Closing the gap

Prioritising thyroid disease in Asia-Pacific



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About this report

Closing the gap: prioritising thyroid disease in Asia-Pacific is a report produced by Economist Impact, supported by Merck. The report addresses the gaps surrounding thyroid disease by focusing on how improvements made in awareness, prevention, screening, surveillance and improved engagement with patients and healthcare providers could lead to better health outcomes for people living with these conditions in the Asia-Pacific (APAC) region.

The research highlights opportunities for change, with a particular focus on better screening in high-risk groups including newborns, pregnant women (as well as those looking to become pregnant), older people and those at increased risk of autoimmune disease.

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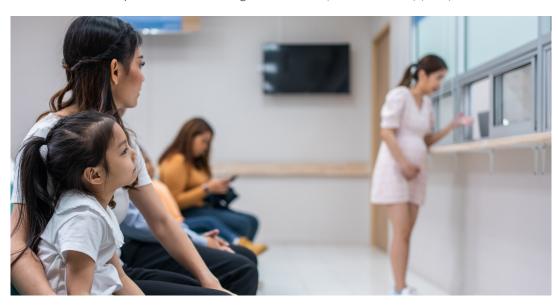
Executive summary

Why thyroid disease matters

Thyroid disease is a major public health concern for the Asia-Pacific region (APAC), requiring urgent action. The most common form—hypothyroidism—affects an estimated 11% of adults, compared with 2-4% of adults elsewhere.¹ Thyroid disease is an umbrella term for several conditions that occur due to abnormal thyroid functioning and production of hormones. They include hypothyroidism, hyperthyroidism, congenital hypothyroidism (CH) and, more rarely, thyroid cancer. Several population groups are at increased risk of thyroid disease, including

pregnant women, newborns, older adults and individuals with certain genetic conditions. Living with thyroid disease can be challenging, especially when undiagnosed, as the conditions impact physical, mental and social functions and quality of life. Economically, they also pose significant and increasing costs to national budgets and health systems.

To research this topic, Economist Impact conducted an evidence review and convened a panel of experts to explore the central issues in the region and support the identification and development of the key policy areas.



Where next? Action areas to improve thyroid health in APAC

Building on the findings of our research, the following key policy takeaways provide next steps in policy development to support a

comprehensive, equitable and sustainable approach to addressing thyroid disease throughout APAC.

KEY POLICY TAKEAWAYS FOR APAC



Implement data gathering through surveillance

Why? Understanding the scale of the challenge is necessary to develop a tailored, evidence-based response to address it.

How? Regularly surveying iodine levels and thyroid prevalence enables health authorities to gauge the scale of thyroid disease and what interventions are needed where. Piloting new approaches such as targeted screening and testing innovations will help determine their feasibility and clinical/cost effectiveness.



Focus screening on high-risk groups

Why? Targeting known high-risk groups will help improve overall detection of thyroid disease.

How? High-risk groups, such as pregnant women, should be actively screened to improve detection. Integrating thyroid screening into existing programmes and services is a potentially cost and resource efficient route to improved detection for exploration.



Raise awareness amongst the public and healthcare professionals

Why? Recognising thyroid disease depends on heightened awareness and proactive diagnostic screening.

How? Educating primary care professionals and the public could lead to more people considering thyroid disease as the cause of non-specific symptoms. Other routes to raising awareness are evidence-based clinical guidelines and categorising thyroid disease as an NCD.



Collaborate on standardised regional clinical guidelines

Why? Guidelines are easier to implement when they reflect real-world practice and relevant stakeholder perspectives.

How? Developing regional guidelines could support resource-limited countries by enabling them to pool resources and expertise. Involving all relevant stakeholders—especially patients—is best practice in guideline production. Working regionally can provide those perspectives for countries where patients are not mobilised to participate.

Introduction

Thyroid disease presents significant challenges to public health, affecting an estimated 200m people globally.² Undiagnosed thyroid disease disrupts various essential bodily functions and exacerbates other health conditions, including cardiovascular disease, pregnancy complications, metabolic disorders, obesity, renal diseases and mental health conditions.²⁻⁶ Estimates indicate that thyroid disease is more common in Asia-Pacific (APAC) than other regions, but data availability is limited.^{1,7}

Left untreated, thyroid disease negatively impacts on individual quality of life and has substantial social, economic and health impacts.^{8,9} Thyroid disease includes hypothyroidism and hyperthyroidism (where the thyroid under- or over-functions), congenital (inherited) hypothyroidism and thyroid cancer. The prevalence of these conditions varies and is influenced by age, gender, ethnicity, healthcare access and dietary iodine intake, meaning that there are specific groups at increased risk of thyroid disease (Figure 1).^{10,11}

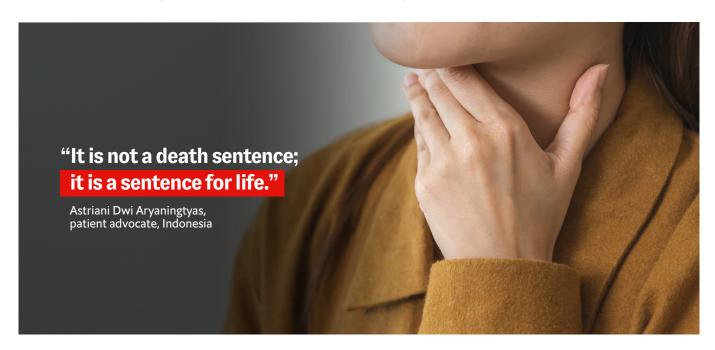
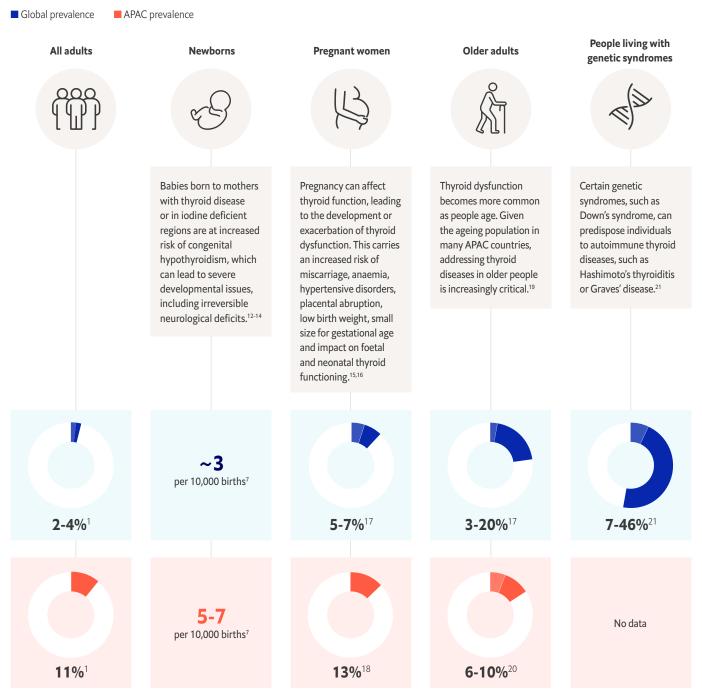


Figure 1: Global and APAC prevalence in high-risk groups



Note. Global and regional statistics are drawn from a number of sources and sometimes reflect data from a single country within the region.

