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Estimates of resource use in the public-sector health-care system and the effect of strengthening health-care services in Malawi during 2015–19: a modelling study (*Thanzi La Onse*)



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Summary

Background In all health-care systems, decisions need to be made regarding allocation of available resources. Evidence is needed for these decisions, especially in low-income countries. We aimed to estimate how health-care resources provided by the public sector were used in Malawi during 2015–19 and to estimate the effects of strengthening health-care services.

Methods For this modelling study, we used the *Thanzi La Onse* model, an individual-based simulation model. The scope of the model was health care provided by the public sector in Malawi during 2015–19. Health-care services were delivered during health-care system interaction (HSI) events, which we characterised as occurring at a particular facility level and requiring a particular number of appointments. We developed mechanistic models for the causes of death and disability that were estimated to account for approximately 81% of deaths and approximately 72% of disability-adjusted life-years (DALYs) in Malawi during 2015–19, according to the Global Burden of Disease (GBD) estimates; we computed DALYs incurred in the population as the sum of years of life lost and years lived with disability. The disease models could interact with one another and with the underlying properties of each person. Each person in the *Thanzi La Onse* model had specific properties (eg, sex, district of residence, wealth percentile, smoking status, and BMI, among others), for which we measured distribution and evolution over time using demographic and health survey data. We also estimated the effect of different types of health-care system improvement.

Findings We estimated that the public-sector health-care system in Malawi averted 41·2 million DALYs (95% UI 38·6–43·8) during 2015–19, approximately half of the 84·3 million DALYs (81·5–86·9) that the population would otherwise have incurred. DALYs averted were heavily skewed to children aged 0–4 years due to services averting DALYs that would be caused by acute lower respiratory tract infection, HIV or AIDS, malaria, or neonatal disorders. DALYs averted among adults were mostly attributed to HIV or AIDS and tuberculosis. Under a scenario whereby each appointment took the time expected and health-care workers did not work for longer than contracted, the health-care system in Malawi during 2015–19 would have averted only 19·1 million DALYs (95% UI 17·1–22·4), suggesting that approximately 21·3 million DALYs (20·0–23·6) of total effect were derived through overwork of health-care workers. If people becoming ill immediately accessed care, all referrals were successfully completed, diagnostic accuracy of health-care workers was as good as possible, and consumables (ie, medicines) were always available, 28·2% (95% UI 25·7–30·9) more DALYs (ie, 12·2 million DALYs [95% UI 10·9–13·8]) could be averted.

Interpretation The health-care system in Malawi provides substantial health gains with scarce resources. Strengthening interventions could potentially increase these gains, so should be a priority for investigation and investment. An individual-based simulation model of health-care service delivery is valuable for health-care system planning and strengthening.

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Introduction

In all countries, important decisions need to be made regarding how to allocate resources for collective health-care provision. Policy makers need to respond to questions about health, such as which interventions to

offer or not offer as part of service provision to maximise health and reduce health inequalities, the ways available resources should be used and configured, the benefits of strengthening specific parts of the health-care system, how parts of the health-care system should be prioritised,

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Research in context

Evidence before this study

We searched PubMed from database inception to Nov 6, 2023, using the search terms “((healthcare system OR health system) AND (low-income) AND (model*) AND (agent-based OR individual-based))” for articles published in English. We found 32 articles, most of which focused on the effect of one type of intervention for one disease. One article was a systematic review of models for health-care system research that found a preponderance of studies in high-income settings focused on acute care, care of older people, and long-term care services and argued that future work should model health-care systems in low-income and middle-income countries to improve understanding. Another systematic review of health-care system modelling found no studies fulfilling the needs they describe for a mechanistic health-system model worldwide and identified an opportunity to advance modelling methods to understand the relationship between health-care system inputs and outputs.

Added value of this study

To our knowledge, this modelling study is the first to model use of a health-care system in a low-income country via an individual-based approach that included most of the diseases in the population and most of the services delivered by the public-sector health-care system. We estimated that the health-care system in Malawi provided health effects during 2015–19, but was overburdened. Interventions that strengthen service delivery could increase health effects.

Implications of all the available evidence

Health-care service delivery can benefit from analytical evaluations of alternative choices for service delivery and system-strengthening interventions in which the constraints and weaknesses of the health-care system are shown. These evaluations can provide crucial additional information for health-policy decision making and help provide resources to increase the beneficial health effects of health-care systems.

and the planning and consequences of future changes in health-care needs. These questions are fundamental to the operation of every health-care system but are especially important in low-income countries, where ineffective choices lead to larger losses in health than elsewhere.^{1–3}

There has been a rapid expansion in analytics, data, and methods to meet this demand.^{4–8} Although these approaches are a substantial advance in our analytical ability, they do not fully respond to all analytical needs. For example, databases of cost-effectiveness have results that are incomparable or partial,^{9,10} the appropriate cost-effectiveness threshold is not known in some analyses,¹¹ diseases and interventions are considered independently, and estimates do not represent health-care production or weaknesses in health-care systems. None of these approaches alone are adequate to guide the long-term redesign of health-care systems or are adapted to the abundance of epidemiological and systems data that are increasingly available.¹² Consequently, an extremely high value is attached to developing a new approach to developing a form of analysis that can fully address all these issues.^{13,14}

We aimed to estimate how health-care resources provided by the public sector were used in Malawi during 2015–19 and to estimate the effects of strengthening health-care services.

