INTRODUCTION
Scientific knowledge from biomedical research and development (R&D) can be considered a public good insofar as it can be used repeatedly (non-rival) and it is difficult or costly to exclude non-payers (non-excludable)3. Private financing is unlikely for R&D with limited excludability, which occurs in the absence of intellectual property rights that allow investors to fully capture the financial benefits from R&D. Economic theory suggests that private sector investments are primarily determined by positive financial returns, while public and philanthropic investments are determined by the likelihood and magnitude of social returns. This research considers how factors theorized to impact investments in R&D are associated with investments by public, private, and philanthropic sources.

RESEARCH QUESTION
How are factors theorized to impact costs and revenues from global health R&D associated with investments in R&D for specific diseases? How do those investments differ across the public, private, and philanthropic sectors?

METHODOLOGY
• The study begins with a literature review exploring factors theoretically associated with investments in early-stage biomedical research, including basic research and Phase I – III clinical trials.
• We analyze evidence on factors that impact how public, private, and philanthropic investments in R&D are allocated for four diseases with high incidence rates in low- and middle-income countries2: malaria, tuberculosis disease (Tb), hepatitis C (HCV) (genotypes 4, 5, and 6), and soil-transmitted helminthiases (STH).
• We then explore whether these factors are associated with distinct levels of R&D funding by disease.

RESEARCH QUESTIONS
1. How do factors associated with costs and revenues from global health R&D investments differ across the public, private, and philanthropic sectors?
2. How are factors associated with costs and revenues from global health R&D investments associated with investments in R&D for specific diseases? How do those investments differ across the public, private, and philanthropic sectors?

FINDINGS
Multiple factors influence estimated returns to global health R&D investments and allocations of R&D funding by public, private, and philanthropic sources, including disease pathology and epidemiology, the cost effectiveness of existing interventions (which may affect market share and willingness-to-pay), regulatory environments, and market conditions (Table 1). Figure 1 compares global R&D investment to neglected disease R&D investments by sector. Figure 2 illustrates levels of R&D funding and Disability-Adjusted Life Years (DALYs) by disease and sector.

Table 1. Factors associated with costs and revenues/benefits from R&D investments

<table>
<thead>
<tr>
<th>Factor</th>
<th>Aspects</th>
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<tbody>
<tr>
<td>Costs</td>
<td>Fixed and variable costs, political and public budgeting processes, time-to-market, stage of research of candidates for treatment or prevention, regulatory systems, disease pathology, partnerships (risk-sharing)</td>
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<tr>
<td>Revenues/Benefits (financial &amp; social)</td>
<td>Market size, share, and growth, willingness-to-pay (WTP), existence of effective treatment, intellectual property rights, likelihood of knowledge advancement, partnerships, discount rate</td>
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Figure 1. Percent of R&D investment by sector for global health R&D and neglected disease R&D

Figure 2. Investments in R&D by disease and by sector, with DALYs

MALARIA
• Market Size: The global burden of malaria is high, but the ability-to-pay of consumers and high-burden country governments is low, limiting market size and purchasing power. Funding mechanisms have been developed to increase the purchasing power of consumers and demand-side incentives for further R&D.
• Stage of Research/Time-to-Market: The majority of vaccine candidates in the clinical trial stage are in Phase I (22) and II (5). The high risk and long time-to-market of early-stage trials indicates limited incentives for private sector investment and are reflected in increasing private investment after Phase I.

TUBERCULOSIS DISEASE (Tb)
• Existence of Current Treatment: The current BCG vaccine has limited effectiveness and current treatments take over 6 months, providing opportunity for returns on new vaccines and drugs.
• Location of Returns: Investments by middle-income countries with high incidence can provide domestic returns when considering averted treatment costs5.

HEPATITIS C
• Market Size: Surveillance for HCV in low-income countries (LICs) is limited, indicating an unknown market size in these regions, as most diagnostic tools were developed for genotype 1.
• Willingness-to-pay: The majority of interventions are designed for genotype 1, the most common genotype in high-income countries (HICs), while genotypes 4, 5, and 6 are more prevalent in low-income countries and receive less funding.

SOIL-TRANSMITTED HELMINTHIASES (STH)
• Market Size: Because of the cost effectiveness of presumptive treatment and the non-specificity of signs and symptoms, estimates of the global burden vary, such that the market size is unknown.
• Prevalence of Cost Effective Treatment: There is little early-stage research being conducted on STH, likely due to the cost-effectiveness of treatment and the feasibility of eliminating STH with existing interventions.

KEY FINDINGS
• There is a limited association between global burden (in DALYs) and investments in R&D across all diseases.
• Accurate disease surveillance is key for identifying market size; diseases with poor diagnostics have more uncertain estimates of potential revenues/benefits.
• Diseases with incidence in HICs and LICs show some association with increased private sector investment; dual markets can increase the likelihood of financial returns.