This report explores the challenges around detecting, diagnosing and managing thyroid disease in APAC. It also includes the insights of a panel of regional experts to identify key regional policy action areas and examples of current progress within the region.

Challenges in thyroid care in APAC

The key themes to emerge from the evidence review and the insights of the regional expert panel cover the whole spectrum of thyroid disease care, from prevention and detection to management and awareness raising. The broad range of these themes reflects the scale of the challenge facing the region. Here we discuss areas for improvement for APAC, then identify specific policy takeaways for the region that are supported by case studies of successful action that has been taken to address these challenges.

Primary prevention—addressing population iodine levels

Iodine is a key contributor to the healthy functioning of the thyroid.^{5,6} Too little iodine (iodine deficiency) can impair the cognitive and motor development of children, can affect the productivity and ability to work of adults, and is associated with an intelligence quotient (IQ) up to 15 points lower than comparable communities with sufficient iodine.²² Insufficient iodine intake

"We need to push the government to focus on certain subpopulations. We still have many pregnant women who are iodine deficient."

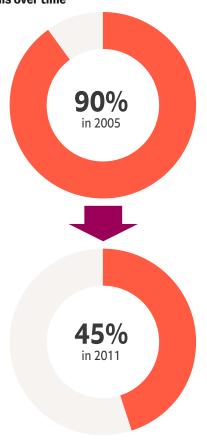
Cecilia A Jimeno, endocrinologist, Philippines

during pregnancy can affect the neurological development of foetuses and infants. Indeed, iodine deficiency is considered the most common cause of preventable brain damage globally.^{22,23} Thus, an effective way to prevent thyroid disease is to monitor population iodine levels and address them as needed.

Monitoring iodised salt availability and iodine deficiency

Two surveillance systems monitor iodine intake globally. The first is part of the Vitamin and Mineral Nutrition Information System (VMNIS), managed by the Iodine Global Network and the World Health Organisation (WHO).^{24,25} It collates country-level data on iodine status using the globally standardised measure of Median Urinary Iodine Concentration (UIC) in various populations, including school-age children. The second surveillance system is the UNICEF Global Database on Household Consumption of Iodised Salt. This monitors the percentage of households consuming iodised salt (>0 ppm), particularly in low- and middle-income countries. At the time of the last survey, most APAC countries recorded high proportions of households consuming iodised salt and adequate iodine sufficiency among school-aged children (Table 1).26 However, much of the data in both the VMNIS and UNICEF databases are outdated.

Figure 2: lodised salt intake in Vietnam falls over time²⁷



Furthermore, such progress should not be taken for granted, and continuous monitoring of population iodine levels is crucial to ensure rapid and targeted action. Although in Vietnam in 2005 more than 90% of households were using adequately iodised salt (>15ppm), this fell to just 45% in 2011.²⁷ The reason was the removal of subsidies and non-mandatory legislation leading the food industry to end iodisation.²⁷ In another example, New Zealand

"lodine deficiency is an underlying problem for the health of pregnant women, newborns and children."

Paul Yen, endocrinologist, Singapore

introduced iodised salt in the 1930s, yet saw a sudden rise in iodine deficiency in the 1990s.²⁸ It addressed this by making iodised salt mandatory in commercially made bread products in 2009 and then mandating the provision of iodine supplementation for all pregnant and lactating women in 2010.^{28,29}

Legislating national salt iodisation

Fortifying foods, especially with iodised salt, is a key mechanism to prevent iodine insufficiency. Most countries in APAC have mandatory iodised salt legislation in place, with Malaysia being the latest country to adopt this into law in 2020 (Table 1).30 Of the APAC countries with mandatory iodised salt legislation in place, only Vietnam still has insufficient iodine intake among its general population, suggesting that this approach is generally effective in improving population iodine levels (Table 1).24 However, as Roland Kupka, regional nutrition advisor, UNICEF East Asia and Pacific Regional Office, explained, there is a need to strike a balance between the risks of insufficient and excessive iodine intake to prevent the latter, which can lead to iodine-induced hyperthyroidism.

Focus on at-risk sub-populations

lodine deficiency is a public health issue in those population groups at increased risk of thyroid disease. In several countries, such as the Philippines, Mongolia and Myanmar, pregnant women still fall below WHO-recommended iodine levels (Table 1).²⁵ Programmes to boost iodine intake can target specific populations such as weaning infants, preschool children, pregnant and lactating women. Other sub-groups to target include "difficult-to-reach" populations such as those who live in remote regions of Southeast Asia, who may not have access to iodised salt.³¹ The targeting of such interventions requires accurate and current data.

Table 1: Salt iodisation status and urinary iodine levels in APAC

(see Appendix 1 for a detailed version of this table)

■ Above threshold ■ Below threshold ■ No data ■ Highest % ■ Lowest %

	Median uri (μg/L of iod	nary iodine ine in urine)	lodised salt		
Country	In school-age children (recommended level ≥100 µg/L)	In pregnant women (recommended level ≥150 µg/L)	Is there salt iodisation legislation?	% of households consuming iodised salt	
Afghanistan	171	37.5	Yes	56.9	
Australia	175	-	Yes	-	
Bangladesh	146	158	Yes	76.5	
Bhutan	183	-	No	98.4	
Brunei	-	-	Yes	-	
Myanmar	139	121.8 Yes		85	
Cambodia	235.9	63 Yes		68.9	
China	217	172	Yes	96.6	
Timor-Leste	-	-	No	84.5	
India	175	173.4	Yes	94.3	
Indonesia	215	163	Yes	91.9	
Japan	269	-	No	-	
Laos	103	-	Yes	94.8	
Malaysia	109	-	Yes	28.2	
Mongolia	145	120.5	Yes	75.6	
Nepal	314	241.3	Yes	94.9	
New Zealand	116	114	Yes	-	
North Korea	97	-	No	37.5	
Pakistan	123	108	No	80.4	
Papua New Guinea	-	-	Yes	99	
Philippines	180	121	Yes	57	
Singapore	-	-	Yes	-	
South Korea	449	-	No	-	
Sri Lanka	233	157.9	Yes	98	
Thailand	179	154.9	Yes	93.9	
Vietnam	84	83.4	Yes	62.4	

Sources: Salt iodisation legislation.^{30,32,34} Households consuming iodised salt.^{26,35} Iodine levels in school-age children.^{24,25} Iodine levels in pregnant women.^{25,36,37}



"Screening pregnant women for thyroid disease will help us to identify and treat them properly and prevent congenital issues from developing due to maternal hypothyroidism."

