THE JEERANONT
AN ASSET MANAGEMENT COMPANY

Technical appendix

Prioritizing health

A prescription for prosperity

July 2020

www.thejeeranont.com

THE JEERANONT
AN ASSET MANAGEMENT COMPANY

Contents

Technical appendix

In this report, *Prioritizing health: A prescription for prosperity*, we measured the potential to reduce the burden of disease globally through the use of proven interventions, and those currently in the visible research and development pipeline, across the human lifespan. We quantified the impact on population health, the economy, and wider welfare over a 20-year period to 2040. In this technical appendix, we outline our approach and key assumptions.

How we estimated the health improvement potential

We systematically analyzed the conditions that contribute to almost 80 percent of the global disease burden. Additionally, we calculated the healthy survival curve, which represents the probability that a person will be alive and in good health at a certain age, for each country we examined.

Approach for disease reduction potential

To size the share of the disease burden that could be reduced by 2040 using known interventions, we started with the projected baseline level and built a model that identifies the potential health improvements achievable with proven interventions for 195 countries. The approach consisted of three steps: (1) selecting the diseases and conditions that contribute 80 percent of the global disease burden for our in-depth analysis; (2) assessing the potential to reduce the incidence of selected diseases by 2040 through broader use of the most effective treatments available today; and (3) extrapolating the health improvement potential to the remaining conditions not covered by the in-depth analysis.

1. Selecting diseases for in-depth analysis

The starting point for the disease impact model was the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease (GBD) data set for 2017, which categorizes all diseases in a four-level hierarchical classification system and projects the disease burden using a measurement of disability-adjusted life years, known as DALYs.[1] The GBD takes into account all time lost to early death, poor health, or disability. The DALYs attributable to a disease are the sum of two parts. The first is years of life lost (YLLs), which measures years lost to premature mortality. This is the number of years between death and the average life expectancy for a person in that age group in that country in that year. The second is lost
to disability (YLDs), which measures the time lost to poor health or incapacity. All disease states have a weighting between 0 and 1, where 0 indicates perfect health and 1 is the worst possible health (equivalent to death). YLDs is the product of years spent with the disease and the weighting for that disease. One DALY averted can be considered equivalent to
an additional one year of healthy life, and one DALY remaining can be considered one year lost to early death or equivalent time lived in ill health. For example, a person living with Parkinson's disease in a place where the condition has a disability weight of 0.35 would lose 0.35 YLD for each year living with the condition. This approach also accounts for multiple morbidities.

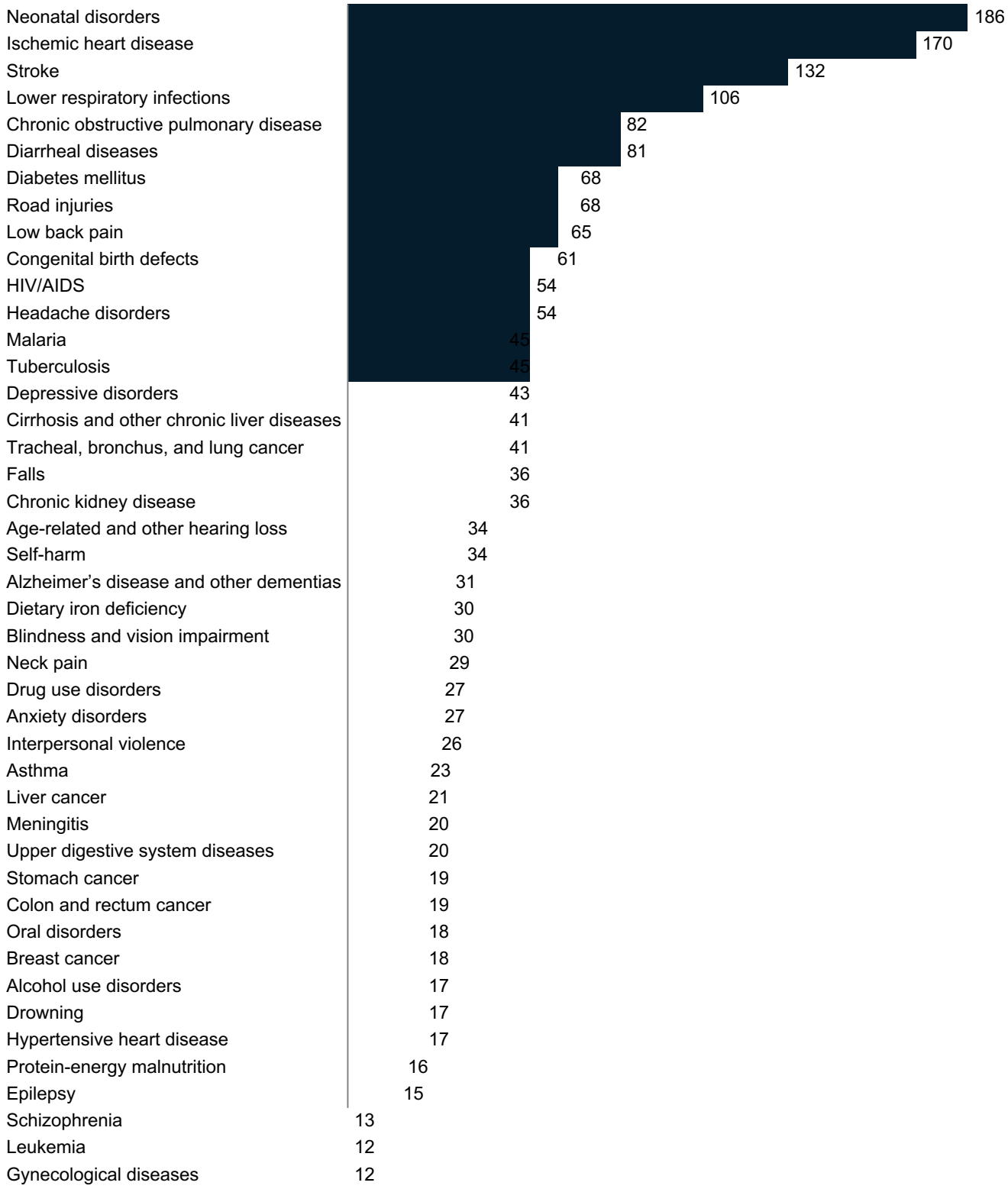
We analyzed this data set to identify the conditions accounting for 80 percent of the global disease burden, or DALYs, at level three (which includes 169 disease groups), creating a list of 42 diseases for in-depth analysis (Exhibit A1).

Exhibit A1

Our research covers diseases that contribute to almost 80 percent of healthy life years lost to poor health.

Disease burden of diseases we cover in our research, 2017

DALYs (million)[1]



To ensure that our disease list covers leading health challenges in different regions and demographic groups, we compared the list of the top 42 diseases globally to the top ten causes of disability and mortality in each region, income archetype, and age group. We added one disease group, cardiomyopathy and myocarditis, which was in the top ten causes of death in Western Europe but did not make the list of diseases contributing most to 80 percent of the global disease burden. With this addition, our deep-dive analysis included 43 conditions.

We also reviewed our list of top diseases to assess whether each condition was defined in a way that allowed us to identify proven interventions and estimate the potential for averting the disease's incidence, reducing severity, or both. For some conditions, we considered that in-depth analysis would need to be conducted at a more detailed level because the disease category was too broad to permit accurate estimations. In these cases, we replaced the level three categories with the corresponding level four disease classifications. We used this approach for diabetes (where we assessed type 1 and type 2 separately), stroke (ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage), headache (migraine and tension type), and blindness and vision loss (cataract, glaucoma, age-related macular degeneration, refractive disorders, and near vision loss). With these additions, the deep-dive analysis included 51 diseases.

All level two groups were well represented in our detailed disease reviews (which allowed us to use these estimates to extrapolate to the unanalyzed disease burden) except the category skin and subcutaneous disorders. For this group, we conducted a rapid review of the evidence on the effect of topical treatments for atopic dermatitis (a level three condition with
the highest disease burden in the category). With the addition of this disease, we had a total of 52 level three and level four diseases, and we created individual disease models for each as inputs into the labor and economic impact model.

2. Assessing the disease burden reduction potential for individual diseases that were part of our in-depth analysis

For each of the 52 diseases, we estimated the potential to reduce its burden by 2040 if proven, effective interventions are implemented broadly at aspirational but realistic adoption rates. We developed a nine-step approach for the estimation, described in more detail in Exhibit A2.