Methods

Model design and parameters

For this modelling study, we used the *Thanzi La Onse* model, an individual-based simulation model (figure 1; appendix pp 61–560). The model comprised a representation of how resources (ie, health-care workers, consumables, facilities, and equipment) were used for

effective health-care services, a representation of the population served by the public-sector health-care system, needs for health care, and policies that governed how resources for health care were arranged to meet these needs. Source code is publicly available¹⁵ and core components of the model have been described elsewhere.^{16–22}

There were four levels of public-sector health-care facilities included in the model (ie, 0=community, 1=primary care, 2=regional referral hospitals, and 3=national referral hospitals).¹⁶ Facilities were specific to each district or region of Malawi; we assumed that resources were pooled among all facilities at level 0 in the same district, among all facilities at level 1 in the same district, among all facilities at level 2 in the same region, and among all facilities at level 3 nationally. Each set of facilities included health-care workers, for which there were nine types (ie, clinical, community, dental, laboratory, mental health, nursing or midwifery, nutrition, pharmacy, and radiography). Each type of health-care worker was assumed to be able to deliver health-care services for a specific number of minutes per day, calculated from the number of staff employed, their contracted hours, and expectations for absences and leave.²³

Health-care services were delivered during health-care system interaction (HSI) events, which we characterised as occurring at a particular facility level and requiring a particular number of appointments (appendix p 2).²⁴ We organised HSIs into groups that provided particular treatment for a particular condition (appendix p 3).

We calculated the difference in the number of appointments with and without a particular service being provided. We defined appointments as a unit of care delivered by one or more types of health-care worker. For example, one HSI could be one antenatal care

See Online for appendix

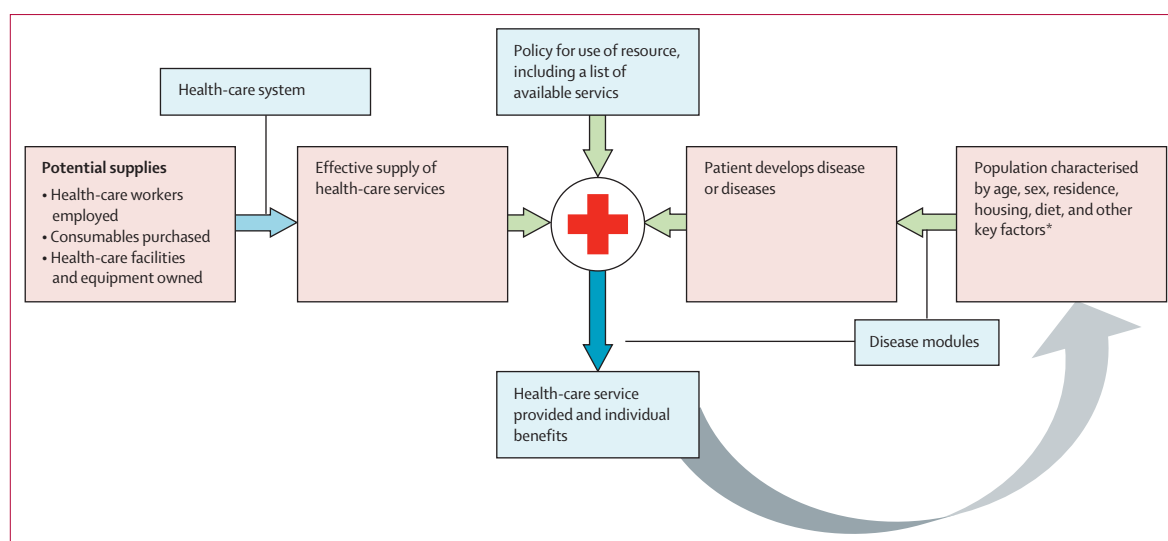


Figure 1: Model design

Grey arrow indicates feedback that was incorporated on the characteristics of the population between health care that was received or not received and patterns of health-care need in the future. *Other key factors are shown in the appendix (p 72).

appointment at a primary care facility with a requirement for 1.0 min of time from a clinician, 11.0 min of time from a nurse or midwife, and 0.4 min of time from a pharmacist. We defined 50 different types of appointment (appendix pp 88–89), grouped into broad categories: consultation with a disease control and surveillance assistant (DCSA); dental; general inpatient or outpatient care; HIV clinic; laboratory services; mental health clinic; nutrition clinic; pharmaceutical dispensing; radiography; reproductive, maternal, newborn, and child health; and tuberculosis clinic.²³ During an HSI event, consumables (ie, medicines, diagnostics, and other items needed to provide care such as gloves and syringes) could have been required; the *Thanzi La Onse* model tracked whether those consumables were available at each facility level in each month and in each district.¹⁷

We developed mechanistic models for the causes of death and disability that were estimated to account for approximately 81% of deaths and approximately 72% of disability-adjusted life-years (DALYs) in Malawi during 2015–19, according to the Global Burden of Disease (GBD) estimates (appendix p 2).^{25,26} The disease models could interact with one another and with the underlying properties of each person to estimate, for example, the risk of several diseases due to the same risk factor and of one disease increasing the risk of acquisition or the severity of another. We collectively and phenomenologically modelled causes of death for additional risks of death that matched age-specific, sex-specific, and period-specific GBD estimates.²⁶ Generic symptoms that might arise from these causes could occur and, as with other symptoms, could have led to health-care seeking.

