.6%) which had the lowest stunting prevalence rate.⁴⁸

South Korean authors have used the NNS to compare maternal nutrition among women living in North and South Korea from 2004⁴⁹ and 2012 surveys.⁵⁰ A study conducted in 1997 examined 3984 children under 7 years of age in 40 Government-selected institutions to identify the prevalence of acute malnutrition across four provinces (16.5%, n=654, out of total of 3965, as 19 children with weight-for-height Z-score<-4.0 were excluded) and chronic malnutrition (38.2%, n=1513, out of a total of 3960 as 24 children with height-for-age Z-score<-5.0 were excluded).⁴⁶ Schwekendiek has conducted in-depth analysis using NNS data by comparing regional⁵¹ and seasonal variations in malnutrition in the DPRK,⁵² height-weight differences of North and South Korean children,^{53 54} determinants of nutritional status,⁵⁵ and nutritional impact during the famine.⁵⁶

In contrast to several observational, cohort and secondary data analysis studies, only one randomised controlled trial was identified. The authors (all from the DPRK) recruited 234 infants aged 6–12 months from 36 nurseries in the DPRK and demonstrated that iron supplementation to rice group was superior to placebo, reducing prevalence of anaemia (24.3% vs 48.1%, p<0.01) and increasing Hb levels (117.6 g/L vs 109.8 g/L, p<0.001) and serum ferritin levels (40.7 vs 26.8 mcg/L, p<0.001).⁵⁷

There were several malnutrition studies on iodine deficiency and hypothyroidism.^{58–60} The first comprehensive national iodine deficiency survey conducted between 2009–2010 by the DPRK Institute of Child Nutrition, with assistance from the International Council for Control of Iodine Deficiency Disorders and WHO, examined rates among 1200 children aged 6–12 years from 30 clusters (40 children in each cluster). The total goitre rate was 19.5% (n=234) nationally, and

by province it was highest in Ryanggangdo (30.8%) and lowest in Pyongyang (11.8%).⁶¹

Health system

Health system strengthening (HSS) is a health policy priority; yet, few studies have analysed the health system in the DPRK.⁴ Grundy and Moodie provide an analysis of the current health system and strategic frameworks to adopt for further strengthening.⁶² However, studies analysing the DPRK health system are mainly by South Korean authors. Health system studies have examined broad political, legislative and economic conditions^{63–70} including analysis of potential unification scenarios that could involve the integration of the health systems,^{71–73} as well as drawing on comparative analysis from German unification and transitions of former Soviet bloc states.^{74–76}

International organisations' reports offer insight into the health system. WHO provides a HSS analysis in its Country Cooperation Strategy (CCS),⁷⁷ and Unicef publishes annual reports,⁷⁸ analysis of the situation of children and women in the DPRK⁷⁹ and MICS data,⁸⁰ outlining the broader systems and data challenges facing RMNCH populations. Amnesty International produced a report on the North Korean health system⁸¹ and nutrition issues⁸² based on interviews with refugees and experts. Drawing from an operational perspective, Médecins Sans Frontières published a 189-page report detailing activities and challenges working in the DPRK using excerpts from emails, fax and interviews while working in the DPRK between 1995 and 1998.⁸³ Moreover, the Global Alliance for Vaccines and Immunization has made their documentation on in-country activities publicly available.⁸⁴

DISCUSSION

To our knowledge, this is the first systematic review and narrative synthesis of the published literature on public health in the DPRK. Earlier analysis was limited in scope and explored English language articles published by DPRK authors from 1997 to 2017,⁸⁵ refugee populations,^{86–88} or DPRK Journals only.^{89–91} Research and policy development should be informed by evidence,⁷⁷ yet we identified gaps in evidence.

The DPRK faces a triple burden of disease from NCDs, CDs and injuries and disasters. Increasingly, NCDs form the major burden of disease in the DPRK. NCDs are a major contributor towards the increase in life expectancy gap between the North and South.⁹² The MOPH has already developed a national strategic plan for prevention and control of NCDs,⁹³ recently updated for 2014–2020.⁹⁴ However, only 1 of the 16 MTSP research priorities was on NCDs (mental health). We identified 138 articles addressing NCDs and the vast majority (n=110) explored the mental health of people living outside the DPRK and hence offer limited inference about populations living in the DPRK. Future NCD

research could focus on cardiovascular disease, cancer and respiratory disease—which constitute a significant share of the estimated NCD burden in the DPRK.