Muhammad Yazid Jalaludin, paediatric endocrinologist, Malaysia

Early detection—identifying and screening at-risk populations

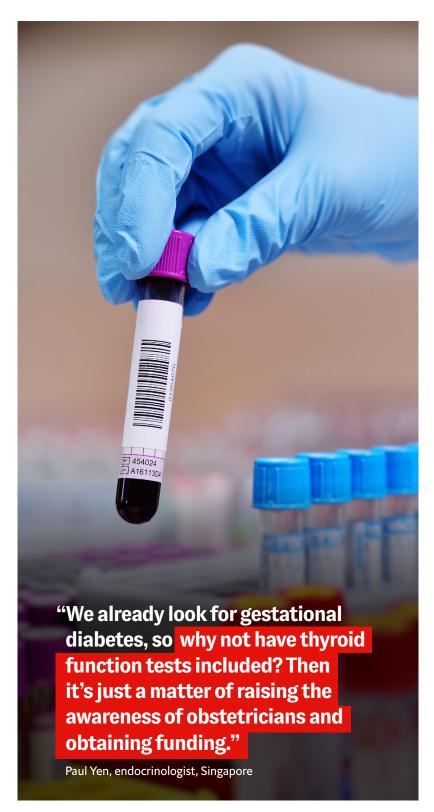
Integrated thyroid screening in maternal and child health

Pregnant women are at higher risk of thyroid disease. This is, in turn, associated with adverse maternal and foetal outcomes, including preeclampsia, spontaneous abortion, preterm delivery and intrauterine growth retardation.³⁸ Congenital hypothyroidism can impair the development of newborns and lead to long-term disability and intellectual impairment.^{7,39}

The impacts of hypothyroidism can be addressed through early diagnosis and management. However, universal screening for maternal thyroid disease has not been adopted in APAC. Many countries, such as Malaysia, currently recommend a targeted case-finding approach towards maternal hypothyroidism, whereby pregnant women are only screened when they have additional risk factors, such as a family history of thyroid dysfunction.⁴⁰

The expert panel that we consulted emphasised that adopting a universal approach to maternal thyroid screening could have major health benefits for mothers and babies in the region. In addition to impacts on health outcomes and development, several studies have proven the cost-effectiveness of universal screening in pregnancy for hypothyroidism as a means of managing costs and improving quality-adjusted life years (QALYs).

Universal screening for congenital hypothyroidism in neonates has been more widely accepted and adopted in APAC than maternal screening (Table 2). For example, the Japanese Society of Paediatric Endocrinology has had guidelines for mass screening of congenital hypothyroidism since 1998. 41 Muhammad Yazid Jalaludin, professor of paediatrics and senior consultant paediatric endocrinologist at Universiti Malaya Medical Centre in Malaysia, reported that that country's integration of thyroid functioning testing into the national neonatal screening programme helped reduce the number of children with the most severe effects of hypothyroidism.



Older adults

There is evidence of a high prevalence of thyroid disease in older people in APAC, which could be detected through universal screening for subclinical hypothyroidism. However, this has not been shown to be cost-effective at a population level, leading to lack of consensus on universal screening and warranting further research. 42-44

People with family history or genetic disorders

People with a family history of thyroid disease and those living with certain genetic disorders (Down's syndrome, for example) are at an increased risk of thyroid disease. There are no standardised clinical guidelines for most of these groups. An example where such guidance is available is the Royal Australian College of GPs' guidance on Down's syndrome that recommends thyroid disease testing at birth and annually throughout childhood and adulthood, or more frequently if signs or symptoms are observed.⁴⁵

Integrating thyroid screening into existing programmes

Several APAC countries have screening programmes to identify conditions such as diabetes in pregnant women and older adults.⁴⁶⁻⁴⁹ The expert panel suggested that integrating thyroid disease into these screening programmes could improve health outcomes while requiring limited additional resources. Dicky L Tahapary, an endocrinologist in the University of Indonesia's Department of Internal Medicine and head of the Indonesian Thyroid Association Jakarta Branch, analysed the benefits of universal maternal thyroid-health screening and found that, rather than simply being low cost or cost-neutral, such screening could in fact save "quite a lot of money by preventing the negative health outcomes that result from undetected conditions."50

Integrating thyroid screening into existing screening programmes for pregnant women and babies could improve detection in these high-risk groups. Whilst many of the newborn screening programmes in APAC include screening for congenital hypothyroidism, many countries still have limited or no newborn screening programmes in place (Table 2).⁵¹ Geographical factors can limit the reach of maternal and newborn services and, therefore, screening opportunities. For example, in Bangladesh 62% of births occur at home.^{52,53} There is also regional inconsistency in newborn congenital hypothyroidism screening. For

example, Malaysia didn't include congenital hypothyroidism in newborn screening for the first 23 years of the programme, whereas routine congenital hypothyroidism screening is the only mandated and regulated newborn screening in Indonesia.^{54,55}

It can also be challenging to create an enabling environment to implement such policy initiatives. Cecilia A Jimeno, professor of endocrinology, diabetes and metabolism, University of Philippines College of Medicine, highlighted clinical guidelines as an important first step to raise awareness and get policy buy-in.

Table 2: Status of newborn thyroid-screening programmes⁵¹

- Established neonatal screening programmes
- Progress in implementing neonatal screening programmes
- Limited/no neonatal screening programmes

Australia	
Bhutan	
Brunei	
Myanmar	
Cambodia	
China	
Timor-Leste	
India	
Indonesia ⁵⁵	
Japan	
Laos	

Malaysia	
Nepal	
New Zealand	
North Korea	
Pakistan	
Papua New Guinea	
Philippines	
Singapore	
South Korea	
Thailand	
Vietnam	

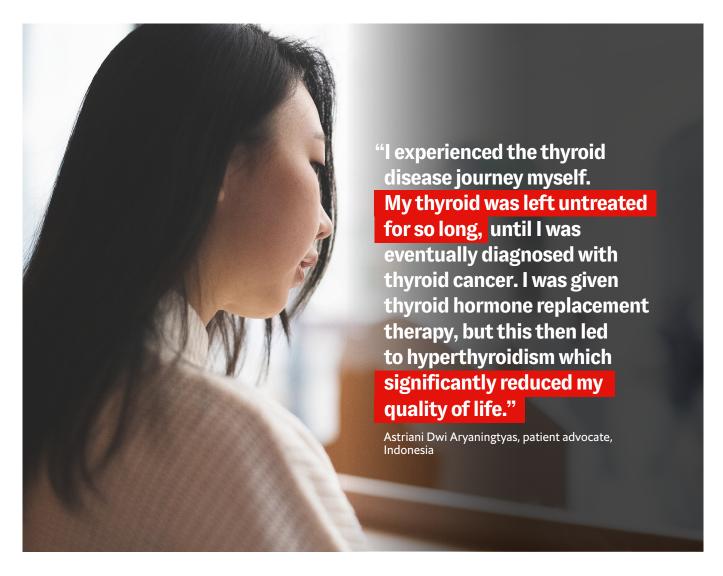
Note. This table is designed to give a regional overview; the data are from 2019. Data for Indonesia have been updated based on information identified during the literature review and cited above. The rating criteria are defined in the source material.⁵¹

Barriers to optimal care

Receiving optimal care can be hindered by barriers such as poor awareness and knowledge among healthcare professionals, patient-related delays, limited access to health services and other resource limitations. Individuals with thyroid disease are much less likely to seek and receive a diagnosis if they do not recognise their symptoms. For hypothyroidism specifically, symptoms are typically nonspecific and often mimic those associated with variations in lifestyle or with other conditions. 56,57 These obstacles can significantly impact overall patient outcomes.

Healthcare professionals' awareness

The clinical presentation of thyroid disease is mainly through nonspecific symptoms such as fatigue, insomnia and constipation. According to Azraai Bahari bin Nasruddin, a consultant endocrinologist at the Hospital Putrajaya Endocrine Institute in Malaysia, diagnosis can therefore often depend on clinician awareness of thyroid disease. Because these symptoms are associated with many conditions, patients may visit several healthcare professionals before anyone recognises that a thyroid function test is needed. As a result, people are more likely to be



diagnosed in the later stages of the disease, when specific clinical signs are more apparent, leading to increased costs and poorer outcomes.