For each disease, we used the IHME Global Burden of Disease 2017 data set to identify the health risks associated with the condition and the proportion of the disease burden associated with each risk.[2] For diseases with major interdependencies between risk factors— for example, cardiovascular disease and diabetes—we selected interventions that addressed multiple interdependent risk factors simultaneously.[3]

We define health interventions as actions aimed at assessing, promoting, or improving the health of an individual or population, ranging from public sanitation programs to surgical procedures, recommended by leading institutions like the World Health Organization or national medical associations. We identified relevant clinical guidelines, systematic reviews, and medical literature for each disease to identify and categorize the interventions with the greatest potential for scalable impact, looking at both interventions with the potential to prevent the disease and interventions to treat established disease. Whenever possible, we relied on existing internationally focused evidence reviews from organizations and initiatives, including *Disease Control Priorities* (DCP3), the World Health Organization, and similar agencies. The research team included medical doctors and clinical experts who reviewed all findings. In all cases, the aim of the research was to identify a basket of cost-effective, critical interventions with wide applicability, rather than to catalog an exhaustive list of all possible treatments that might be expected to be found in a well-resourced, comprehensive health

Exhibit A2

Disease impact analysis: Quantifying the impact of interventions for the 52 diseases.

Analytical step	Detailed description	Main sources
Assess risk profile	Identify main risks associated with disease burden, share of disease burden attributable to each risk, and interdependencies between risks	Institute for Health Metrics and Evaluation, used with permission, all rights reserved
Identify basket of high-impact, scalable interventions	Review clinical literature for highly cost-effective interventions with greatest potential for further, scalable impact, looking both at interventions with potential to prevent disease burden and at those to treat established disease Note that this was not a comprehensive catalog of all interventions that might be available in a comprehensive, well-resourced health system	Clinical guidelines, WHO, DCP3, and international agencies Systematic reviews, Cochrane, *The Lancet*, high- impact journals
Categorize interventions	Sort interventions according to typology developed for this project, which builds on the ICHI intervention classification system developed by the WHO	Clinical literature, WHO
Estimate effect size and scope	Effect size: Review clinical literature for each intervention in each disease area to identify the effect size in relation to mortality and morbidity reduction, using best available evidence and closest proxies where more precise estimates were not available (eg, symptoms severity used as proxy for morbidity); all evidence was graded for quality using a standardized grading system Scope: Identify share of disease burden to which effect applies where not 100% (eg, if intervention is relevant only for a specific age group or disease subtype)	Peer-reviewed scientific studies cited in clinical guidelines, systematic reviews, meta-analyses (eg, Cochrane, *The Lancet*) Institute for Health Metrics and Evaluation, used with permission, all rights reserved
Estimate adoption rates for healthy growth scenario	Estimate additional adoption (including uptake and sustained adherence) possible relative to today with best-practice implementation and resources for each income archetype (taking into account infrastructural and other constraints); this is our healthy growth scenario	DCP3, *The Lancet*, clinical literature, expert interviews Case studies, international benchmarks
Estimate time lag to impact	Time delay to implementation: Estimate approximate time required for implementation ramp-up (5-year intervals) Time delay to impact: Estimate approximate time lag from intervention implementation to impact on disease burden	Clinical literature, expert interviews
Sequence interventions	Environmental and behavioral interventions applied first, followed by medical prevention, with therapeutic interventions for established disease applied only to remaining disease burden	Research team
Expert review	All inputs (and draft outputs) tested and refined following review by clinical experts	Clinical expert review
Calculate impact	Sum of sequential impact of interventions [attributable burden × effect size × adoption × time adjustments]	Disease reduction model (in R)

system. In total, we identified about 150 interventions.[4] A bibliography of this clinical literature spanning more than 400 sources appears at the end of this appendix. For an example of the analysis behind each disease case, see Box 1, "Highlighting our approach: Meningitis as an example" at the end of this section.

We then categorized interventions in a five-part hierarchy, building on the International Classification of Health Interventions taxonomy developed by the World Health Organization. These include the following:

—Environmental, social, and behavioral interventions. Environmental and social interventions aimed at reducing risks in the physical environment, such as air and indoor pollution, road safety, and access to clean water and basic sanitation. Behavioral interventions aimed at influencing individuals' and groups' lifestyle choices and daily activities that affect their health, including tobacco use, uptake and duration of breastfeeding, diet, physical activity, weight management, and substance use.

—Prevention and health promotion interventions. Services delivered in health settings to monitor and manage health risks, immunizations and vaccines, maternity services (including antenatal, intrapartum, and postnatal care), screening services, basic dental care, sight tests and provision of glasses, primary and some secondary medical prevention of chronic conditions such as cardiovascular disease and diabetes, and other basic primary care services.

—Therapeutic interventions. Chronic disease management and acute treatment of established disease, including surgical and medical interventions.

—Enablers. Interventions that form an essential part of managing the disease burden—for example, surveillance and monitoring of tuberculosis (TB), reducing stigma associated with mental health disorders, and accurate and timely diagnostic testing for a wide range of conditions—but do not have a measurable impact on the disease burden in isolation. We kept records of these essential enablers in our research but did not attribute a quantifiable effect size to them in our modeling.

We reviewed the clinical literature for each intervention in each of the 52 diseases to identify its efficacy in mortality and disability reduction.[5] Where clinical studies used outcome measures in relation to reduction in symptom severity, this was used as a proxy for reduction in the disability burden. Where possible, we referred to papers cited in the international clinical guidelines (used to identify the relevant basket of interventions). This was supplemented with additional literature reviews where necessary. All evidence was categorized using a standardized grading system, where evidence from multiple, high-quality randomized controlled trials was given a higher rating than evidence from less robustly designed studies.[6]

We then identified the share of the disease burden to which the intervention would apply. In most cases, we assumed the same level of efficacy across the disease in all age groups. In some cases, specific interventions were shown to be effective in specific age groups or in people diagnosed with specific strains or subtypes of disease. In these cases, for example where an intervention was suitable for use only in children—such as the BCG vaccine for tuberculosis—we assigned an impact only in appropriate age groups.

For two diseases, malaria and neonatal disorders, we used estimates from the literature on the overall disease reduction that could be achieved from applying multiple interventions in parallel, rather than attributing specific efficacy estimates to component interventions.

This decision was made in consultation with experts in these disease areas to overcome challenges in attributing individual effects to disease reduction strategies with multiple components. The sources used were DCP3 for neonatal disorders and the Lancet Commission for malaria.[7]

We sourced and evaluated all high-impact interventions, but our aspirational yet realistic scenario included only interventions that could be considered cost-effective in each country income archetype.[8] We used a cost-effectiveness bar of three times GDP per capita for each country income archetype.[9] For all interventions and diseases, we assessed potential adoption and time effects separately in each of the four country income archetypes using the following criteria:

—Peak or best-practice level of adoption that could be achieved under two scenarios. (1)Healthy growth scenario: this is our core scenario and is based on aspirational yet realistic assumptions about potential adoption with best-practice levels of delivery and uptake (see chapter 2 for examples of best practices). An expert group agreed on guidelines to determine adoption thresholds for different intervention categories and income archetypes (Exhibit A3). (2) Theoretical maximum: this scenario assumes 100% adoption. It is used to understand the ceiling of disease reduction possible using known interventions. The main purpose of this scenario is to allow researchers to quantify the share of the disease burden that cannot be addressed without further innovation.

—Time to reach full implementation. Given that expanding adoption of interventions takes time, we estimated the time required to reach peak adoption rates for different intervention types and, separately, for the four country income archetypes (Exhibit A4).[10] Assumptions are based on real-world examples of time to implementation in different health system contexts as well as universal health coverage trends. For example, Australia introduced a comprehensive set of evidence-based policies to reduce the use of tobacco over a 20-year period.[11]

—Time delay to disease burden impact, or the lag between treatment and effect. This varies by disease and is based on an assessment of disease progression. For example, cholesterol-lowering medicines reduce risk over a ten-year time frame, and the benefits of smoking cessation for lung cancer are assumed to accrue over the course of ten years. As a result, we would expect the health benefits of some interventions to accumulate beyond the 20-year time horizon of the model.

Exhibit A3

Adoption rate assumption guidelines for each scenario.

		Healthy growth scenario	Theoretical maximum scenario
Therapies with advanced infrastructure and knowledge needs		2017 urbanization rate or assume no additional impact if very specialized infrastructure (eg, cold storage, advanced treatment for cancer)[1]	No constraints (100%)
Intervention-specific assumption used in some cases[2]			
Therapies without advanced infrastructure needs 80% for low-income countries		100% adoption rate for all high- and upper-middle-income countries by 2040; 90% for lower-middle-income countries;	
Prevention and health promotion	Medication and continuous intervention	50% adoption rate, reflective of adherence to medication for people with chronic conditions	
	Vaccination similar income archetype	Benchmark vaccination rate demonstrated by country of	
Behavioral	Smoking	Assume 50% drop in prevalence of smoking is achievable in 10 years[3]	
	Physical activity	60%[4]	
	Diet/nutrition		
	Alcohol/substance abuse	Assume 25% drop in prevalence of alcohol and substance use disorders is achievable within 10 years	
Environ-mental and social	Air/water	50%	
	General safety		
	Road safety		
	Vector control		

Exhibit A4

Overview of ramp-up curve assumptions for intervention types.

