

## Supplementary Material

### 1 Supplementary Methods

#### **Database construction**

Since 1990, the World Health Organization and collaborating organizations have attempted to generate comparative data on the global burden of diseases and injuries and update this dataset over time. Here we used the recently updated Global Burden of Disease (GBD) estimates for 2000–2019 as a foundation to identify major categories of infectious and parasitic diseases of global health importance, for which disability-adjusted life years (DALYs) and years of life lost due to disability (YLDs) have been calculated (20). We used ICD-10 codes provided for “infectious and parasitic” Global Health Estimates (GHE) to identify causative agents of disease to species, but excluded diseases categorized in “other” causes and any ICD-10 codes associated with unspecified causes of disease (20). This resulted in 150 individual species, which we refer to as 150 “infectious diseases” throughout. For each infectious disease, we characterized the dominant transmission strategy, identified obligate and relevant non-human host ranges, and estimated the amount of time each infectious organism spends in human, animal, and environmental reservoirs during the course of its life cycle (distinguishing incubation periods from duration of infectiousness).

Transmission strategies included: human-to-human; fecal–oral; food-borne; soil-borne; water-borne; vector-borne; zoonotic (i.e. direct contact between humans and wild or domestic vertebrates); and sapronotic (saprophages, free-living organisms that consume dead plant and animal biomass, infect humans opportunistically (22)). Among helminths, only schistosomes use water-borne transmission as a primary transmission strategy, so we merged water-borne helminths with soil-borne helminths for visualizations and descriptive statistics. Diseases acquired through fecal–oral transmission are often characterized as human-to-human transmission, but we distinguished the fecal–oral strategy from direct transmission via respiratory droplets and close, intimate contact. For diseases that can be transmitted via multiple routes, we included the strategy assumed to cause the greatest number of infections, but we also provide a “secondary” transmission route in the database. For example, *Vibrio cholerae* is sometimes considered a sapronotic or water-borne disease (22), but because many large outbreaks are associated with fecal-oral transmission within households or communities (41,42), we classify it as a fecal-oral pathogen, with water-borne transmission as a secondary strategy.

For diseases with non-human vertebrate hosts, we classified the animal vertebrate hosts as: (i) obligate hosts, where humans are incidental or dead-end hosts; or (ii) relevant alternative hosts, where vertebrates maintain parasite and pathogen populations independently from humans, and can therefore contribute to disease in certain contexts at the animal–human interface and may compromise long-term control. The primary vertebrate host was classified as: humans only; wild animals (including birds); companion animals (i.e., dogs or cats); livestock; or, mixed, where humans and non-human vertebrates can both maintain pathogen populations. Vertebrate host ranges (i.e., all known host species used by the pathogen), provided descriptively, are therefore likely to change as new data emerges for diseases that are currently less well understood.

Duration was characterized as time (in days) that a single infectious organism spends in the following contexts: in vertebrate hosts (including humans); as free-living stages in abiotic environments; or in obligate vectors or intermediate hosts. We attempted to distinguish the duration of incubation periods

from infectious periods, but this information is lacking for many pathogens. For many parasites and pathogens, human (or vertebrate) infectious periods can be cyclical or interspersed with dormant stages; for consistency, we estimated duration of infectiousness as the average duration of infection, even though this may overestimate the actual period spent shedding enough infectious material to cause infection in other hosts. For these and other reasons, the total time an infectious organism spends in various stages of its life cycle does not represent its generation time. Moreover, disease duration can be highly variable in humans and environmental reservoirs depending on host body condition, temperature, humidity, and other physical and biological factors. For this reason, we include a description of duration according to data found in literature sources in the supplemental database.

We also collected data on the contemporary, or most recently available, total number of cases each infectious organism causes in humans in a given year. Because source estimates of global cases are highly variable, sometimes outdated, and often difficult to find, we reduced the chances of assigning an incorrect estimate of global cases by assigning cases to logarithmic categories (i.e., 0–100; 101–1,000; 1,001–10,000, 10,000–100,000; 100,000–1 million; >1 million; >1 billion). Rare and neglected diseases that lack centralized reporting systems and diseases that do not typically require medical treatment are likely underestimated.

Finally, we included data on the ‘gold standard’ control strategy recommended by global health organizations for each disease or closely related diseases. Control strategies include (i) behavior or lifestyle change (e.g., safe sex); (ii) vaccination or pre-exposure prophylaxis; (iii) water, sanitation, and hygiene (WASH) or safe food preparation; (iv) vector control; (v) reservoir host treatment (e.g., animal vaccination); and (vi) integrated human and environmental control (e.g., combinations of multiple strategies such as mass drug administration and environmental control). We note that some “gold standard” prevention strategies, like pre-exposure prophylactics (PrEP) for HIV, are not accessible or affordable to those who may need them.

Between 2017 and 2020 we conducted extensive literature searches to collect data on the ecology of rare diseases and to estimate duration of time spent in human and environmental reservoirs (incubation and infectious periods). Where possible, data were acquired from peer-reviewed scientific literature, the World Health Organization, the U.S. Centers for Disease Control and Prevention, and health communications resources provided by other academic, national, and global health institutions (i.e., (43)). Peer-reviewed sources used included laboratory experiments, modeling exercises, and reviews.

The life cycles, host ranges, environmental persistence, and control strategies of many diseases are still being investigated, and data presented here is likely to change as more knowledge is generated. Therefore, we encourage users to consider this database as a first step in synthesizing data on the life cycle, host diversity and environmental persistence of parasites and pathogens causing a substantial burden of human infectious disease, and to further investigate specific diseases of interest.

### ***Descriptive statistics***

We used linear mixed effects ANOVAs to describe (i) how duration of infectious stages outside obligate vertebrate hosts varies with primary transmission strategy; (ii) how duration of infectious stages outside vertebrate obligate hosts varies with gold standard control and prevention practices; (iii) how global cases (minimum value of logarithmic range) varies with transmission pathways; and (iv) how global cases vary with obligate vertebrate host range. Both outcome variables (duration of infectious stages and global cases) were scaled using a natural logarithm. We included a random

effect term for the 11 major disease categories assigned in the WHO GBD database (Tuberculosis, STDs excluding HIV, HIV/AIDS, Diarrheal diseases, Childhood-cluster diseases, Meningitis, Encephalitis, Hepatitis, Parasitic and vector diseases, Intestinal nematode infections, Leprosy), excluding ‘Other infectious diseases’. All analyses were performed in the statistical computing software, R, version 1.3 (44) and models were built using the ‘lme4’ package (45). Estimated marginal means for categorical predictors were estimated using the ‘emmeans’ package (46).

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## 2 Supplementary Data

See the attached database.

## 3 References for Supplementary Data

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