Improving thyroid health literacy among healthcare professionals is therefore a crucial step towards addressing the gaps in awareness and diagnosis. ⁵⁹ This is of particular relevance for healthcare professionals who would be the first point of contact for individuals at risk of thyroid disease or experiencing thyroid-related symptoms, including general practitioners, obstetricians and midwives for pregnant women, and paediatricians for newborns. The experts

we consulted suggested that integrating thyroid-related topics into medical education courses and training programmes could enable healthcare providers to better recognise thyroid disease and address it more promptly. The experts felt that particular focus should be given to the identification and treatment of thyroid disease in high-risk population groups, such as older people in countries with rapidly ageing populations.

Patient awareness and understanding of thyroid disease

Seeking a diagnosis

Owing to the non-specific and mild nature of symptoms, individuals often do not think to seek a diagnosis for thyroid-related conditions. This can be particularly true among older people, because symptoms such as confusion, depression, falling, heart failure and changes in bowel habits are often seen as normal signs of ageing. Delays in seeking care can lead to worse health outcomes and increase future care costs for the individual and health system.

Dr bin Nasruddin highlighted that there are "many patient portals, support groups and educators for diabetes, but few, if any, within the thyroid sphere." Other experts agreed that disease-specific patient support groups and online resources would support improved detection and management of thyroid disease.⁴⁸ The expert panel also highlighted the use of social media platforms to promote awareness and disseminate information among patients and the community as a key strategy. Paul Yen, professor of medicine at Duke-NUS Graduate Medical School, Singapore, suggested that government health agencies use "whatever internet platform they use to reach the public to find ways to educate the people who are unaware of thyroid disease."



"The biggest impact on thyroid disease treatment would come from improving communication and access to education.

We must enhance the literacy of our patients, caregivers, family members and doctors."

Azraai Bahari bin Nasruddin, endocrinologist, Malaysia

The expert panel also felt that patient groups can play a major role in advocating for and raising awareness about thyroid health. Experts from the Philippines cited a thyroid cancer support group that has successfully backed the launch of a National Thyroid Cancer Awareness Week, mirroring awareness campaigns for diseases like diabetes. Although for now the initiative is small and mainly active only in the capital city, Manila, it shows the role that such groups can play in launching activities to raise public awareness of thyroid disease.

Receiving and adhering to treatment

For people with diagnosed thyroid disease, the expert panel felt that improved understanding of the health implications could improve patient adherence to treatment and follow-up. The side effects of thyroid disease treatments, the busy lives of patients, lack of disease education and symptom alleviation are some factors that have been shown to contribute to poor adherence to medication. 64,65

Recognising thyroid disease as an NCD

The WHO Non-Communicable Disease agenda currently focuses on five major non-communicable diseases (NCDs): cardiovascular disease, cancer, diabetes, chronic respiratory disease and mental health and neurological disorders. For Distatus for a disease has several benefits, namely inclusion in health policy agendas aimed at prevention, diagnosis and treatment; healthcare professional awareness; and prioritisation for data collection, research and funding. Decay Because thyroid disorders face barriers across many of these fronts, they could benefit from NCD status.

Experts we consulted felt that thyroid disease should be classified as an NCD both because it makes a significant contribution to the global burden of disease and because disruptions

"Some older people don't really want to see the doctor, or they ascribe their symptoms just to "ageing" and don't seek help when they should."

Paul Yen, endocrinologist, Singapore

"Many of my patients don't give importance to their thyroid treatments.

Our clinics have a high appointment default rate, but patients subsequently re-present with complications later on."

Azraai Bahari bin Nasruddin, endocrinologist, Malaysia

"Thyroid disease is everyone's business.

This is a call to action to the WHO to recognise thyroid disease as an NCD and put it in the spotlight."

Astriani Dwi Aryaningtyas, patient advocate, Indonesia

in thyroid functioning are related to other recognised NCDs including cardiovascular disease, cancer and diabetes. In his argument for NCD status, Dr Jalaludin stressed the preventable nature of thyroid disease, especially

congenital hypothyroidism. He and Astriani Dwi Aryaningtyas, founder of Pita Tosca, an Indonesian thyroid health patient organisation, both highlighted the discrepancy between the prevalence of thyroid disease and the limited national and international policy attention it attracts. Categorising thyroid disease as an NCD has the potential to help overcome these barriers.

Although many countries in APAC and globally are starting to focus on thyroid disease in their health policy agendas, only a few countries (including Turkey and Colombia) consider it an NCD for prioritisation. ⁵⁹ Several organisations are actively undertaking advocacy efforts to classify thyroid disease as an NCD. Policymakers including the WHO and global health and development donors are being called on to include endocrine-related conditions, including thyroid disease, into their NCD policies and programmes.

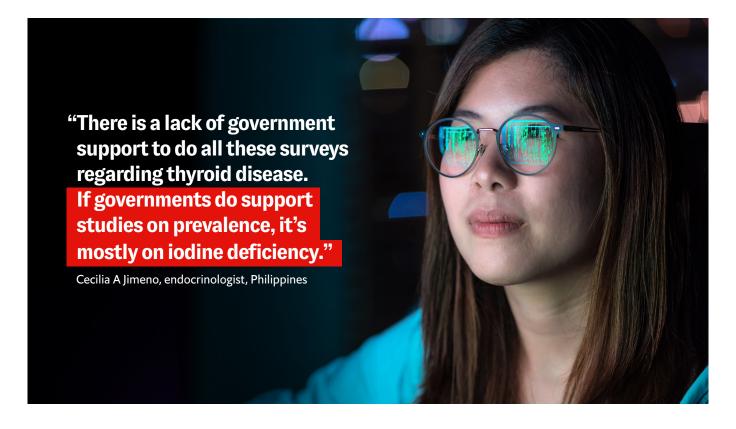
Access to health services

The uneven distribution of healthcare resources and infrastructure lead to variations in access to diagnostic testing, specialist care (such as endocrinologists or obstetricians) and disease management, particularly affecting those living in rural areas.^{70,71} For example, members of our expert panel told us that it can take 3-5 days for foetal cord blood thyroid-stimulating hormone (TSH) test results to be returned to district-level hospitals in Malaysia. As large archipelago island nations, the Philippines and Indonesia face challenges in access to healthcare facilities and provision of necessary diagnostic tests and specialist treatment.^{72,73}

The cost of testing

In general, there is a substantial cost associated with diagnostic tests for thyroid disease, and experts across APAC have cited cost of testing as an ongoing barrier to access.⁷⁴⁻⁷⁶ Widely used diagnostic tests for thyroid function require laboratory processing, whereas point of care (POC) tests are now available that can give results in minutes and do not need to be sent off to a laboratory.⁷⁷⁻⁷⁹ Such POC tests make thyroid testing physically and economically accessible to people living in areas that may be physically inaccessible or lack formal healthcare facilities.^{80,81}





Bridging the evidence and practice gap

National prevalence data

Data are needed on the prevalence of iodine deficiency and thyroid disease to help policymakers better understand the burden of the disease, develop treatment guidelines and effectively allocate healthcare resources.82 Existing data for APAC are often outdated or non-existent (Appendix 2), despite international priority given to iodine deficiency surveillance in recent years.83,84 The two key global sources of data on dietary iodine, UNICEF and the Iodine Global Network/WHO, are based on data from surveys conducted more than ten years ago (Appendix 2). Although outdated, such global sources are helpful when comparing across countries (for example, diagnostic thresholds, assay sensitivities and study populations).85

Funding challenges in research

Securing funding for thyroid disease research is difficult in the context of competing priorities and limited resources. 86-89 This contributes to the lack of comprehensive data and research on thyroid disease, which in turn means a lack of support for its prioritisation—a vicious cycle that is challenging to break. 88,89

One solution proposed by the expert panel to address this funding gap is for non-governmental organisations (NGOs) to fund smaller-scale national studies to either gather prevalence data or to pilot new interventions to test their feasibility and acceptability. Such data could provide the evidence base needed for policymakers to act or further research to be funded to advance understanding and management of these conditions.