CDs still account for a large proportion of disease burden; research on this area will remain an important part of a national CD control strategy. There were several studies on MDR-TB and hepatitis, but none on HIV. Recent publications including the DPRK TB prevalence survey,⁹⁵ national malaria strategy,⁹⁶ and malaria programme review⁹⁷ provide opportunities to better understand and control CD.

There was only one report on injuries, although injuries constitute 12.1% of disease burden (in DALYs, 2016). The DPRK Government has selected the months of November and May as Accident Prevention Months, promoting efforts to reduce traffic and fire injuries through education and prevention programs.⁴ Moreover, one MTSP research priority is on injuries. However, research is needed to characterise and reduce the rates of injuries, occupational hazards and work related-illness.

In RMNCH, there have been limited published studies despite Unicef's role in the DPRK and WHO's Improving Women and Child Health programme. Research is needed to more precisely measure changes to maternal, infant and under-5 mortality rates and to identify interventions to further improve them.⁴ In particular, there is a need for studies that evaluate the impact of programmes and policy interventions, and studies on RMNCH knowledge, access, utilisation and outcomes. The 2017 MICS, published by the Government's Central Bureau of Statistics and Unicef in June 2018—the first since 2009—represents progress in data collection in child and women health in the DPRK.⁸⁰ Moreover, the 2014 Socio-Economic, Demographic and Health Survey, published by the Central Bureau for Statistics and UNFPA, also provides data on RMNCH.⁹⁸

There was limited health systems analysis from the DPRK. According to the MTSP, the DPRK health system faces challenges in delivering basic 'operational funds, infrastructure, referral systems and logistics'.⁴ Engaging in health system research with policymakers represents an opportunity to improve population health.

Limitations of this study

We have identified six limitations of our study. First, we attempted to identify all empirical (qualitative and quantitative) articles on public health in DPRK populations. Of the 465 studies included (1988–2017), 294 (63.2%) were published in 2010 or afterwards, suggesting increasing scholarly interest in health research on DPRK populations. However, the heterogeneity of articles meant conducting a quantitative synthesis was not possible. We classified study quality by Oxford Evidence Level, but did not assess inherent article quality (eg, bias). Over half (n=241; 51.8%) of articles were qualitative or mixed methods studies. Many studies used cohort or cross-sectional designs and were based on self-reported data. Although the majority were original empirical

studies (n=246; 52.9%), a large proportion relied only on previous empirical studies (n=190; 40.9%).

Second, the distribution of included studies was skewed towards the refugee population (142 of 290 Korean articles and 79 of 175 English articles) with the majority of refugee studies focused on those living in South Korea. Studies on refugee populations were often small, limiting generalisability. Only 165 of the 465 articles (35.5%) were directly on populations living within the DPRK. 25 articles (5.4%) articles included an author from the DPRK, compared with 376 articles (80.9%), which had a first author from South Korea.

Third, we were unable to search DPRK journals. It would be of interest to determine the degree of overlap of articles and topics with articles from the DPRK.⁸⁹ Moreover, several South Korean articles had English abstracts but not all articles did, limiting accessibility to an international audience.

Fourth, burden of disease estimates were obtained from IHME.⁶ Although IHME estimates are derived from a limited data sample, often using secondary data analysis, since there is limited publicly available health data, it remains an important source of information on public health in the DPRK.

Fifth, not all health policy topics (e.g. social determinants of health) and articles were included in the narrative review due to space constraints.

Sixth, this study is limited by the date range we searched; some relevant articles could have been published earlier and additional articles will be written in the future.

While these limitations reduce the generalisability of findings beyond the populations studied and indicate the need for high-quality studies in settings *within* the DPRK, to our knowledge, this study offers the most comprehensive overview of the literature published on DPRK populations to date.

CONCLUSION

In sum, we found gaps in the public health evidence on the DPRK.

Further research should focus on addressing evidence gaps on the most significant and under-studied burdens of disease. In addition, obtaining more accurate estimates on magnitude and distribution of disease burden, and analysis on health systems, can contribute towards future gains in population health.

There are significant opportunities to improve health in the DPRK and wider region - a better understanding of public health through data collection, knowledge and research can help achieve this goal.

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Contributors JJP, KBP, HYS, AYL, SYC and HSA conceived and designed the study. JJP, OLP, DHO, AYL, SYC and HSA searched the literature. SJJ offered statistical support. JJP, DHO, OLP, AIK, SYK, AYL, SYC and HSA extracted, analysed and interpreted the results. JJP drafted the initial report. AYL, SYC and HSA commented on the first draft, and RA and JBB revised the draft. All authors critically commented on and revised subsequent versions of the report.

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