When a person developed symptoms of ill health or became pregnant they might have sought health care,

either immediately or after a delay and at a particular facility level. In the *Thanzi La Onse* model, the probability of care seeking depended on symptoms, sex, age, wealth, and residence (eg, urban or rural) based on previous self-reports of behaviour.^{20–22} If a person never sought health care, then no health care was provided.

When health care was needed, we entered the corresponding HSI for that individual into a queue at the relevant facility level and district. Each day in the simulation, and for each queue, we compared the total requirement for time of health-care workers with the time of health-care workers that was available. If there was sufficient time for each health-care worker to meet all calls, all HSI events were run. If there was insufficient time for at least one type of health-care worker, two assumptions were possible: elastic constraints, whereby all HSIs were run but the time allocated to each was reduced or the time of health-care workers was increased, or hard constraints, whereby each appointment took the time expected and health-care workers did not work for longer than contracted, so low-priority HSIs were postponed to the next day or did not happen at all.

When an HSI event was run, we logged consumables used during the treatment and simulated the beneficial effect of treatment provided. If the effectiveness of a treatment was contingent on a consumable (ie, a medicine) that was not available at the time and at the facility, we did not simulate the beneficial effect of the treatment and the HSI event might have been rescheduled, depending on the health-care seeking behaviour assumptions made for that HSI.

The various appointment types could be requested through multiple types of treatment (appendix p 4), all of

which used the same available time of health-care workers, and all HSI events had the same pattern of consumables availability. Consequently, the model represented all different types of care with the same finite resources.

We estimated the effect of different types of health-care system improvement (table). Improvements were those for which many health-care systems aim²⁷ and represent changes that provide easy and quick access to care; improved service delivery; and improved availability of medicines, diagnostics, and other consumables.

The scope of the model was health care provided by the public sector in Malawi during 2015–19. The public sector provided 66% of all facilities and more than 98% of all outreach and village clinics in 2016.²⁸ To test the external validity of our model, we compared our outputs with the 2018 Malawi Census,²⁹ World Population Prospects (WPP),³⁰ GBD data,^{25,26} and data from preprint publications.^{31,32}

The *Thanzi La Onse* project received ethical approval from the Malawi College of Medicine research ethics committee (P.10/19/2820).

Data sources

Each person in the *Thanzi La Onse* model had specific properties (ie, sex, district of residence, wealth percentile, smoking status, and BMI; appendix p 72), for which we measured distribution and evolution over time using demographic and health survey data.^{15,33}

We compared both demographic outputs of the model (appendix p 6) and total number of deaths that occurred in the model with available data.

The total number of each type of appointment delivered during 2015–19 was compared with records in the electronic medical records system of all public-sector health-care facilities in Malawi.^{16,34}

We modelled the method of contraception used by each woman, or use of no contraception, to match the detailed contraception calendar data in the demographic and health survey data.¹⁸ Together with estimates of fertility and the effectiveness of the contraceptives, we established the chance of conception for each woman. We

mechanistically modelled pregnancy, labour, and delivery and calibrated them to match available data, as shown in a preprint paper (appendix p 1).¹⁹

Consumable data were empirical estimates of frequencies at which consumables went out of stock.¹⁷

Processes regarding how the quality of data was assessed and how the model was calibrated are provided in the appendix (pp 100–263).

Only publicly available, anonymised, secondary data were used in the *Thanzi La Onse* model. Therefore, individual informed consent was not required, as deemed by the Malawi College of Medicine.

Statistical analysis

Our simulation started on Jan 1, 2010, with a representative model population (ie, one person in the model represented approximately 145 real people in Malawi). Jan 1, 2010, was chosen as a start date to allow for 5 years of burn-in (ie, the initial period of the simulation that is discarded to minimise the effect of initial value of model results). The central estimate of computed statistics was the median; uncertainty intervals (UIs) were the 2·5th to 97·5th percentiles across ten runs of the model with the same parameter values.