Economic assessment and policy implications

In addition to prevalence studies, our expert panel felt that economic assessments to quantify the financial impact of thyroid disease on APAC healthcare systems and economies are another key tool to support policymakers in prioritising thyroid disease as a public health concern.90 This includes evaluating the cost-effectiveness of screening programmes, treatments and other preventive measures to optimise resource allocation and improve health outcomes.91 For example, one 2019 analysis estimated that 1.6m newborns across APAC were iodine deficient, which could lead to lifelong productivity losses totalling US\$2.9bn.92 These are the type of data needed to alert policymakers to the scale of the problem and catalyse further action. The expert panel suggested that an in-depth economic study on the cost of undiagnosed congenital hypothyroidism or iodine deficiency could be piloted in one APAC country and used by others as a proxy.

There is ongoing debate globally regarding universal screening for thyroid dysfunction in pregnant women, as studies show mixed conclusions about its cost effectiveness. This is despite the fact that many organisations, such as The Endocrine Society in the US, advocate for implementation of this policy. Lack of consensus reinforces the need for regionally focused research that reflects the local epidemiological context and other regional factors.

Collaboration on clinical guidance and policy development

The expert panel discussed the urgent need for collaborative efforts to set global standards in promotion, prevention, medication and management of thyroid disease. Bringing patients, healthcare providers, policymakers and industry stakeholders together is necessary to

tackle the complexities in care coordination that may be inhibiting optimal thyroid care. Collaboration at the national level can also help establish evidence-based clinical guidelines on improving thyroid care. For example, Indonesia's clinical practice guideline for hyperthyroidism, developed by the Indonesian Task Force on Thyroid Disease, serves as a valuable resource for healthcare professionals in accurately diagnosing and treating hyperthyroidism.95 The Korean Thyroid Association's national guidelines for subclinical hypothyroidism take a countryspecific approach that considers patient age, health conditions and treatment implications, offering personalised recommendations for optimal care.96

"By developing a set of recommendations and guidelines specific to APAC,

it will give every country something to aspire to."

Paul Yen, endocrinologist, Singapore & APAC

The experts we consulted also emphasised the potential for regional collaboration among major thyroid and endocrine associations to develop common guidelines and recommendations. Organisations specific to APAC include the Asia and Oceania Thyroid Association and the Asia-Pacific Society of Thyroid Surgery. Our expert panel felt that such collaborative guidelines could provide a framework for localisation, thereby promoting consistency and quality in thyroid care across different settings. The existence of such a framework could help prevent neglect of certain types of thyroid care in national clinical guidance, such as measuring thyroid hormone levels in women before they conceive.

Policy takeaways

The following policy takeaways reflect the findings of the research programme, providing direction on next steps for regional and country-level action on thyroid disease in APAC.

Key strategies for implementing data gathering through surveillance

- Regularly surveying iodine levels and thyroid prevalence enables health authorities to gauge the scale of thyroid disease and what interventions are needed where.
- Piloting new approaches such as targeted screening and testing innovations helps policymakers to understand their feasibility and clinical/cost effectiveness.

Key strategies to focus screening on high-risk groups

- Actively screening high-risk groups, such as pregnant women, helps improve detection.
- Integrating thyroid screening into existing programmes and services is another route to improved detection that could be explored.

Key strategies for raising awareness amongst the public and healthcare professionals

- Raising awareness among primary care professionals and the public through education could lead to more people considering it as the cause of non-specific symptoms.
- Evidence-based clinical guidelines and categorising thyroid disease as an NCD are other routes to increased awareness.

Key strategies for collaborating on standardised regional clinical guidelines

- Developing regional guidelines—using an inclusive and participatory methodology could support resource-limited countries by enabling them to pool resources and expertise.
- Working regionally can also provide perspectives for countries where patients are not mobilised to participate.

Making it happen ongoing APAC efforts to tackle thyroid disease

Implement surveillance and prioritise research

Existing research initiatives

Several countries in APAC currently have research initiatives underway to advance the understanding of thyroid disease. Countries looking to do the same may want to explore these examples as research best practice.

In **Malaysia**, the nationwide MyEndo-Thyroid study commissioned by the Malaysian Endocrine and Metabolic Society is examining the prevalence of thyroid disease and its association with ethnicity and iodine status, offering valuable insights into disease epidemiology.⁹⁷

Similarly, **Indonesia** is leveraging data from the National Health Survey, newborn screening programmes and targeted screenings of highrisk populations to assess thyroid disease prevalence and its impact on quality of life and productivity, as well as advocating for increased government focus in this area. This initiative, run by government bodies and medical associations, has led to significant policy changes, including the introduction of screening programmes for high-risk populations like pregnant women. Although these initiatives

are in progress, they show how existing data can be harnessed to inform policy practice.

In the **Philippines**, the Expanded National Nutrition Survey, which is conducted every five years, has consistently tracked iodine deficiency trends.98 However, challenges persist in comprehensively capturing data on related thyroid disease. For instance, the survey does not capture diseases related to iodine deficiency, such as goitres or other forms of thyroid dysfunction. The 2008 National Nutrition Survey aimed to address this gap and included a sub-study (PhilTiDes) to understand the prevalence of both goitres and thyroid disorders in the Philippines, covering all 17 regions and 80 provinces.58 However, the data are now outdated, emphasising the need for ongoing research and sustainable funding to address gaps in thyroid disease surveillance.

Focus on high-risk groups

Tackling congenital hypothyroidism in Malaysia

In Malaysia, congenital hypothyroidism affects approximately 1 in 3,000 live births and it is estimated that at least 180 babies are born with congenital hypothyroidism each year.⁷⁷ Screening for congenital hypothyroidism has



been included in neonatal universal screening programmes in government hospitals since 2003. Despite this, its implementation and postscreening management has varied between institutions and healthcare facilities over the years. In 2021, to standardise the quality of care across all healthcare facilities, the Ministry of Health and the Malaysian Endocrine and Metabolic Society (MEMS) jointly released the Consensus Guidelines on Screening, Diagnosis and Management of Congenital Hypothyroidism in Malaysia.⁷⁷ These guidelines offer practical step-by-step guidance for healthcare staff caring for newborns, to ensure systematic screening of hypothyroidism, follow-up actions and preventing mental retardation because of congenital hypothyroidism.⁷⁷ By developing these guidelines and standardising care, MEMS and the health ministry additionally hope to

improve the quality of data collection to support research efforts and allow for the ongoing improvement of management strategies to address congenital hypothyroidism.