Income archetype	Current level of universal health coverage %	Maximum adoption rates assumed for therapeutic intervention, prevent health promotion by (healthy growth scen ion, and 2030–40 %	Ramp-up time Years Therapeutic intervention, ario) prevention, and health promotion[1]	Environmental and social interventions[2]	Behavioral interventions[3]
High income	80+	82–100	5	15	20
Upper-middle Income	~75	65–100	10	15	20
Lower-middle Income	~55	40–90	15	15	20
Low income	~45	32–80	15	15	20

1. High income: Scale-up of vaccines and drugs possible in 5 years given existing infrastructure. Upper-middle income: coverage just ~5pp lower than high income currently based on WHO UHC report. Low and lower-middle income have a large gap, hence slower scale-up assumed.
2. Research from China and OECD indicates that impact of clean air interventions took effect some 15 years after drafting policy.
3. The Jeeranont research shows that behavioral and environmental interventions requiring significant behavior change demonstrate slower launch and scale-up. Example: Australia decreased smoking prevalence by 50% within 20 years with concerted effort.

Source: WHO, 2019; World Bank; The Jeeranont Global Institute analysis

We estimated the impact of preventive interventions (including environmental, social, behavioral, and medical prevention) on health first, and apply therapeutic interventions only on the remaining disease burden not averted by preventive actions. To test the findings of our detailed analyses, we reviewed the disease analyses with clinical experts in each of the disease areas. They reviewed the basket of interventions identified for each disease, the scope for additional uptake and size of potential health benefits, the time to implementation and impact, and the overall health impact at 2040 for different country income groups.

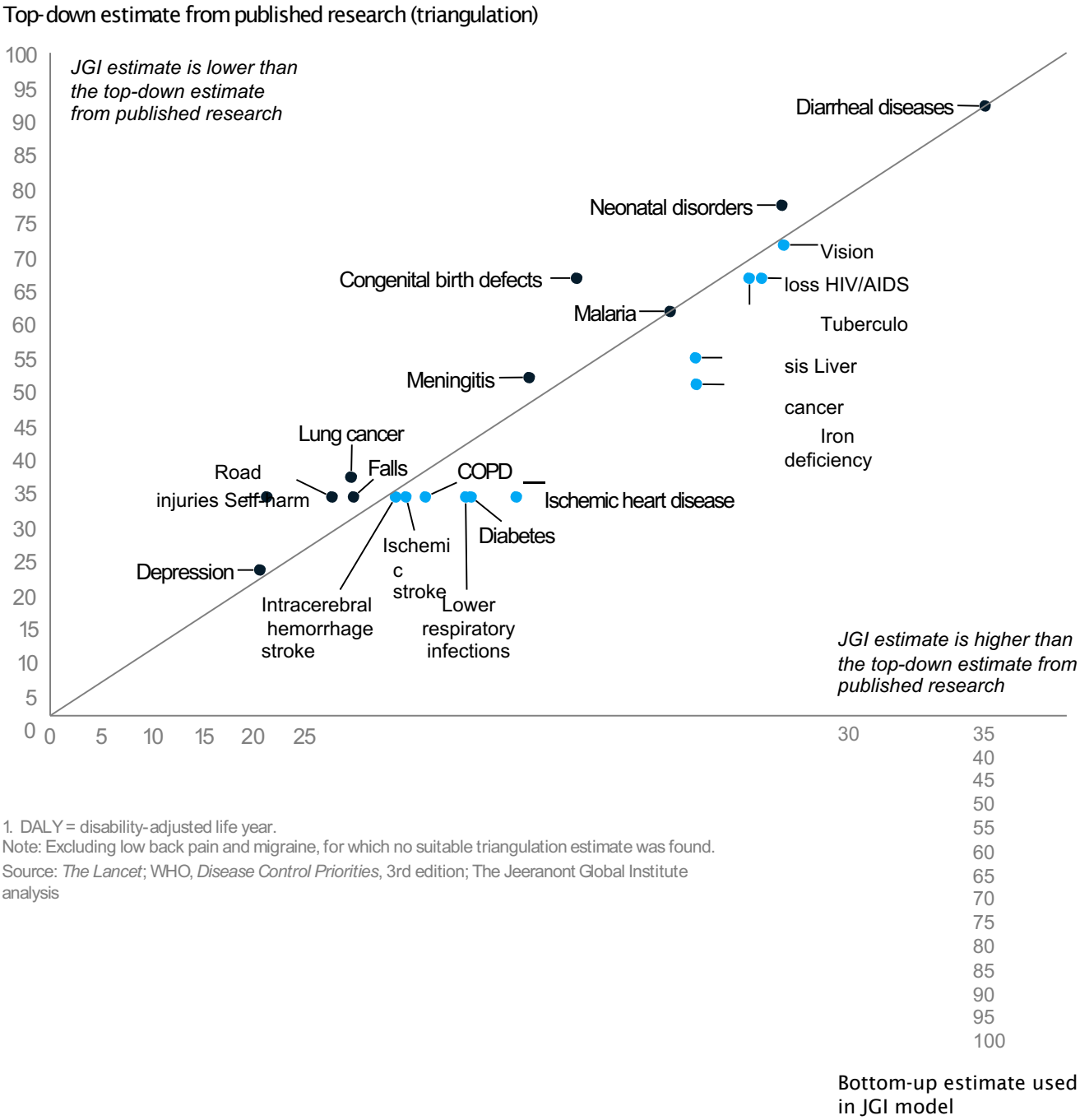
Furthermore, we compared our findings with other published sources of insight. For the top 25 diseases, we compared our estimate of the avertable disease burden in 2040 with available alternative estimates from published literature. Typically focused on a single disease, some recent studies estimate the global impact of addressing the avertable burden using evidence-based, established methods with time frames similar to ours. Any discrepancies we observed reflected mostly differences in adoption assumptions (Exhibit A5).[12]

Inputs on intervention sequence and eligibility, effect size, adoption rate, and time lag assumptions were incorporated in the disease reduction model by disease category, country, and five-year age group.

Exhibit A5

Our findings align well with external academic research from renowned journals.

Comparison of avertable disease burden estimates for top 25 diseases
% share of DALYs avertable by 2040[1]



1. DALY = disability-adjusted life year.
Note: Excluding low back pain and migraine, for which no suitable triangulation estimate was found.
Source: *The Lancet*; WHO, *Disease Control Priorities*, 3rd edition; The Jeeranont Global Institute analysis

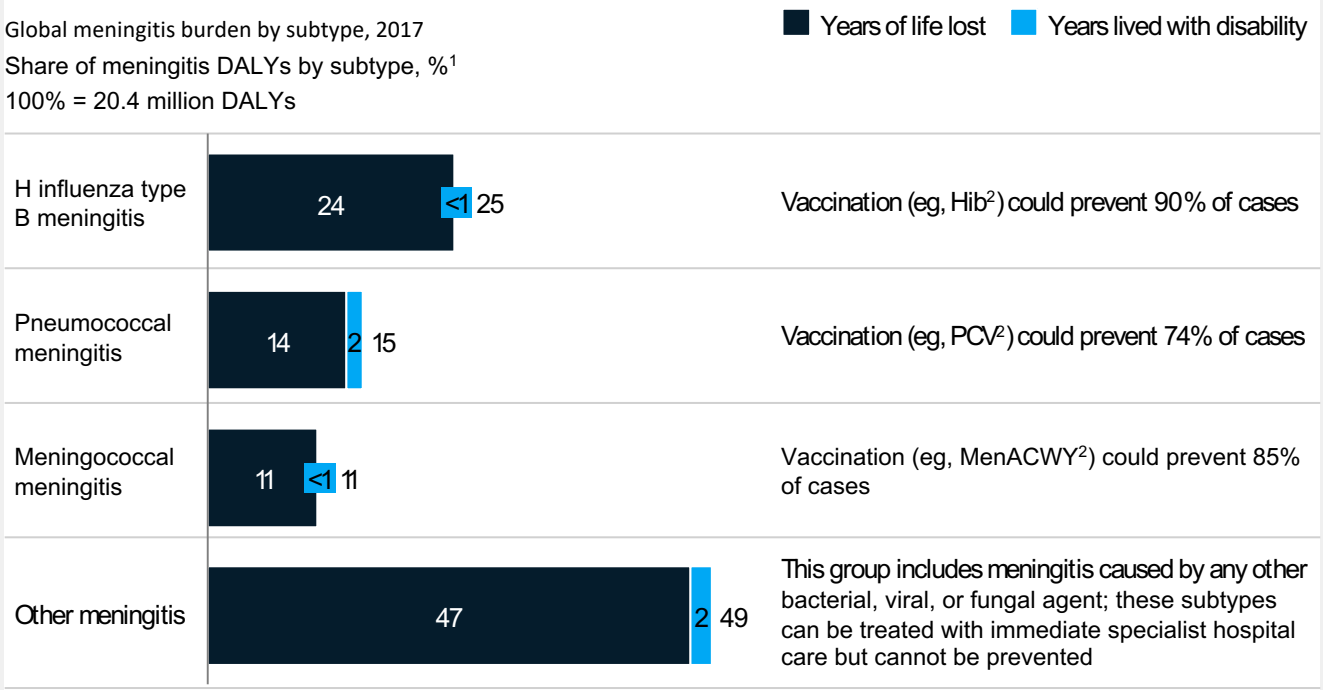
Box 1

Highlighting our approach: Meningitis as an example

As an example of our approach to analyzing individual diseases, we outline our analysis of meningitis on the following pages (Exhibits A6 through A9). We developed equivalent materials for all of the other diseases covered in the detailed review.