The *Thanzi La Onse* model logged the date and nature of all demographic characteristics, disease-related events, and HSI events. We computed DALYs incurred in the population as the sum of years of life lost (ie, when a death occurred, the number of life-years lost was equal to the difference between the age at death and a reference value for life expectancy)³⁵ and years lived with disability (ie, the disability for each individual from all conditions was measured monthly and combined additively).³⁶

We programmed the model in Python language version 3.8 and used pandas data analysis library 2.³⁷

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

	Constraints on human resources for health	Health-care seeking	Function of the health-care system	Availability of consumables
Status quo	Elastic*	As per data ^{18–20}	As per data†	As per data ¹⁷
Perfect health-care seeking	Elastic*	All people with a new symptom of ill health seek care immediately	As per data†	As per data ¹⁷
Perfect health-care seeking and function	Elastic*	All people with a new symptom of ill health seek care immediately	All routine and specifically indicated screening, diagnostics, and referrals were completed and health-care worker performance was optimal‡	As per data ¹⁷
Perfect health-care seeking, function, and consumables availability	Elastic*	All people with a new symptom of ill health seek care immediately	All routine and specifically indicated screening, diagnostics, and referrals were completed and health-care worker performance was optimal‡	All consumables available at all facilities all the time

*We assumed all health-care system interaction scheduled to occur at a particular facility on a particular day could occur if the necessary health-care workers were present, which could have involved the time taken for the interaction being reduced or health-care workers doing overtime. †Direct data on the performance of health-care workers in clinical diagnoses, probability of referrals, self-reported diagnosis status, and inference from data on health-care system use. ‡Full specification of each assumption included health-care workers making accurate diagnostic decisions and all necessary screening and referrals occurring (eg, outreach testing for HIV and routine screening for hypertension; appendix pp 45–60).

Table: Scenarios to estimate effects of strengthening of the health-care system in Malawi