One area of concern noted during the establishment of these clinical guidelines was the potential for inadequate follow-up of newborns for thyroid function testing. Given the fluctuations in thyroid hormones following birth, the gold standard for testing is venous blood sampling at 48-72 hours of life, when TSH levels have stabilised. 99-101 However, this was not considered viable in the Malaysian health system owing to early discharge practices postlabour and long laboratory turnaround times. As such, cord blood TSH testing was prioritised to maximise the number of infants screened and allow for timely identification, re-call and further evaluation of infants if abnormalities are detected. 102 This example highlights the importance of countries adapting policies to achieve context-specific best practice.

Ramping up newborn screening in Indonesia

The Indonesian Ministry of Health mandated newborn congenital hypothyroidism screening in 2014, making it the only condition covered by newborn screening in the country.⁵⁵ The cost of screening was not covered by national health insurance, meaning that costs shifted onto states and individuals, limiting its reach.⁵⁵ By 2020 only 2% of newborns were being screened for congenital hypothyroidism.⁵⁵ The government has taken key steps to address poor uptake, firstly increasing laboratory capacity from five to 11, which translated into a rise to 10% coverage of newborns.⁵⁵ In 2023 the government introduced a policy that linked newborn screening for congenital hypothyroidism to national insurance to further boost screening rates.39

Targeted screening and treatment of thyroid disease during pregnancy in India

The prevalence of hypothyroidism in pregnant women in India is estimated to be between 4.8% and 13%.18 In addition, cities located inland—Delhi, Ahmedabad, Kolkata, Bangalore and Hyderabad—report a significantly higher prevalence (11.7%) than those in coastal regions-Mumbai, Chennai and Goa, with prevalence of 9.5%.¹⁰³ In 2014 the Ministry of Health and Family Welfare developed a set of national guidelines for the screening and treatment of hypothyroidism during pregnancy aimed at reducing maternal, foetal and neonatal complications associated with the disease.104 These guidelines were part of the wider reproductive, maternal, newborn, child and adolescent health strategy launched in 2013 by the National Rural Health Mission. 105 This was implemented across India in a phased manner, starting with medical colleges in the first phase, followed by district hospitals, community health centres and primary health centres in phase 2. These guidelines outline screening and treatment protocols for earlier diagnosis and treatment.104

In 2017 the American Thyroid Association (ATA) released new guidelines that outlined more extensive criteria for identifying pregnant women considered to be at high risk of hypothyroidism. ¹⁰⁶ It is estimated that if these criteria were incorporated into India's national guidelines, a significant proportion of pregnant women in India would be classified as high risk. It has therefore been suggested that this, alongside the ongoing high rates of iodine deficiency and gestational hypothyroidism, make a case to transition from targeted screening to universal screening for thyroid disease in pregnant women. ¹⁰⁷

There are also concerns that important aspects of India's current guidelines are outdated and do not reflect the current evidence base. For example, they currently do not include a national pregnancy-specific TSH reference range, whereas the ATA now recommends defining criteria for this based on evidence that the fixed cut-offs used previously were leading to high false-positivity rates for hyperthyrotropinemia (7.4%-27.8%). 106,107 In addition, a consensus statement from the Indian Thyroid Society recommends screening



for Thyroid Peroxidase Antibodies (TPO Ab, an indicator of hypothyroidism) in pregnant women with a TSH concentration of 2.5-10.0 mU/L.108 ATA guidelines also provide specific treatment recommendations in cases of TPO Ab positivity. TPO Ab screening is not currently included in India's national guidelines and there is no specific mention of a treatment and management plan for those who test positive for TPO Abs. There is therefore a need for India to review its guidelines to ensure that they reflect the current evidence base.



From preconception to neonatal thyroid care—a holistic approach to maternal and child health in China

In 1981 the Chinese government introduced newborn screening as a public health policy to prevent genetic diseases with "significant preventative effects".⁵¹ As of 2017, the coverage of congenital hypothyroidism and hyperphenylalaninemia screening is 97.5% nationwide.⁵¹

In 2010 the Chinese government rolled out a nationwide preconception care programme as a part of a wider welfare project. The preconception programme, which is comprised of several routine check-up test items, including thyroid function tests to determine maternal thyroid status, has been found to be effective in reducing birth defects and adverse pregnancy outcomes due to thyroid dysfunction. ¹⁰⁹ China's social insurance system provides maternity insurance, which is funded by employer contributions, that includes immunisations and disease screening. ^{110,111}

The Chinese Society of Endocrinology and the Women's Health Care Branch of the Chinese Preventive Medicine Association jointly developed guidelines for preventing and managing thyroid disease during pregnancy and the perinatal period. The guidelines establish a rating system that can be used to assess "low, average, moderate-high, and high risk" based on the severity of the thyroid disease. 113

Overcoming geographical isolation for adult and newborn screening in the Philippines

In 2023 the Thyromobile project (partsponsored by Merck) was launched, with the aim of increasing national awareness on thyroid health and taking thyroid disorder prevention, diagnosis and therapeutic services into remote, iodine deficient areas via vehicle.¹¹⁴ Fifteen provinces were included in total, all with median iodine intakes below 100ug/L at last survey, undertaken in 2018/19.¹¹⁵ Services provided include goitre screening, thyroid ultrasounds, and blood tests for thyroid hormones and iodine levels, with a particular focus on targeted pregnant and lactating women.¹¹⁵ This initiative is a public-private partnership that includes the lodine Global Network, the Philippine Thyroid Association, and other local and international partners.¹¹⁶

Newborn screening in Indonesia has been limited to certain areas owing to geographical challenges.⁵⁵ The Philippines has overcome similar geographical challenges by switching to dried blood samples for newborn screening, so that samples can be taken in remote locations then processed in labs elsewhere.¹¹⁷ A key enabler of this change in practice is that the cost of taking, transporting and processing the sample are covered by national health insurance.¹¹⁷

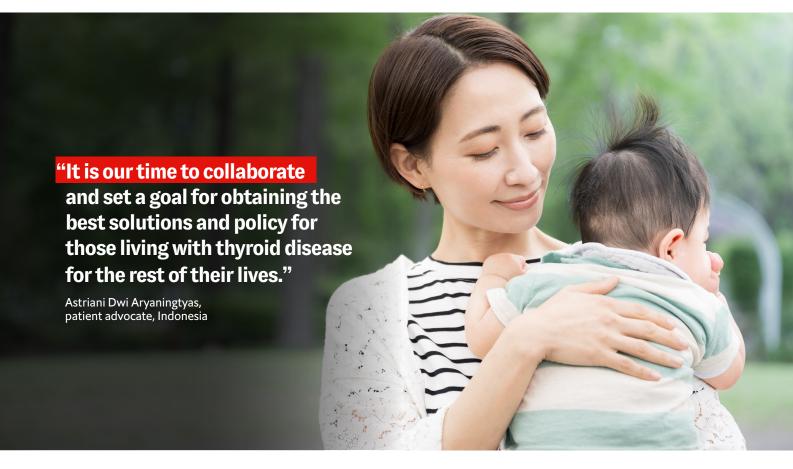
Addressing thyroid disease in older people in China