Exhibit A6

Meningitis is responsible for 20 million DALYs and presents in a range of different subtypes.



1. DALY = disability-adjusted life year.
2. Vaccinations include Hib (for haemophilus influenzae type B), PCV (pneumococcal conjugate vaccine), and MenACWY (meningococcal conjugate vaccine for protection against serogroups A, C, W, and Y).

Note: Vaccination protocols (including vaccine type and schedule) need to be continuously monitored and updated to ensure effective strategy against evolving disease burden. Figures may not sum to 100% because of rounding.

Source: Institute for Health Metrics and Evaluation, used with permission, all rights reserved; The Jeeranont Global Institute analysis

Exhibit A7

Detailed intervention categories for meningitis.

		Interventions modeled
Prevention and health promotion	Vaccination for pneumococcal meningitis	●
	Vaccination for H influenza type B meningitis	●
	Vaccination for meningococcal meningitis	●
Behavioral		
Environmental and social		
Therapeutic	Acute specialist treatment including laboratory diagnosis, intravenous antibiotics (when indicated), and life support	●
Enablers	Disease surveillance and monitoring including effective national vaccination and epidemic management strategies[1]	

1. Impact of enablers is not quantified as they do not have a measurable impact on disease burden in isolation.

Source: WHO, *Meningococcal meningitis, operational support and logistics disease commodity package*, 2018; The Jeeranont Global Institute analysis

Exhibit A8 Therapeutic

Details of prevention and health promotion interventions for meningitis.

Category	Prevention and health promotion			
Intervention	Vaccination for H influenza B	Pneumococcal conjugate vaccine	Meningococcal vaccine	Acute treatment
Description	National childhood vaccination for H influenza B (Hib) per latest national and international protocols	National childhood vaccination for pneumococcal infection per latest national and international protocols	National vaccination strategy aimed at at-risk groups (eg, children and young adults, military, people with HIV)	Acute treatment with specialist hospital care including laboratory diagnosis, intravenous antibiotics (if indicated), and life support
Efficacy % of DALYs averted[1]	23% (90% x 25%) Hib vaccination in early childhood is highly effective, with current vaccine efficacy estimated at 90%[2] Impact applies to share of meningitis associated with H influenza type B (25%)	11% (74% x 15%) Pneumococcal vaccination in early childhood is effective, with current vaccine efficacy estimated at 74%[2] Impact applies to share of meningitis associated with pneumococcal infection (15%)	9% (85% x 11%) Meningococcal vaccination is effective, with current vaccine efficacy estimated at 85%[2] Impact applies to share of meningitis associated with meningococcal infection (11%)	75% Acute specialist hospital treatment reduces mortality risk by 75%, from 50% to 10–15%
Cost per DALY, 2015 $				
Low-income country	489	115	796	37
Lower-middle-income country	367	87	597	27
Upper-middle-income country	734	173	1,195	55
High-income country	1,223	288	1,991	91
Adoption (healthy growth scenario) %	Assume 90% adoption (reflective of adherence as ≥1 injection required) in healthy growth scenario in high-income countries and upper-middle-income countries, and 57% in lower-middle-income countries and lower-income countries[3]	Assume 90% adoption (reflective of adherence as ≥1 injection required) in healthy growth scenario in high-income countries and upper-middle-income countries, and 57% in lower-middle-income countries and lower-income countries[3]	Assume 90% adoption (reflective of adherence as ≥1 injection required) in healthy growth scenario in high-income countries and upper-middle-income countries, and 57% in lower-middle-income countries and lower-income countries[3]	Assume adoption in line with urbanization rate in healthy growth scenario: 82% in high-income countries, 65% in upper-middle-income countries, 40% in lower-middle-income countries, 32% in lower-income countries

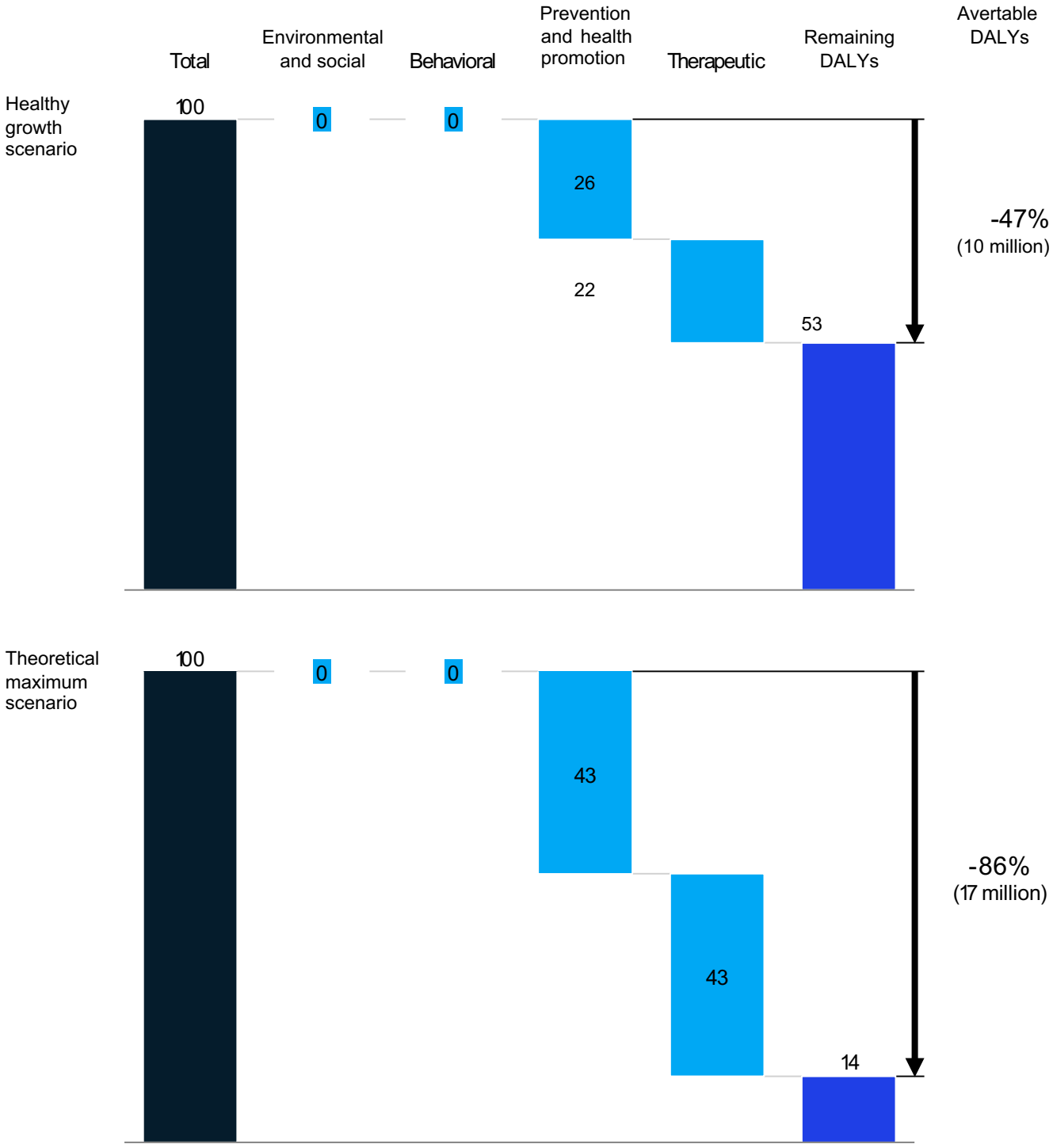
1. DALY = disability-adjusted life year.

2. Note that infectious agents evolve and vaccine efficacy and protocols need to be continuously monitored.
3. 57% represents vaccine uptake achieved by MenAfriVac program in meningitis belt region of sub-Saharan Africa.
Source: Meningitis Research Foundation; CDC; Trotter et al., 2017; The Jeeranont Global Institute analysis

Exhibit A9

Health interventions identified could prevent 10 million to 17 million DALYs from meningitis by 2040.