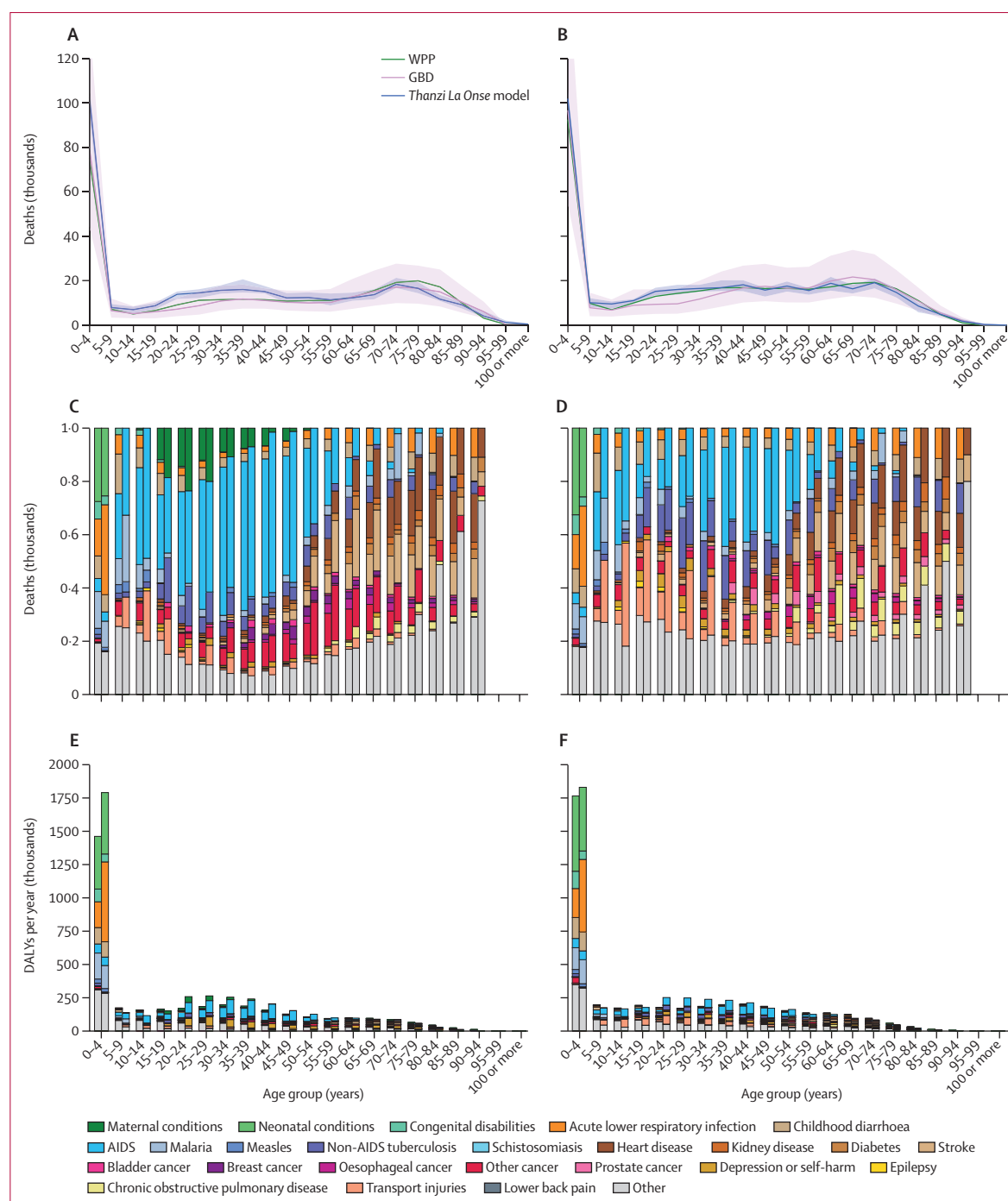


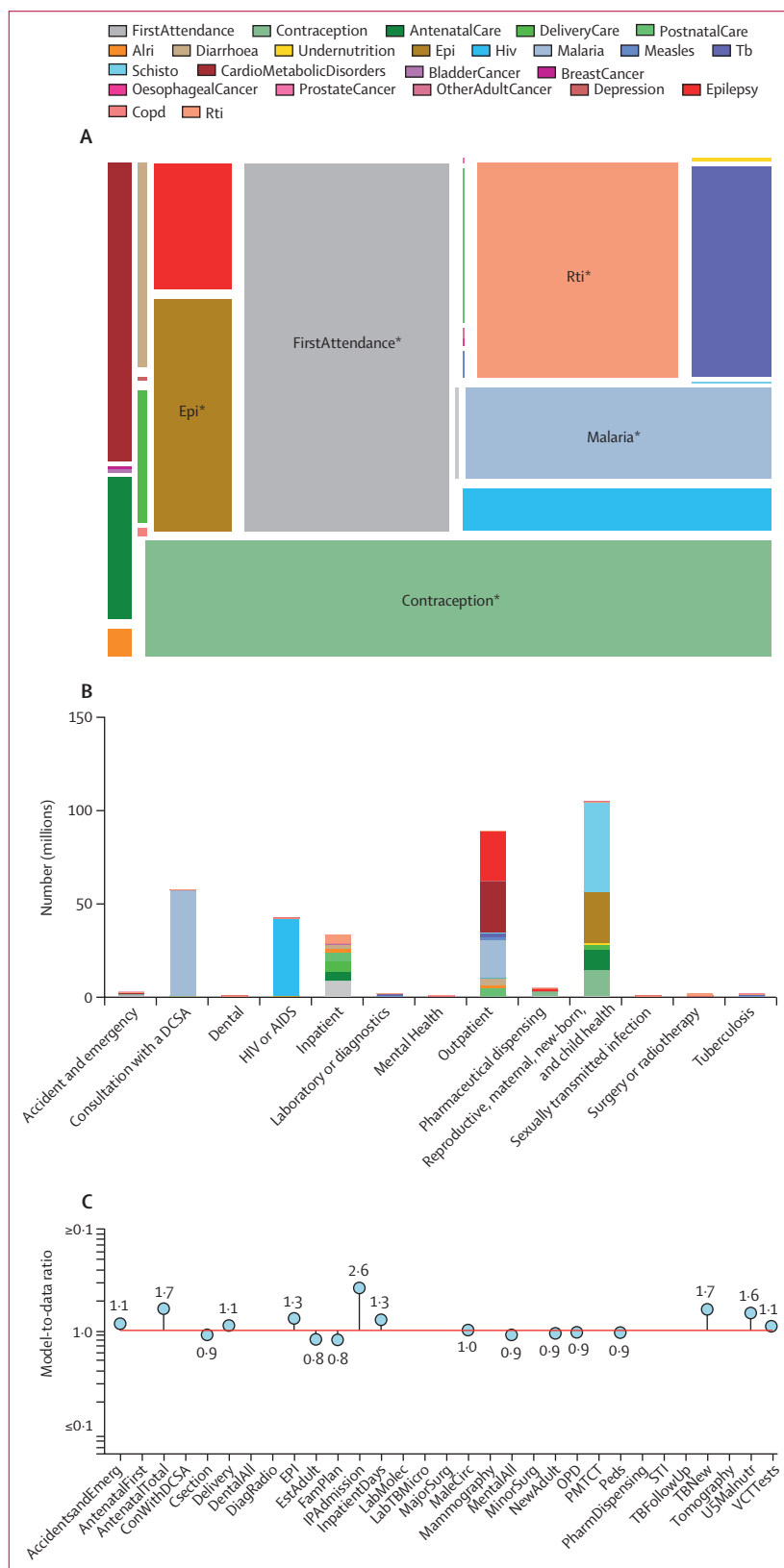
Figure 2: Estimated burden of diseases in Malawi during 2015–19

Estimated number of deaths by age group for female individuals (A) and male individuals (B). Shaded areas show 95% CI. Estimated causes of death by age group in the *Thanzi La Onse* model (right bars) and by GBD (left bars) for female individuals (C) and male individuals (D). Other indicates causes that were not mechanistically represented in the *Thanzi La Onse* model. Estimated DALYs per year by age group in the *Thanzi La Onse* model (right bars) and by GBD (left bars) for female individuals (E) and male individuals (F). All mechanistically modelled causes are listed in the figure key. DALY=disability-adjusted life-year. GBD=Global Burden of Disease. WPP=World Population Prospect.

