Annex 4

Methodology for return on investment (ROI) calculations

The economic return on investment (ROI) projected to be made during the Global Fund Seventh Replenishment period was estimated for each country and disease via two methods: "intrinsic" and "instrumental" valuation of the averted burden of the three diseases over the period 2024-2030. Estimates of the "intrinsic" value of health are based on what individuals are willing to pay for improvements in their own health (Section 1), whereas the "instrumental" valuation considers the extent to which reductions in sickness and premature deaths increase productive work (Section 2).

The Investment Case scenario was compared to a "constant coverage" counterfactual scenario in which the coverages of key interventions were assumed to be maintained at 2023 levels. For the investment and counterfactual scenarios, the modeling that has been conducted as part of this Investment Case (see Annex 3: Methodology for impact modeling) has estimated the annual number of cases, deaths, disability-adjusted life years (DALYs) and cost. The cost of the investment compared to the counterfactual scenario is a net cost that includes both the cost of the interventions, i.e., those that prevent cases of disease or improve treatment, as well as health sector cost savings from not having to treat as many cases. For both valuations, and following standard approaches,[1,2] the present value of the projected stream of future costs and benefits was calculated by applying a discount rate of 3% per year. As Global Fund investment in countries varies as a proportion of the total cost of the investment scenario, a Global Fund-specific ROI ratio was derived by weighting the disease-specific costs and benefits according to the countries' share of Global Fund allocations during 2027-2029.

Section 1: Intrinsic valuation

Following the methodology of recent Benefit Cost Analysis (BCA) guidelines[1,2] an adjusted Value of a Statistical Life-year (VSLY) calculation was used to calculate country- and year-specific VSLYs that anticipate economic growth in Global Fund-supported countries:

[1] Departmental Guidance on Valuation of a Statistical Life in Economic Analysis. U.S. Department of Transportation, 2022 [cited 2022 January 15]. https://www.transportation.gov/office-policy/ transportation-policy/revised-departmental-guidance-on-valuation-of-astatistical-life-in-economic-analysis.

[2] Valuing nonfatal health risk reductions in global benefit-cost analysis. Robinson LA, Hammitt JK, O'Keefe LO. Journal of Benefit-Cost Analysis 2019;10(Suppl 1):1-36.

$$VSLY_{it} = \frac{VSL_{USA}\left(\frac{GDP_{it}}{GDP_{USA}}\right)^{e}}{\frac{1-(1+r)^{-0.5*LEB_i}}{r}}$$

Value of Statistical Life in the United States, VSL_{USA}
Per capita Gross Domestic Product, purchasing power parity adjusted, GDP_{it}
Income Elasticity, e
Life Expectancy at Birth, LEB_i
discount rate, r
year index, t
country index, i

Where *VSLYit* is calculated using the 2019 estimate of the Value of a Statistical Life (VSL) for the USA of US$12.31M[3], and transferring it to Global Fund-supported countries based on the difference in income between the USA (GDP_{USA}) and the country (GDP_{it}), where GDP_{it} is purchasing power parity (PPP)-adjusted gross domestic product (GDP) per capita of country *i* in year *t* in international dollars, which was obtained from the October 2024 World Economic Outlook;[4] GDP_{USA} is the PPP-adjusted GDP per capita of the USA (estimated at US$82,715 for 2023); *e* is a conservative estimate of income elasticity of 1.5, reflecting that poorer individuals are willing to pay a lower portion of their income for a given incremental of health risk reduction, compared to higher income individuals; and the term in the denominator is the present value of remaining life expectancy for a person in middle-age. As a proxy (recommended in BCA guidelines),[5] we used one-half of life expectancy at birth of country *i* in the year 2023 obtained from the World Bank.[6] We deviated from the BCA guidelines by discounting the remaining life expectancy at 3% per year when converting VSL to VSLY, but this was necessary in order to be consistent in discounting all health benefits and costs, accounting for the year in which they occur. To calculate the ROI, the total number of discounted DALYs averted in each country and year as predicted by the modeling underlying the Investment Case was multiplied by the country/year-specific VSLYs. In this way, we made a choice to value deaths proportionally to the remaining life expectancy associated with the counterfactual of

[3] Productivity Costs: Principles and Practice in Economic Evaluation. Pritchard C, Sculpher M. London: Office of Health Economics, 2000.