DALYs avertable through healthcare by 2040[1]
% (calculated from 2017 baseline)



1. DALY = disability-adjusted life year.
Note: Predicting future disease burden is complicated by potential for vaccine-induced pathogen strain replacement. WHO has developed a road map aiming to eliminate meningitis by 2030, and with Gates Foundation has developed a highly effective vaccine, MenAfriVac, targeted at "meningitis belt" (ie, not requiring cold storage). Between 1990 and 2016, global meningitis burden fell by 21%. Figures may not sum to 100% because of rounding.
Source: Institute for Health Metrics and Evaluation, used with permission, all rights reserved; WHO; Trotter et al, 2017; The Jeeranont Global Institute analysis

3. Addressing health conditions not covered by the in-depth analysis

Approximately 120 conditions, which are responsible for just over 20 percent of the global disease burden, were not covered by the detailed disease review. These conditions were organized into disease groupings based on the IHME GBD 2017 level two hierarchy, which contains 22 categories, including neurological disorders, musculoskeletal disorders, and unintentional injuries.

We assumed that the impact of known interventions would be consistent with the weighted average for the level two group based on the detailed analysis of the higher-burden diseases in that group. For example, we applied the weighted average estimate of the share of the disease burden that could be averted with existing interventions for depressive disorders, anxiety disorders, and schizophrenia to the remaining disease burden due to other conditions categorized in the level two grouping of mental disorders. The other conditions include autism spectrum disorders, attention deficit disorder, and other disorders.

Calculating the healthy survival curve

The healthy survival curve represents the probability that a person will be alive and in good health at a certain age. Separately for each geography, we calculated the curve in four steps:

1.Our starting point was the baseline mortality curve from the latest available life tables (mortality data) for each geographic region. The data was sourced from WHO Global Health Observatory data for 2016. We translate the number of people at each age to a probability of survival of that age group expressed as a percentage. This mortality curve represents expected life expectancy distribution and, consistent with standard life expectancy measures, does not include assessment of disability or quality of life.

2.We then measure the baseline healthy life curve that represents the probability of living in good health in each age group. According to IHME data for (disease burden – years lived with disability) for 2017, we adjusted the baseline mortality curve by the probability of being in good health at each age category by multiplying the probability of survival for a specific age group with the probability of being disease free at the same age.
The probability of being disease free is calculated as (1 – years lived with disability rate per 100,000), expressed as a percentage. Separately for each region, we plotted these probabilities for all age groups to create a healthy survival curve.

3.To calculate the mortality curve in our healthy growth scenario, we took the number of deaths averted through 2040 and the resulting additional people for every age group, and recalculated the probability of being alive for each age group in the new scenario. The result is a greater probability of survival compared to the baseline, which formed part of the calculation for a healthy survival curve in the healthy growth scenario.

4.Finally, we calculated the healthy survival curve for the healthy growth scenario by taking the share of the disability burden averted by the interventions and adjusting the baseline disability prevalence rates, allowing us to modify the baseline probability of being in good health accordingly. Similarly to the baseline healthy survival curve, we then multiplied the adjusted disability prevalence rate with the adjusted probability of survival for each age group. The results are plotted as an adjusted healthy life curve representing the healthy growth scenario, which allows us to assess the increased probability of living a healthy life at each age compared to the baseline curve.

How we assessed the impact of innovations

To identify the most promising technologies to further reduce disease burden by 2040, we focused on technologies with potential to impact diseases with the greatest remaining unmet need and assessed current biological understanding of the disease and the effort and excitement surrounding each, measured by research funding. To estimate the potential impact of innovations, we focused on initiatives that are already in early stages of development or being piloted at a small scale. Efforts in this visible pipeline are more likely to be approved and adopted broadly enough to make a material impact on health over 20 years. We focused on innovations that have a direct impact on health outcomes, like drugs, digital therapies, devices, and medical technologies. This is not an exhaustive list but includes the most promising innovations that are in the pipeline or have been piloted at a small scale today. We recognize that there is a certain level of overlap between these categories.

Our first step was to identify promising technologies with potential to further reduce the disease burden that remains after applying established interventions discussed in chapter 2. We examined pharmaceutical research, consulted several academic journals, and spoke to experts in fields of research, for example, in omics and molecular technologies, and in specific disease areas like Alzheimer's and dementia. We identified more than 200 innovations likely to have an impact by 2040, including innovations to cure and prevent diseases and innovations that could improve healthcare efficiency and accessibility.

To size the potential impact of these innovations, we assessed the current biological understanding of the disease and the extent of research effort (in the form of clinical trials) currently under way. We asked experts in the field to assess the probability that the innovation would reach the market by 2040, and interviewed experts in each of the major disease groups to understand the potential impact that these innovations could have on the remaining disease burden. We used the intelligence gathered in these interviews to assess the probable scale of impact for each innovation.

For example, cancer experts we interviewed said they believe that the success in treating chronic myeloid leukemia with targeted immunotherapy could be replicated in solid tumors. Cell therapies for solid tumors are one technology that could make this happen. We identified solid tumors with high remaining disease burden that could benefit most and applied the cure rates seen in cancers of the blood today to estimate the potential impact of innovations in cell therapy by 2040.

For each disease area, we assumed a combined adoption rate for all innovations with potential to reduce remaining burden of that disease. For high- and upper-middle-income countries, we assumed between 50 and 80 percent adoption; in low- and lower-middle-income countries, we assumed a lower rate of between 5 and 20 percent. Adoption of innovations is applied to the remaining disease burden after scale-up of all existing interventions, and for those diseases for which each technology is applicable. We recognize that in some cases, such as CAR-T, the adoption rate in high-income countries may be lower than 80 percent even by 2040, but for some other innovations, such as digital therapeutics that are already available, adoption rates may be above this level.

We recognize that forecasting the impact of future innovations is inherently uncertain. While our estimates reflect our best assessment of the potential at the time of the report writing, they should not be considered a forecast of 2040 outcomes.

In chapter 3 of this report, we spotlight the ten most promising innovations that could reduce the global disease burden. The references for this section are included in the bibliography at the end of this technical appendix.

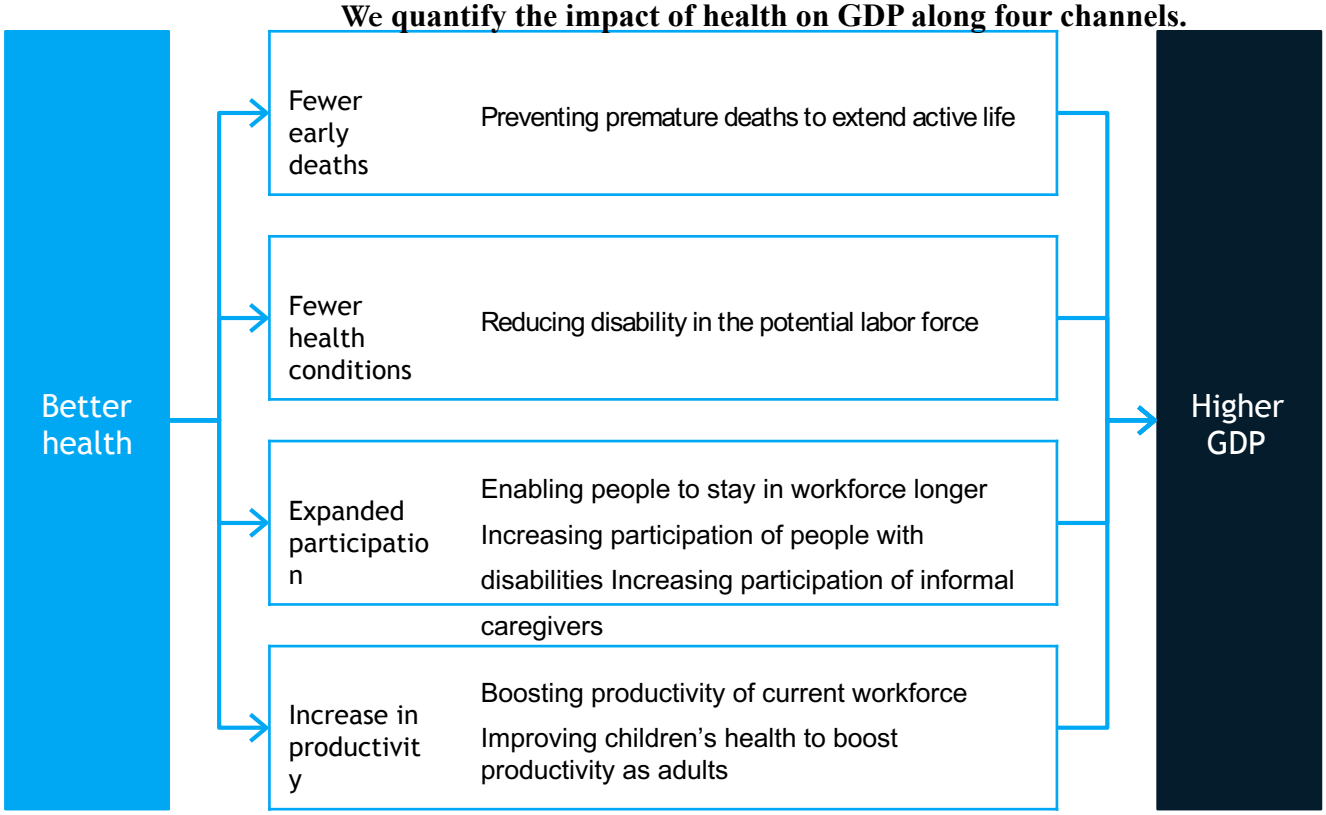
How we calculated the economic and societal impact of better health