Results

During 2015–19, population-size growth, the population pyramid, the number of live births, and the

distribution of ages of mothers estimated by the *Thanzi La Onse* model matched census²⁹ and WPP³⁰ data (appendix p 6). Number of deaths, both total and



by age group or sex, estimated by the model were similar to GBD^{25,26} and WPP³⁰ data (figure 2A, B). Distributions of causes of deaths and DALYs estimated by the model were similar to GBD^{25,26} estimates (figure 2C–F; appendix p 7). Discrepancies between the model and other data were mostly for transport injuries, depression or self-harm, and HIV or tuberculosis (figure 2C–F; appendix p 7). However, in these domains, model outputs matched previous national or preprint data.^{31,32}

Most HSIs were attributable to initial triaging, contraceptive services, routine immunisation, care needed for malaria, care after road traffic injuries, and care for HIV and tuberculosis (figure 3A). Appointment types needed most frequently were reproductive, maternal, newborn, and child health; outpatient care; consultation with DCSA; and HIV clinic (figure 3B). No data were captured at facility level 0.

Numbers of each type of appointment delivered during 2015–19 estimated by the model matched records in the electronic medical records system; the model-to-data ratio was close to 1.0 for most types, including the appointment types needed most (figure 3C). Some less common appointment types had a model-to-data ratio of more than 1.0, up to 2.6.

We estimated that the public-sector health-care system in Malawi averted 41.2 million DALYs (95% UI 38.6–43.8) during 2015–19, approximately half of the 84.3 million DALYs (81.5–86.9) that the population would otherwise have incurred. DALYs averted were heavily skewed to children aged 0–4 years due to services averting DALYs that would be caused by acute lower respiratory tract infection, HIV or AIDS, malaria, or neonatal disorders (figure 4A; appendix p 8). DALYs averted among adults were mostly attributed to HIV or AIDS and tuberculosis (figure 4A). The distribution of DALYs averted by wealth percentile showed a modest skew in favour of those in the highest wealth percentile (figure 4B; appendix p 9).

Service types with the largest DALYs averted were for HIV or AIDS, contraception, malaria, acute lower respiratory tract infection, tuberculosis, and routine vaccination (figure 4C). Interaction between diseases led to the effects of a health-care service being distributed across several causes of DALYs. For example, HIV services averted deaths due to childhood diarrhoea as well as to AIDS, and contraceptive services averted deaths

Figure 3: Estimated resource use in the health-care system in Malawi during 2015–19

(A) Estimated health system interaction events that occurred in the model health-care system, by service provided. (B) Estimated number of appointments for each service provided. (C) Model-to-data ratio of appointments per year in the *Thanzi La Onse* model with electronic medical records. Please note that model scenario names have not been edited. DCSA=disease control and surveillance assistant.