Thyroid disease is particularly common among older adults in China, with this age group accounting for 50% of thyroid disease cases. 118 However, the diagnosis and treatment of thyroid disease in older adults are challenging for several reasons. This includes physiological changes in the hypothalamic-pituitary-thyroid axis (which regulates metabolism and stress), comorbidities, and the decline in various organ functions. To improve the clinical management of thyroid disease and promote healthy ageing in China, a cross-discipline team from the Endocrine Metabolic Diseases Group of the Chinese Geriatrics Society and the Thyroid Group of the Chinese Society of Endocrinology developed a consensus statement on the diagnosis and treatment of Chinese elderly

with thyroid disease. Published in 2021, the guidelines highlight that older people are at high risk for thyroid disease and have a high rate of multimorbidity with metabolic diseases and that this should be taken into consideration by healthcare professionals.¹¹⁹ Among other recommendations, the guidelines also advise that screening for hypothyroidism should be conducted during admission to nursing institutions or hospitals, and as part of routine health check-ups, demonstrating how integration into existing pathways can work. The consensus aims to provide the basis for clinical decisions and health management in older people by geriatricians, endocrinologists and general practitioners.¹¹⁸

Improve awareness among the public and healthcare professionals

The NCD Alliance, an NGO set up to drive prevention and control of NCDs, plans to approach the 2025 UN High-Level Meeting on NCDs, where governments will discuss plans to meet global NCD targets as well as the Sustainable Development Goals (SDGs), to advocate for thyroid health promotion and education and the inclusion of thyroid disease as an NCD.¹²⁰ Within the thyroid community, the Thyroid Federation International launched International Thyroid Awareness Week and World Thyroid Day (May 25th) as platforms to encourage national societies and thyroid working groups to provide the public with information about the diagnosis and treatment of thyroid disease. Several organisations in APAC, including the Asia-Oceania Thyroid Association and national bodies, have aligned activities with these awareness-raising calendar events. The theme for World Thyroid Day 2024 was "Thyroid Diseases are NCDs", reflecting the importance that the thyroid community places in recognising thyroid disease as an NCD.¹²¹



Foster multidisciplinary collaboration on standardised clinical guidelines

A multidisciplinary approach to congenital screening in India

Congenital hypothyroidism affects about 1 in 1,031 term neonates from non-endemic iodine deficient regions of India, 1 in 13 term neonates from endemic iodine deficient regions, and 1 in 20 neonates born to mothers with thyroid disorders.14 The government has also recognised that low screening rates for congenital hypothyroidism are an issue in India.14 The Rashtriya Bal Swasthya Karyakram (RBSK) programme for child health screening and early intervention services was first launched in 2013. This programme involves the screening of children from birth to 18 years of age for the so-called four Dsdefects at birth, diseases, deficiencies and development delays. This has grown over the

years to include 32 common health conditions, including congenital hypothyroidism.¹²² Although the implementation of RBSK varies across different states, it aims to utilise community public healthcare resources for screening and relies on referrals and crossreferrals between secondary and tertiary healthcare units for efficient diagnosis and treatment management of these conditions. 123 This multidisciplinary and holistic approach of the RBSK programme allows for effective collaboration between experts, which can help to streamline the screening and identification of diseases and allow for comprehensive and integrated care to be provided to all children, leading to improved child health outcomes.¹²⁴ The RBSK initiative emphasises the importance of multi-sectoral coordination among public health professionals, endocrinologists and paediatricians to make screening for and identifying thyroid conditions efficient.125

Appendices

Appendix 1: Background to thyroid disease

Normal thyroid function is critical for optimal body functions such as metabolic regulation, body temperature, heart rate and menstruation. The term "thyroid disease" describes several conditions that prevent the thyroid from producing hormones within a healthy range: hypothyroidism, hyperthyroidism, congenital hypothyroidism (CH) and, more rarely, thyroid cancer. They are associated with the risk of developing more serious conditions, including cardiovascular diseases, pregnancy complications, metabolic diseases, obesity, renal disease, and depression and anxiety disorders. 2-4

Diagnosis and treatment

Thyroid disease has a broad range of presentations, impacting a range of bodily functions and affecting almost every organ system.³ The diagnosis of thyroid dysfunction is predominantly based on biochemical confirmation of thyroid-stimulating hormone (TSH) levels—the most sensitive marker of thyroid status—alongside thyroxine (T4) and triiodothyronine (T3) levels. High TSH and low

T4 levels equate to an underactive thyroid (hypothyroidism), whereas low TSH and high T4 levels equate to an overactive thyroid (hyperthyroidism).³

One of the main goals of thyroid disease treatment is to return the individual to a euthyroid state (normal thyroxine levels), resolve the signs and symptoms, and improve or at least preserve—quality of life. 130,131 Treatment of thyroid disease depends on the type of disorder. Hypothyroidism is treated using medicines that replace the hormones that the thyroid gland is unable to produce.¹²⁷ This is usually through the once-daily intake of an oral pharmaceutical, levothyroxine. 127 An underactive thyroid is a lifelong condition, so a patient will normally be required to take levothyroxine for the rest of their life. Hyperthyroidism is treated with medicines, radioiodine therapy or thyroid surgery to bring thyroid hormone levels back down to normal. 132 Pharmaceutical treatment for hyperthyroidism consists of taking thioamides, a group of medicines that stop the thyroid gland producing too much thyroid hormone. Radioiodine therapies use iodine to kill overactive thyroid cells and shrink the enlarged thyroid gland to limit its thyroid hormone production. 128,133,134

Epidemiology and risk factors

Thyroid disease is among the most commonly encountered endocrine disorders globally.3 It is associated with significant physical, mental, social and economic burden.8 It is estimated that 200m people globally have a thyroid disorder.² National-level prevalence and incidence of thyroid dysfunction are difficult to compare across countries owing to differences in diagnostic thresholds, assay sensitivities, population selection and fluxes in iodine nutrition and population dynamics. Although thyroid disease is not a major cause of mortality, it contributes to disability and reduced quality of life.9 In India it is estimated that approximately 42m people are living with a form of thyroid disease.1 Hypothyroidism is the most common, with a prevalence of 11%, which is significantly higher than in countries such as the US (4.6%) and the UK (2%).1 Overall, there are minimal data available for APAC, limiting the ability to understand the current epidemiology of thyroid disease; available data are largely outdated.

Thyroid disease does not affect all populations equally, and prevalence of thyroid dysfunction can vary by age, sex, race/ethnicity and geographical location (through variations in dietary iodine intake). ¹⁰ In Khyber Pakhtunkhwa, Pakistan, it was found that 75.8% of people diagnosed with thyroid disease were female. ¹³⁵ In China prevalence of hypothyroidism is estimated to be around 13.95%, totalling almost 10.7m people, of which 2.8m are men and 7.9m are women. ¹³⁶

Other population groups at increased risk of thyroid disease include:

Pregnant women

During pregnancy, the thyroid gland typically increases in size by 10% and by 20-40% in areas with iodine deficiency. ¹⁰⁶ As such, the

production of thyroid hormones and iodine requirement in the body increases by around 50% during pregnancy, putting strain on the thyroid gland and potentially affecting its functioning.^{15,137,138} Thyroid dysfunction is estimated to affect up to 5-7% of all pregnancies.¹⁷ A study in India found that 13.3% of pregnant women had hypothyroidism.¹⁸