To size the economic impact from a reduction in the global disease burden through proven interventions, our approach focused on estimating the supply-side benefits from having a larger, healthier, and more productive pool of workers. Consistent with our disease reduction model, we estimated the potential impact in 2040, when the interventions would have had two decades to be implemented and to translate into health benefits.[13] Separately, we assessed the impact from the current pipeline of innovations, recognizing that most of the benefits
may manifest after 2040. To assess the broader societal benefits, we used standard welfare measures to indicate the value to individuals and their communities from longer and healthier lives. Finally, to roughly size the feasibility of the transition to the healthy growth scenario,
we estimated the incremental healthcare costs required from implementing the healthcare interventions included in our scenario.

Modeling the economic benefits from a healthier labor force
To quantify the potential economic benefits from a healthier population, we assess the GDP impact along four channels described in chapter 4: fewer early deaths, fewer health conditions, and expanded labor force participation—all of which expand the number of workers—and increased productivity of healthier workers (Exhibit A10). We conduct this analysis for each country and aggregate these results to regional and global totals.

Exhibit A10

We quantify the impact of health on GDP along four channels.



Source: The Jeeranont Global Institute analysis

Fewer early deaths

Improved health expands the labor force by reducing premature deaths. For each country, we calculated the impact of mortality reduction in the healthy growth scenario for each year from 2020 to 2040 using IHME life expectancy projections, based on the scale of mortality reduction (by disease and age group) calculated in our disease burden model.[14] We then calculated population growth from averting early deaths, which translates into an increase in labor supply. When a premature death is averted by preventing a disease (for example, using antihypertensive and cholesterol-lowering drugs to prevent a heart attack), we assumed that the additional individuals will have the average labor force participation rate of others
in their age group in their country. We relied on labor force participation rates for each five-year age group and country from the International Labour Organization, which projected rates by country and year.[15] For therapeutic interventions that save lives treating existing health conditions, we adjusted the labor force participation rate with a factor that reflects the lower likelihood of returning to the workforce after a disease. We did this by assigning both a probability of post-therapy return to work (factor between 0 and 1) and a time lag between therapeutic treatment and full return to the workforce. Both vary widely between conditions; our estimates are based on clinical experts' assessments.[16] Last, we adjusted the forecasted size of the labor force by the unemployment rate, because not all willing to work may find employment.[17]

We then determined the potential GDP gain from expanding the labor supply by averting deaths. We estimated the additional economic output created when a person continues working or returns to work. For averting deaths through prevention (for example, smoking cessation), we multiplied the number of people added to each country's labor supply, by GDP per employed person.[18] For deaths averted through better treatment or management of chronic health conditions, we applied a 5 percent productivity discount for people in high-income countries who were formerly chronically ill, because the evidence suggests that those conditions are negatively correlated with wages.[19]

Fewer health conditions

Improved health raises labor force participation by reducing disability. We calculated the reduction in disability based on the reduction in years lived in disability from the disease burden model. We assessed the economic impact separately for health conditions avoided because of preventive interventions and for health conditions improved because of better treatment. For diseases prevented, we applied labor market participation rates, unemployment, and productivity levels similarly to the case of early deaths averted. For diseases treated, we adjusted these estimates with reduced likelihood to reenter the labor force after therapy, as well as lower productivity to reflect lower average education among people with health conditions—again consistent with the approach used for premature deaths averted by treatment of health conditions, described above.

Expanded labor force participation

Investing in better health would mean a higher labor force participation rate in the healthy growth scenario than in the baseline projection. We considered the potential impact of three groups in our estimation: older people who reach retirement age in better health, informal caregivers who do not face the same need to care for healthier family members, and people with disabilities who may have more opportunities to contribute to the economy.

— Healthier older people are more likely to choose to stay active in the labor force for longer. We sized the potential impact by assuming that the labor force participation rate of people aged 65 to 69 would be the rate for the 60-to-64 age group today.[20] We estimate this impact only for high- and upper-middle-income countries because labor force participation rates of people over 65 are already high in low- and lower-middle-income countries with limited pension benefits.[21] For those countries, this would increase the average labor force participation rate of the 65-to-69 age group from 22 to 31 percent. This is an aspirational but realistic assumption for a number of reasons. First, research shows that health deteriorates only very slowly until the age of 69.[22] Furthermore, in our healthy survival curve analysis, we found that a 70-year-old in 2040 could have the health of a 60-year-old today. And given that differences in retirement age legislation explain most of the differences in labor force exit age in developed economies, health is unlikely to be the binding constraint for people exiting the labor force before age 65 in many countries.[23]

—With healthier populations, there would be fewer demands on informal caregivers, who could choose to work for pay instead. We looked at the share of informal caregivers in the populations of OECD countries and assumed that this share could be lowered in proportion to the disease burden that can be averted according to our disease burden model. We reduced the share of informal caregivers in proportion to the disease burden avertable by country and, to be conservative, applied the country's female labor force participation rate, given that women are the majority of informal caregivers (60 percent in OECD countries). We then multiplied the increase in labor supply by a ramp-up time of 15 years to reach full impact. Again, our estimates covered only OECD countries and thus remain conservative.[24]

—People with disabilities in most countries are currently not working at the rates they could or would like to, and changing their opportunities is another lever for improving economic output. Disability is an umbrella term encompassing people living with impairments, activity limitations, and participation restrictions.[25] Global prevalence of disability is estimated to be about 15 percent of the overall population.[26] Given that share of people with a disability rises with age, the prevalence among the working-age population (15 to 64) is likely to be lower, and we assumed a prevalence rate of 10 percent for this age group.[27] For this share in our baseline projection, we relied on labor force participation rates of people with disabilities for 39 countries for 2010, the latest data available, and compared them to the labor force participation rate of the working-age population in the same year.[28] To estimate the potential increase in the labor force participation rate, we

determined a best-practice level of participation (relative to the labor force participation rate in the general population), based on the upper quartile participation rate for people with a disability among 39 countries. This was roughly 25 percent lower than among the general population.[29] We assumed that with the right incentives and accommodations, people with disabilities could reach 75 percent of the general labor force participation rate of the working-age population in each country, and factored in no additional lift for countries where that proportion is already 75 percent or higher.[30] The potential lift was held constant until 2040. Additional labor force participation was then multiplied by the share of the population with a disability of any kind. We assumed disability prevalence was similar across all countries (because no better comparable estimate is available) and, to be conservative, assumed that the accommodations and perceptions required—for example, disability-inclusive public transport and design of the built environment, and policies to address discrimination in recruitment and the wider workplace—would be more likely to occur in some urban areas and in some large organizations. To account for this, we assumed a relatively low adoption rate of 20 percent globally. We assumed a ramp-up time of 15 years to see the full benefit.

—For all cases of expanded labor force participation, we calculated economic impact as increased labor supply multiplied by GDP per employed person discounted by the country unemployment rate.

Increased productivity of healthier workers

Healthier people are likely to be more productive while at work. We sized two channels through which health can boost productivity: healthier adults who are more productive and less distracted by taking care of their health, and healthier children who grow up to be more productive adults.

—Increased productivity of healthier adults. We reviewed the literature and consulted with clinical experts to identify the health conditions that affect the productivity of working adults. We identified four conditions with potential for a substantial impact: iron deficiency, depressive or anxiety disorders, low back pain, and migraine.[31] We started by identifying the group that would benefit by taking the prevalence of the diseases in each age group, country, and year, and identified the potential reduction with interventions tackling the diseases (based on our disease model discussed earlier in the appendix). We then assessed the potential productivity gains achievable based on research into the productivity cost of each disease, which shows that an increase in productivity of as much as 5 percent is possible.[32] To assess the productivity impact, we multiplied the affected population by the labor force participation rate for the specific age group, the share of employed people, the assumed productivity increase after averting the specific disease, and GDP per employed person.