[4] World Economic Outlook, April 2024 update. International Monetary Fund, 2024.

[5] Valuing nonfatal health risk reductions in global benefit-cost analysis. Robinson LA, Hammitt JK, O'Keefe LO. Journal of Benefit-Cost Analysis 2019;10(Suppl 1): 1-36.

[6] World Development Indicators Databank. World Bank. https://data.worldbank.org/indicator/SP.DYN.LE00.IN [cited 2018 Dec 4].

that death (how long they would live if they had not died), and we are also valuing the reductions in non-fatal morbidity associated with these diseases.

Section 2: Instrumental valuation

When cases are prevented or effectively treated, household members can continue or return to productive work. Following a standard human capital approach for calculating "indirect cost" in cost-of-illness studies,[7] the productivity loss per case was calculated by multiplying an average duration of temporary disability by a wage rate for both investment and counterfactual scenarios. The duration represented the average days of lost work by the patient (or the patient's parent for childhood malaria cases).

For both TB and malaria, the episode duration was not affected by treatment access, but for malaria, the episode duration depended on whether the case was severe or not. The episode duration for HIV cases was assumed to be the period of symptomatic untreated disease, which include untreated adult patients (>15 years old) with CD4 count below 200 in any one year.[8] During this period, we assumed a 15% reduction in productivity.[9] Wage rate was derived from GDP per capita after subtracting natural resource rents obtained from the World Bank and a further downward adjustment to account for the disproportionate concentration of disease burden in groups of lower socioeconomic status.

Productivity loss due to premature death (i.e., remaining lifetime earnings had the death not occurred prematurely) was calculated by multiplying remaining working years at age of death by a wage rate, assuming that people work until age 65. For persons dying from malaria under 5 years old, we assumed a lag of 10 years before the working age period would begin.

Over 90% of the productivity-based ROI is due to averting productivity losses due to death. Our approach does not account for the potential societal-level impacts on other households not experiencing the disease-related death. It is possible, in settings where much labor is unskilled and unemployment levels are high, that when workers leave the workforce due to death or disease, they are replaced quickly by another – previously unemployed – person, so the net loss at the society level may be reduced. In addition, our analysis does not consider the future consumption (costs) associated with avoiding a premature disease-related death. Finally, we do not consider other macrolevel economic changes that may occur, such as a shift toward lower fertility and

[7] Productivity Costs: Principles and Practice in Economic Evaluation. Pritchard C, Sculpher M. London: Office of Health Economics; 2000.

[8] Data from nine country Population based HIV Impact Assessment (PHIA) surveys, showing the unweighted average proportion of patients not on antiretroviral therapy (ART) who had CD4<200 was 17.5%, which is taken as a proxy for "symptomatic." Personal communication with John Stover, Avenir Health.

[9] Work and home productivity of people living with HIV in Zambia and South Africa: Evidence from the HPTN 071 (PopART) trial. Thomas R, Friebel R, Barker K, Mwenge L, Kanema S, 2019.

greater per-child investment as child survival increases, and the resulting increase in education levels and economic productivity.

To see the method to estimate historical ROI, see https://www.theglobalfund.org/en/results/methodology/.

The Global Fund commissioned a health decision scientist[10] on the faculty of the Health Policy and Management Department at the Harvard T.H. Chan School of Public Health to conduct this study.

[10] Stephen C. Resch, lecturer on Health Decision Science. Health Policy and Management, Harvard T.H. Chan School of Public Health. https://hsph.harvard.edu/profile/stephen-c-resch/.