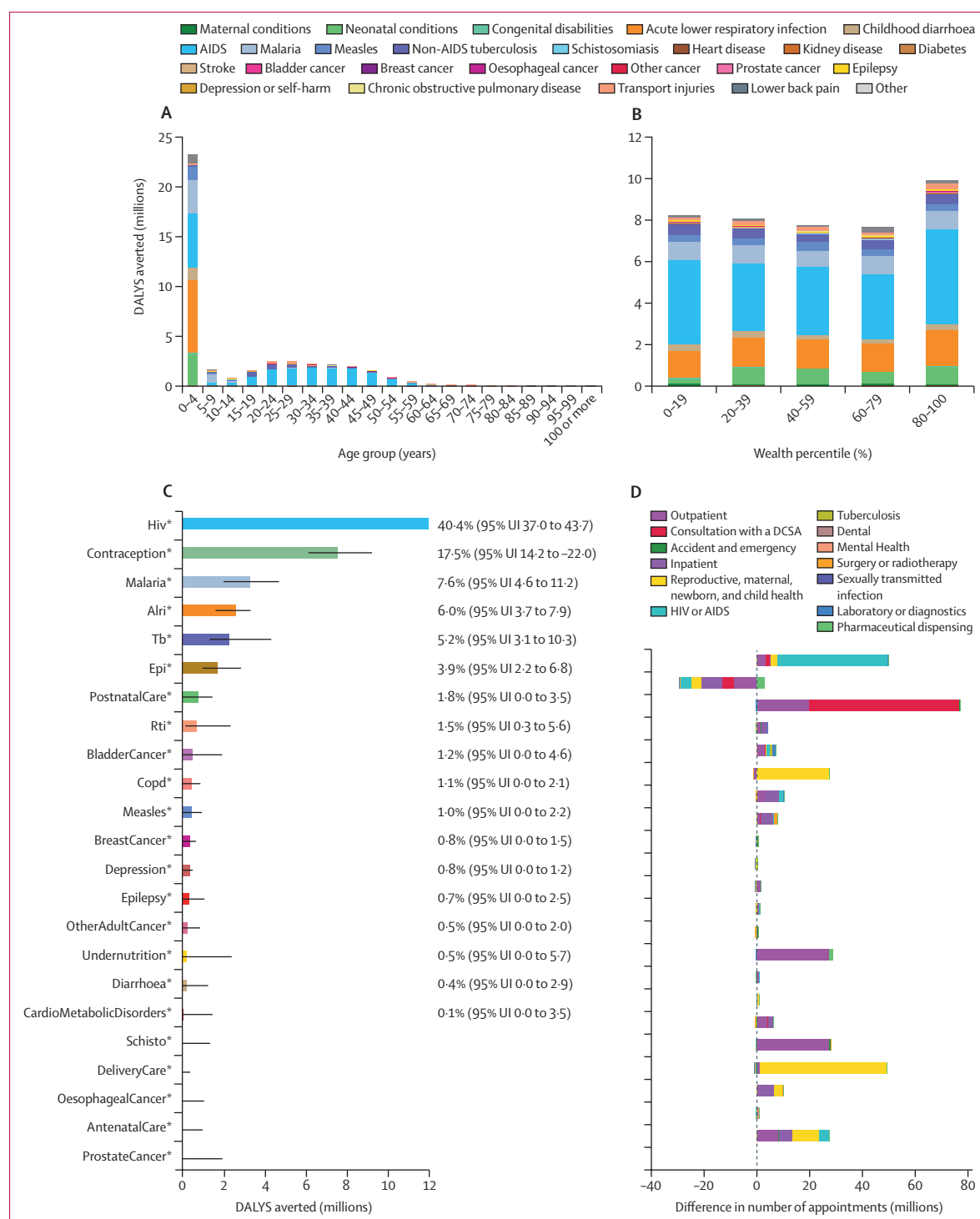


Figure 4: Estimated effect of health-care services in Malawi during 2015–19

Estimated DALYs averted by all health-care services in Malawi by age group (A) and wealth percentile (B). (C) Estimated effect of each service as number of DALYs averted (bars; black lines show 95% UI) and percentage of DALYs incurred when all interventions were available (annotations). (D) Difference in number of appointments needed when each service was provided. Please note that model scenario names have not been edited. DALY=disability-adjusted life-year. UI=uncertainty interval.

among children aged 0–4 years due to neonatal disorders, acute lower respiratory tract infection, malaria, and childhood diarrhoea (appendix p 10).

We estimated that different services had different magnitudes of and requirements for resources (figure 4D), which were not necessarily in proportion to the health

effect they generated. For example, appointments required for tuberculosis services were relatively few but the health gain they generated was among the greatest of all services offered (figure 4C). Furthermore, providing contraceptive services, which had a large health effect (figure 4C), led to fewer appointments overall as there were fewer interactions associated with care for neonates, more than compensating for increased needs for pharmacy dispensing appointments for contraceptives.

In the status quo scenario, there was a mismatch between the total amount of services provided, the time of health-care workers that was available, and the time expected to be required to provide each service. This mismatch affected some types of care more than others (appendix p 11); for example, relevant health-care workers were less available for emergency care and surgical services than they would have needed to be to meet all health-care needs. Under the hard constraints assumption, the effect of the health-care system was reduced as fewer services could be provided. In that scenario, the health-care system in Malawi during 2015–19 would have averted only 19·1 million DALYs (95% UI 17·1–22·4; appendix p 12), suggesting that approximately 21·3 million DALYs (20·0–23·6) of total effect were derived through overwork of health-care workers.

Many HSIs had at least one essential consumable not be available; many of the most frequently needed items were not available on up to 40% of occasions (appendix p 13). For acute conditions, people might not have benefitted from treatment, whereas for long-term conditions, there could have been delays or additional HSIs.

Compared with the status quo scenario, if people becoming ill immediately accessed care, 8·4% (95% UI 4·8–12·1) more DALYs (ie, 3·7 million DALYs [95% UI 2·0–5·3]) could be averted (figure 5). If, in addition, all referrals were successfully completed and the diagnostic

accuracy of health-care workers was as good as possible, 20·9% (95% UI 16·5–22·9) more DALYs (ie, 9·0 million DALYs [95% UI 7·0–10·2]) could be averted. If, in addition to those two, consumables were always available, 28·2% (95% UI 25·7–30·9) more DALYs (ie, 12·2 million DALYs [95% UI 10·9–13·8]) could be averted. Despite all the weaknesses, we estimated that the health-care system in Malawi during 2015–19 was functioning almost 80% as well as an idealised system that provided the same set of services (figure 5).

Discussion

We estimated that in Malawi during 2015–19, approximately half of all potential DALYs were averted by the public-sector health-care system. There were strong effects for children aged 0–4 years and, overall, DALYs were largely mediated by programmes for HIV, tuberculosis, malaria, and acute lower respiratory tract infection and by contraceptive services.

In this Article, we present a new approach to answering fundamental questions about service delivery in a public-sector health-care system and applied this approach to data from Malawi. We also showed how the health-care system operated with appointment times or working hours for health-care workers beyond what clinical expectations or contracts allow. However, without flexibility to reduce the time for appointments or for overtime, the effect of the health-care system would be reduced by approximately half. We quantified consequences of other weaknesses in the system during 2015–19, such as delayed health-care seeking, imperfect referral completion and diagnostic accuracy, and consumables being unavailable. If these weaknesses were overcome, the overall effect of the health-care system could have increased by almost 30%. We believe that our individual-based simulation modelling approach could be used to evaluate other issues that have not yet been able to be directly analysed.