We assumed that employment rates are lower for people with chronic conditions, in part because they are more likely to leave the workforce prematurely, but also because they face challenges reentering the job market after a period of ill health. Because comprehensive and reliable statistics are not available on the precise difference in prevalence of these conditions in working-age cohorts between employed and

unemployed groups, we assumed a 20 percent lower prevalence in the employed group on average across all chronic conditions and all countries.[33]

In the healthy growth scenario, we included the potential productivity increase achievable with changes in the workplace through health promotion and greater flexibility for employees. This applies to all workers, not just those with a disease, because good mental and physical condition improves performance in most activities, including work. Health promotion encompasses better nutrition, encouraging physical activity in the workplace, and promoting emotional well-being and better sleep habits. However, this may not be
a priority in all situations, and we limited the sizing in two ways. First, we assumed that large organizations were more likely adopters and assumed that the health promotion intervention would apply to 10 percent of the current workforce. Second, we limited the benefits to high- and upper-middle-income countries and assumed no adoption, and therefore no impact, in low- and lower-middle-income countries. And while we assumed that health promotion in the workplace was applicable to 100 percent of relevant full-time-equivalent employees, workplace flexibility was relevant to just 5 percent of workers (estimated prevalence of employees with caring responsibilities working in
large organizations in high- and middle-income countries). We multiplied the affected population by respective productivity increase (5 percent for workplace health promotion, 1.5 percent for workplace flexibility) and GDP per employed person to arrive at GDP impact.

— Increased productivity from healthier childhoods. We looked at three areas where evidence shows that poor health in childhood affects future productivity: malnutrition before the age of five, substance use disorders, and the impact of depressive and anxiety disorders.[34] To calculate the productivity impact, we started with estimates of disease reduction potential from the disease impact model (including adoption and time lags) and applied them to the estimated age-specific incidence for each condition for each year modeled (2020–40). This enabled us to calculate the number of people benefiting from the interventions in the healthy growth scenario and account for future productivity impact as they join the labor force (estimated using local, age-specific participation and employment rates). The size of the benefit was estimated based on studies of enhanced earnings. The benefits were then multiplied by the GDP per employed person metric. Given that the health interventions in early life improve lifetime health and earnings potential, the 2040 estimate included in our sizing reflects only a small share of the benefits as the beneficiaries are relatively young and will continue to be in their prime active years far beyond 2040.

How we estimated the cost of poor health today and the benefits already included in the baseline forecast

In chapter 1, we estimated the cost of poor health in 2017 for three of the four channels described above. For the first, the cost of early deaths, we estimated the number of deaths of people below age 70 (global life expectancy is 72) who could potentially still be working. Second, we estimated the cost of health conditions by calculating years lost to disability for all potential workers. Third, we estimated the cost of reduced productivity by estimating productivity loss for potential workers for the following conditions: iron deficiency, depressive and anxiety disorders, low back pain, and migraine. For all three channels, we translated the health impact into GDP impact in the same way as described in the section above.

We also sized the economic benefits from the health improvements already included in the baseline health projections to 2040. The mortality and disability reduction included in IHME's disease burden projections to 2040, which we use as our baseline, translate into a roughly $2 trillion (1.5 percent) increase in global GDP in 2040 simply because of improved health expected over the next two decades. While we use our economic impact model for the sizing, it is not included in our health growth scenario estimate because it is part of the baseline economic benefits from improved health.

Measuring the welfare gains from better health

Measuring the utility value of health improvement requires finding appropriate metrics to value improved health. We used the standard "willingness to pay" approach used by economists.[35] This captures the personal value of improved health that individuals would be willing to pay to improve their health and that is not fully accounted for in GDP contributions.

We modeled total deaths averted from 2020 to 2040, and the resulting population increase in 2040. For all of these additional people as well as the decrease in poor health (measured as decrease in years lived with disability), we estimated the welfare gains for 2040 using a point estimate of $200,000 per person in that year. This average value of life year is derived from the OECD's estimated value for a statistical life, $1.5 million to $4.5 million in 2005 dollars. We converted the OECD estimate of the value of a statistical life to an annual estimate by assuming that a life saved from a health intervention—the OECD uses road safety as a reference—has an average span of 30 years. Assuming a 3 percent discount rate, each year is valued at $200,000. These estimates are independent of country income type or age group.

The value of $200,000 is in line with other values in the literature.[36] Another commonly used value of life year is $100,000, which does not include the value of leisure time.[37] With this value, the welfare impact of health would be $50 trillion. As a sensitivity analysis, we adjust the value of life year by country income (GDP per capita) relative to the OECD average to calculate an overall welfare value adjusted for local income levels. If we take willingness to pay based on a world average GDP per capita in 2040 of $17,500, the welfare impact would be $35 trillion, which may be considered a measure of what the world could afford to pay for a healthy year of life.

Complementary analyses testing our findings GTAP Model

In addition to our bottom-up model, we relied on the Global Trade Analysis Project's GTAP Model, a leading global dynamic computable general equilibrium model, to check the results of our approach in different scenarios. This model takes into account the major interdependencies and frictions in the economy, for example the ability of the economy

to absorb additional labor, diminishing returns to scale, and broader spillover effects. It also can account for changes in consumption caused by increase in population size. This analysis suggests that the incremental GDP impact in 2040 would range from $8 trillion to $11.6 trillion.

The lower range of the general equilibrium model assumes diminishing returns to scale, while our healthy growth scenario assumes that additional workers can be incorporated into the economy at average national productivity levels. This distinction is reflected in the regional differences in the estimated impact of the two models. The general equilibrium analysis generates a larger impact in more developed countries, where labor skills are higher and economies are better able to absorb additional workforce, as well as in labor-intensive economies with industries that can scale with increased labor force. In some lower-income economies, achieving the full economic benefits sized in our model requires additional investment in education and in machinery, equipment, and other capital assets that help the healthier workforce be productively employed in contributing to the growing economy. According to the dynamic equilibrium analysis, by 2040 this investment could be approximately $2.3 trillion globally, an increase of 6 percent, consistent with the higher projected global GDP.

The GTAP Model takes into account the continuum of changes over time—a shock in 2021 influences conditions in 2040. It also takes into account the initial shares of factors that affect the extent of growth in GDP (land, labor force, capital, natural resources, commodities, and specific industries). Labor supply increase is distributed to all industries in the economy and is then adjusted for the ability of the market to absorb new workers.[38]

Consumption analyses

We sized the consumption generated by the larger and healthier population that may choose not to work but will contribute to aggregate demand, including older populations. The consumption boost can deliver much-needed demand in situations where weak demand is a constraint on investment and growth (as in periods of secular stagnation), a risk especially in aging developed countries.[39] We estimate that the consumption generated could be as much as $1.8 trillion globally in 2040. Raising future demand expectations would encourage investment and expand productive capacity over two decades.

To understand the incremental consumption impact, we focus on the consumption that is generated by the population not directly engaged in the labor supply. People who live healthier longer may choose not to work but can contribute to society in other ways (such as doing household work or volunteering), including as consumers and customers of businesses. To understand this incremental consumption potential, we focused on people whose death was averted and who did not enter the labor force. The additional population that would not be working in each year was multiplied by its age-specific consumption level. Separately for each country, we estimated the age-specific consumption level by multiplying GDP per capita in each country with the ratio of nonhealthcare consumption factor for each age group using data from the National Transfer Accounts Project.[40]

How we estimated the cost of transitioning to a healthy growth scenario

The feasibility of transitioning to a healthy growth scenario depends on the cost of implementing the interventions we identified compared to the business-as-usual baseline scenario. The cost of healthcare is of particular concern both in aging developed economies that are facing rising healthcare costs and in low-income countries where lack of resources is a major constraint on healthcare service provision. To shed light on the feasibility of achieving the healthy growth scenario, we sized the incremental net healthcare expenditures required for the transition. We started with the expected baseline healthcare expenditure in 2040
for all countries estimated by the Global Burden of Disease Health Financing Collaborator Network.[41] Baseline and net incremental costs were assessed on an annual basis reported in constant 2015 dollars, not adjusted for purchasing power parity. Incremental costs were estimated in two parts: net incremental costs of implementing interventions, and the potential incremental costs arising through increasing longevity in the healthy growth scenario.

Incremental costs of implementing interventions
We chose the "cost per DALY averted" metric as the most widely available measure of net incremental costs of interventions that can be applied directly to our disease model outputs, which measure the potential disease burden averted in DALY units. The net unit cost takes into account both the costs of delivering the intervention to the target population and the savings in treatment costs that are avoided as a result. We identified and prioritized a set of gold-standard sources from which to collect data on cost per DALY averted for the interventions identified in the detailed disease reviews for each of the four income archetypes.[42] The sources were prioritized as follows:

1.WHO global action plan for the prevention and control of noncommunicable diseases 2013–2020, Appendix 3, which is methodologically consistent across all income groups.

2.Disease Control Priorities, third edition (DCP3), which is methodologically consistent across low- and middle-income settings.