Newborns

Congenital hypothyroidism is one of the most common neonatal endocrine diseases, with a number of genetic and environmental factors contributing to the increased risk of developing the disease. 139 Congenital hypothyroidism incidence was estimated to be higher in several APAC countries (Taiwan, at 5 per 10,000; China, at 4.8 per 10,000; and Japan, at 6.8 per 10,000 births) than in Western countries (3.2 per 10,000 in the US and 3.4 per 10,000 births in England).7 In Malaysia, congenital hypothyroidism affects around 1 in 3,000 live births, and approximately 180 babies are born with the disease annually.77 A study carried out in India showed the impacts of the disease in endemic versus non-endemic iodine-deficient regions among neonates.¹⁴ Neonates born in endemic regions and born to mothers with thyroid disease were most affected by congenital hypothyroidism. The disease affects around 1 in 1,031 neonates from non-endemic regions and 1 in 13 neonates from endemic regions. In addition, 1 in 20 neonates born to mothers with thyroid disease and 1 in 71 preterm neonates were affected by congenital hypothyroidism.14

Older adults

Older adults are also at greater risk for thyroid disease, especially hypothyroidism. Globally, hypothyroidism has been found to affect 5-20% of elderly women and 3-8% of elderly men.¹⁴⁰

A study in Korea found that hypothyroidism affected 3.8% of its population overall, but that the frequency increased in older adults.²⁰ A study in Japan found that older adult patients with subclinical hypothyroidism, a mild form of hypothyroidism, were at increased risk of developing overt hypothyroidism.¹⁴¹ Another study, carried out in India, also found older age to be significantly associated with hypothyroidism.¹⁰³ Evidence has also noted high rates of thyroid dysfunction within the elderly population in Singapore.¹⁴² The rapid global growth in the elderly population has the potential to contribute a significant burden and public health issue.¹⁹

Genetic syndromes

Autoimmune thyroid disease (ATD) is the most frequent cause of acquired thyroid dysfunction in children and adolescents. It most commonly presents as either as Hashimoto's thyroiditis or Graves' disease. A higher incidence of ATD is observed in the context of specific genetic syndromes, such as Down syndrome, Klinefelter syndrome and Turner syndrome.²¹ Thyroid dysfunction may also be observed in other genetic syndromes, such as Prader-Willi or Williams syndrome, but is usually not the result of thyroid autoimmunity. The incidence of congenital hypothyroidism in those with Down syndrome is estimated to be between 1 in 113 and 1 in 141 live births.143 The prevalence of Hashimoto's thyroiditis in these individuals ranges from 13% to 46% and that of Graves' disease is 6.5%.21

The physical, mental, emotional, social and economic burden

Thyroid disease, if left untreated, can significantly reduce overall quality of life, owing to the array of associated physical and mental

symptoms that have emotional, relational, social and working-life impacts. 144-146

Symptoms of hyperthyroidism include nervousness, anxiety, hyperactivity, mood swings, sleeping difficulties, tiredness, muscle weakness, diarrhoea and loss of interest in sex, among others.¹⁴⁷ Physically, those with hyperthyroidism often experience weight loss, vision and hair loss, loose nails, excessive sweating, heart palpitations, and a swelling of the neck caused by an enlarged thyroid.147 Psychological symptoms include anxiety, depression and brain fog; these are often less obvious than physical symptoms but isolating and distressing for people experiencing them.¹⁴⁸ Hyperthyroidism is associated with severe work disability and significant income loss. 149 Conversely, with hypothyroidism, patients experience weight gain, constipation and a slower heart rate. 150 These individuals also have a high prevalence of psychological disorders, including anxiety, cognitive impairment, psychomotor retardation and sleep disorders, all of which can contribute to social isolation and feelings of loneliness.151,152

Thyroid disease is associated with significant and increasing economic cost. In South Korea, the cost-of-illness of thyroid disease was found to be KRW762.2bn (US\$609m) in 2010, 3.4 times higher than in 2002.¹⁵³⁻¹⁵⁵

There are several key areas of focus for addressing the unmet needs of thyroid disease in APAC and to identify opportunities for change. This includes the critical role of primary prevention, screening and early detection, integration of services, patient engagement strategies, data collection and research, and increasing recognition of thyroid disease globally.

Appendix 2 lodised salt legislation, household iodised salt availability and iodine sufficiency in school-age children and pregnant women in APAC

Country	Is there existing salt iodisation legislation? ^{30,32-34}	Mandatory or voluntary legislation ^a	Year of current legislation	% of households consuming salt with any iodine, among all tested households with salt >0 ppm (HIS) ^{26 35}	Date of Survey	Median urinary iodine concentration in school-age children (µg/L of iodine in urine) ^b [Ideal level for school-age children: ≥100 µg/L] ^{24,25}	Date of survey	Median urinary iodine concentration in pregnant women (µg/L of iodine in urine) ^c [Ideal level for pregnant women: ≥150 µg/L) ^{25,36,37}	Date of survey
Afghanistan	Yes	Mandatory	2011	56.9	2015	171	2013	37.5#	2004
Australia	Yes	Mandatory	2009			175	2011/2012		
Bangladesh	Yes	Mandatory	1989	76.5	2019	146	2011/2012	158	2005
Bhutan	No			98.4	2008	183	2010		
Brunei	Yes	Voluntary	2000						
Myanmar	Yes	Mandatory	1998	85.0	2018	139	2016/2017	121.8#	2018
Cambodia	Yes	Mandatory	2003	68.9	2014	235.9	2011	63#	2016
China	Yes	Mandatory	1994	96.6	2018	217	2021	172	2021
Timor-Leste	No			84.5	2016				
India	Yes	Mandatory	2011	94.3	2020	175	2016/2018	173.4	2019
Indonesia	Yes	Mandatory	1994	91.9	2013	215	2013	163	2013
Japan	No					269	2014/2019		
Laos	Yes	Mandatory	1991	94.8	2017	103	2013		
Malaysia	Yes	Mandatory	2020	28.2	2008	109	2008		
Mongolia	Yes	Mandatory	2003	75.6	2018	145	2016	120.5#	2016
Nepal	Yes	Mandatory	1996	94.9	2016	314	2016	241.3	2016
New Zealand	Yes	Mandatory	2009			116	2015	114#	2015
North Korea	No			37.5	2017	97#	2009/2010		
Pakistan	No			80.4	2018	123	2018/2019	108#	2019
Papua New Guinea	Yes	Mandatory	1995	99.0	2005				
Philippines	Yes	Mandatory	1995	57.0	2018	180	2018/2019	121#	2019
Singapore	Yes	Voluntary	1998						
South Korea	No					449	2013/2015		
Sri Lanka	Yes	Mandatory	2005	98.0	2022	233	2016	157.9	2015
Thailand	Yes	Mandatory	2011	93.9	2019	179	2015	154.9	2021
Vietnam	Yes	Mandatory	2016	62.4	2010	84#	2013/2014	83.4#	2019

Notes

a Mandatory versus voluntary. Mandatory salt iodisation legislation requires the iodine fortification of all salt intended for human consumption. Voluntary iodisation legislation allows salt producers to fortify salt only if they choose to do so.

b In population monitoring of iodine status using urinary iodine concentration (UIC), school-age children serve as a proxy for the general population. The UIC data for school-age children have been selected for each country using data from the most recent known, nationally representative survey.

c The UIC data for pregnant women have been selected for each country using data from the most recent nationally representative survey, with additional filters applied where necessary to include (i) both urban & rural populations, (ii) all age groups surveyed, (iii) all trimesters of pregnancy, (iv) all mother's educational levels, and (v) all wealth quantiles.

[#] Median urinary iodine concentration value falls below what is considered adequate for that population group (school-age children: ≥100 µg/L; pregnant women: ≥150 µg/L)¹56

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