Our approach had several strengths. First, it captured a large number of health conditions, transmissions of infectious disease, and developments of conditions during the life course. Therefore, our results capture the indirect effects of different decisions through interactions between diseases and underlying risk factors, and feedback via transmission, giving a fuller characterisation than would be possible under separate modelling approaches. Second, systematic integration of available data for interventions meant our results for different diseases or interventions were comparable, by contrast to results available in the literature that vary in terms of perspective, counterfactual, and outcome measurement.³⁸ Although our approach demanded a lot of data, these demands were met in Malawi and, we believe, can be met in other countries too.

There were several limitations to our approach. First, not all causes of disease or associated interventions were mechanistically represented in the model, so the

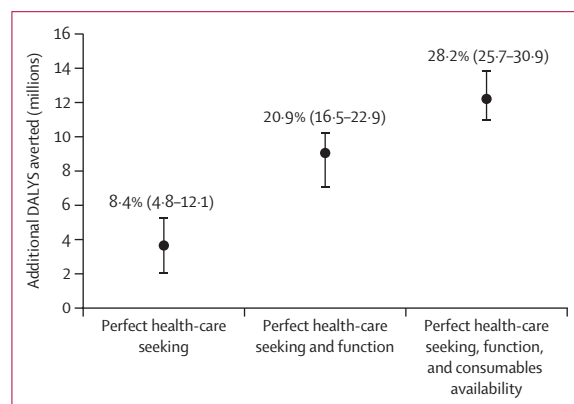


Figure 5: Estimated effect of strengthening the health-care system in Malawi during 2015–19

Estimated additional DALYs averted under each health-care system improvement scenario, relative to DALYs averted by the health-care system in the status quo scenario. Error bars show uncertainty interval. Please note that model scenario names have not been edited. DALY=disability-adjusted life-year.

consequences of decisions for some diseases and interventions were not quantified. Second, the model included only a coarse representation of linkage between time available to deliver a health-care service and its effect; the possibility that a service was not delivered if the full amount of time required was not available. We believe a graduated link exists, and collecting data to characterise it should be a priority. Third, fine detail of the model required assumptions without direct data to support. For example, the behaviour of clinicians and patients when medicines were not available or how much quicker health-care seeking could become. We also assumed that health-care seeking would not automatically change if the performance of the health-care system improved. Furthermore, we did not consider gradations in symptoms that might, in reality, lead to people with the most severe symptoms being most likely to seek care, which would help available health-care resources be directed to those most in need. Fourth, potentially greater uncertainty in our estimates, beyond what has been quantified, could arise from decisions made for the model structure and from parametric uncertainty. Fifth, DALY estimates of the health effects of contraceptive services did not consider the use that would be associated with additional births or the wider economic and demographic consequences.^{18,39,40}

A holistic, integrated, and dynamic approach to modelling service delivery by health-care systems with large amounts of data has been called for to analytically address major questions about options for health-care system strengthening and resource allocation.^{12,13} We believe our approach meets this need, provides important new insights, and enables new analyses to support decision making.

Contributors

This study was conceptualised and led by TBH and ANP, with input from JM-B, MC, TC, DN, GM, PDT, and PR. AUT led the design of the modelling software. TBH, TDM, AUT, JHC, MMG, IH, EJ, BLJ, ILL, RMS, EM, SM, MM, WN, BS, TC, and ANP constructed the model, with supervision and input from MS, NA, AR, and VC. AUT, JC, DS, WG, MSG, SP, MG, and MMG developed the modelling framework and associated infrastructure. TBH and ANP accessed and verified the data. TBH wrote the first draft of the manuscript. All authors reviewed multiple drafts of the manuscript, had full access to all the data in the study, and had final responsibility for the decision to submit for publication.

Declaration of interests

TBH receives research funding from the UK Medical Research Council, UK Research and Innovation, and The Wellcome Trust, paid to their institution. NA receives research funding from the UK Medical Research Council and the Bill & Melinda Gates Foundation, paid to their institution. VC receives research funding from the UK Medical Research Council and UK Research and Innovation, paid to their institution, and consulting fees from Source Market Access. MC receives research funding from The Wellcome Trust, paid to their institution. JHC receives research funding from UK Research and Innovation and The Wellcome Trust, paid to their institution. JC receives research funding from UK Research and Innovation and The Wellcome Trust, paid to their institution. EJ receives research funding from UK Research and Innovation and The Wellcome Trust, paid to their institution. BLJ receives research funding from the UK Medical Research Council and the UK Department for International Development, paid to their institution. SM receives research funding from UK Research and Innovation and The Wellcome Trust, paid to their institution, and

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Data sharing

All data and computer code used in this study are publicly available.¹⁵

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