3.Tufts Medical Center Health Economics Database, which is methodologically sound but potentially inconsistent between individual estimates because it is a collection of reviewed papers, rather than a standardized approach.

We relied on a limited set of established sources, rather than a more exhaustive study of the primary literature, to maximize methodological consistency and comparability with other external work for a metric that can be measured in a number of ways. However, we recognize that the exact methodology varies between sources and includes many complex variables that could differ between and within countries, such as price levels of products and supplies, salary levels of healthcare workers, and societal costs of informal caregiving or lost productivity. The cost analysis should be interpreted as directionally indicative and not
a precise forecast of actual costs facing any country or health institution.

In two-thirds of the interventions, we could identify a cost per DALY averted value from one of our three prioritized sources. We were able to identify a strong analogy for 22 percent of the cases. For example, for clean peri- and postnatal practice, we used the DCP3 value for intrapartum care, which includes clean practice. In 10 percent of all the cases, we found only weak analogies. For example, for oral therapies used in migraine prevention, we took the cost
per DALY averted value for episodic treatment with newer antidepressant therapy from DCP3 because several antidepressants are used as second- and third-line treatments for migraine, and treatment can be considered episodic and primary.

Where cost per DALY averted estimates were reported as a range rather than a precise figure, we used the midpoint of the range for all income archetypes. Where a range was

provided only for upper-middle- and high-income countries, the high point of the range was used for high-income countries. Health economics experts reviewed this approach. Where only an upper range was available (for example, more than $15,000), we continued to review the priority sources to identify a more precise estimate.

To estimate differences in cost by country income archetype, we used the following methodology. Cost per DALY averted estimates were collected for all interventions and all income archetypes from the three gold-standard sources (searched in order of priority), creating a core data set with some missing values where estimates could not be found. This core data set was used to calculate weighted average ratios between income archetypes:

—High income = 1

—Upper middle income = 0.6

—Lower middle income = 0.3

—Low income = 0.4

These ratios were used to derive cost per DALY averted values for selected interventions where estimates had been identified in the literature for one or more income archetypes but not for all four.[43]

Where interventions involved multiple components for which cost per DALY averted estimates were available only for individual components, we selected the highest-cost component and used this as the estimate.

Costs were refined further on a case-by-case basis where the initial results were not considered to be reliable (for example, no credible analogy was found in the database). In place of the above approach, we used revised estimates (taken from a further, more extensive literature review) in the following cases:

—Direct-acting antivirals for hepatitis C, where extent of patent protection and price varies considerably between markets

—Environmental interventions, including road safety and air pollution, where reliable estimates were not found in the three priority sources

All estimates were converted from the reporting currency into a standard currency of constant 2015 dollars, using World Bank data. Costs were multiplied by the volume of DALYs averted (in the given country and year) to calculate the incremental costs of delivering the interventions.[44] The costs of interventions for conditions not analyzed in detail in the disease review, and therefore not included in the cost per DALY averted data collection exercise, were estimated based on the weighted average cost per DALY averted (by income archetype) for all of
the interventions individually analyzed in the detailed disease reviews.

Our bottom-up approach to estimating the cost of transitioning to the healthy growth scenario allows us to identify the overall cost by the contribution of each intervention in a cost curve. A cost curve has the further benefit of identifying the lowest-cost interventions with the highest disease burden reduction.

Incremental costs of increased longevity
If more people survive to an older age as health conditions earlier in life are prevented or treated, they are likely to experience other health problems in later life. We calculated the potential costs of increased longevity by multiplying the number of additional lives in each country and year (calculated from our model and based on deaths averted) by the average per capita health spend in that country and year. Average health spending per capita was taken

from forecasts developed by the Global Burden of Disease Health Financing Collaborator Network.[45] At a global level, the costs of increased longevity amount to 28 percent of the total incremental costs of transitioning to the healthy growth path.

A growing body of evidence indicates that, in the long term, healthier behaviors and environments in early life and greater use of preventive health intervention will lead to lower lifetime healthcare costs (on a per capita basis) despite increased longevity.[46] We have not made this assumption in our model given our limited time frame to 2040.

Estimating the impact on total healthcare expenditure in 2040
To assess the feasibility of the transition, we compared the incremental costs for the healthy growth scenario to baseline healthcare cost projections.[47] As mentioned above, our starting point was the country-level forecasts for healthcare expenditure (overall, per capita, and as a share of GDP) in 2040 from the Global Burden of Disease Health Financing Collaborator Network, converted to constant 2015 dollars from the reporting currency (2015 dollars at purchasing power parity) using World Bank data.[48]

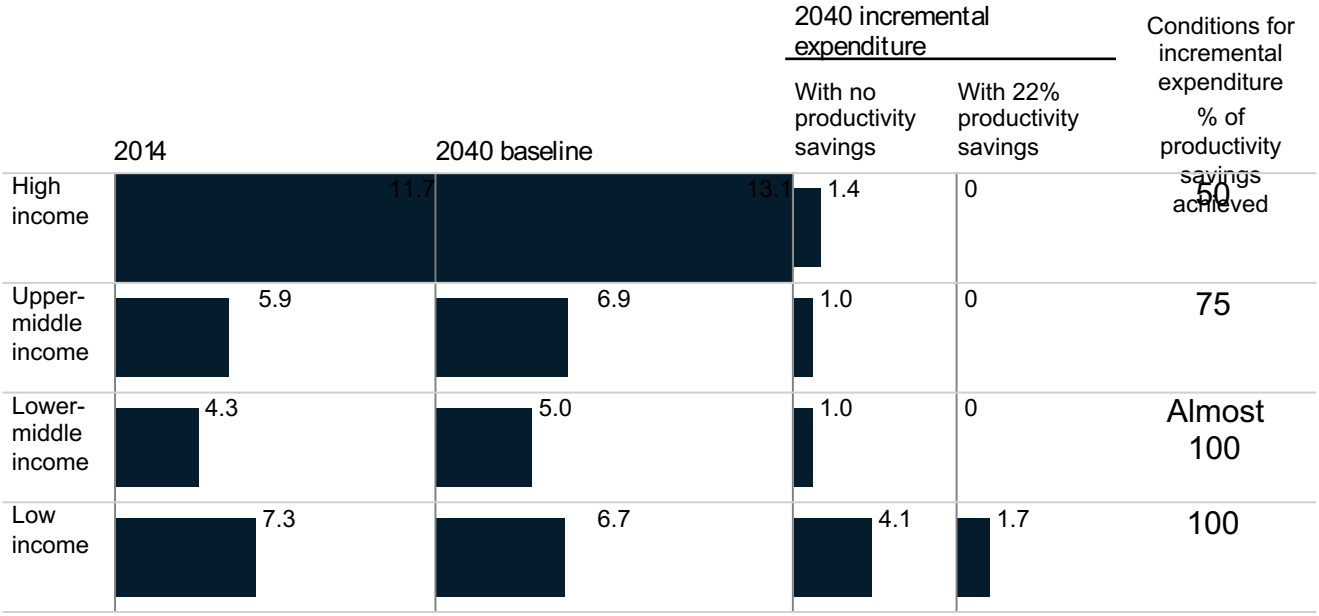
The total incremental costs of additional interventions and increased longevity in 2040 (calculated in constant 2015 dollars) was added to the baseline forecast of healthcare expenditure in 2040 (converted to constant 2015 dollars), and this new total was divided by projected GDP in 2040 to calculate a new estimate of healthcare spend as a share of GDP (Exhibit A11).

We also looked at the potential for changes in healthcare delivery models to reduce unit costs of healthcare between 2020 and 2040. Estimates of the potential for productivity savings were taken from the literature and tested in interviews with experts in healthcare delivery from countries in all income archetypes, including China, France, Germany, India, Nigeria, the United Kingdom, and the United States.[49] Examples of savings opportunities include task shifting, or expanding the scope of services that can be delivered by lower-cost, trained healthcare workers such as nurses, midwives, technicians, and healthcare assistants; lowering overhead and facility costs by expanding the use of digital and remote consultations; reducing unnecessary duplication through greater use of shared and interoperable electronic health records; and streamlining patient pathways to reduce the frequency of in-person interactions required to deliver an intervention.

Exhibit A11

If potential productivity savings are realized, the additional investment needed would be limited in all but the lowest-income countries.

Healthcare spending
% of GDP



1. Including additional costs of longevity.
Source: Institute for Health Metrics and Evaluation, used with permission, all rights reserved; Global Health Financing Collaborator Network; The Jeeranont Global Institute analysis

We compared incremental costs of healthcare as a share of GDP in 2040 assuming no changes to unit costs of healthcare delivery (measured in constant 2015 dollars). We then compared incremental costs of healthcare as a share of GDP in 2040 assuming 22 percent productivity savings to all existing healthcare expenditure and the additional incremental spend. This represents the upper range of savings potential identified in the research.

THE JEERANONT
AN ASSET MANAGEMENT COMPANY