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Misalignment between global disease burden and research efforts through the lens of sex/gender

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Abstract

Men lose more life years to premature mortality (years of life lost, YLL), whereas women live longer but spend more years in ill health (years lived with disability, YLD). Whether biomedical research reflects these differing burdens remains unclear. We linked more than eight million disease-specific publications from 2000 to 2023 to sex/gender-disaggregated Global Burden of Disease (GBD) data across 125 causes to examine research-burden alignment. Across regions and over time, research was 1.8x more aligned with YLL than YLD, disadvantaging women. This gap widened with sociodemographic development. If current trends continue, the global gap is projected to more than double by 2040 relative to 2000 levels, reflecting the growing contribution of disability to disease burden worldwide. Embedding sex/gender-disaggregated research–burden alignment indicators into funding priorities, evaluation frameworks, and national and global health agendas could drive greater equitable healthy longevity for all.

Consideration of sex and gender in this manuscript.

Although the Global Burden of Disease (GBD) framework reports data separately for males and females and labels these categories "sex," the underlying data are drawn in part from self-reported and administrative sources that do not allow for a reliable separation of biological and social determinants of health (see Methods for details). We therefore use the term **sex/gender** throughout this manuscript and refer to men and women to reflect that the burden data refers exclusively to humans[1-3].

Introduction

Health is strongly related to sex/gender. Perhaps the clearest indication is that men lose more years of life to premature mortality (years of life lost, YLL); women live longer but spend a greater share of life in ill health (years lived with disability, YLD). This divergence between lifespan and healthspan is increasingly recognized as a persistent phenomenon in global health[4,5]. Despite this growing awareness, comparatively little is known about how biomedical research engages with these patterns or responds to their evolution over time. Assessing how research priorities reflect sex/gender-specific health needs is therefore essential to delivering optimal medical care for all.

Past research has suggested that a "sex/gender data gap" in biomedical research likely contributes directly to a "sex/gender health gap"[6]. Studies have shown that imbalances in sex representation in preclinical animal models and insufficient consideration of sex and gender in clinical trials can lead to biased evidence bases, suboptimal treatments, and avoidable harms[7-9]. In response, frameworks have emerged to facilitate integrating sex and gender analysis across the research pipeline[10,11]. These approaches have increasingly garnered institutional support reflected in, for example, policies adopted by major research funders, journals, and universities[12-14]. While this literature has advanced our understanding of *how* to better conduct research, far less attention has been paid to *what* gets researched in the first place. Whether global research priorities reflect sex/gender differences in health needs remains largely unexplored. Existing evidence provides only fragmented indications that conditions predominantly affecting women may receive disproportionately less scientific and technological investment. For example, analyses of innovation processes suggest systematic biases in whose health is prioritized[15], and recent reporting has highlighted persistent underfunding of women's health research across major funding systems[16]. These findings indicate that structural disadvantages for women's health needs pervade the research enterprise itself.

A potential misalignment between research efforts and men's and women's disease burden is problematic from both a public health and economic perspective. Recent analyses emphasize that persistent gaps in women's health translate into substantial productivity losses and unrealized economic value[17]. Estimates suggest that improving the diagnosis, treatment, and prevention of conditions disproportionately affecting women could unlock tens of billions of dollars in economic potential, underscoring that gender imbalances in research priorities carry broad societal costs beyond individual health outcomes[18].

With this study, we conducted the first systematic, longitudinal assessment of how biomedical research aligned with sex/gender patterns of disease burden. Using an expansion of our previously established large language model-based method[19], we constructed a crosswalk between research output indexed in PubMed and sex/gender-specific health data, linking more

than eight million disease-specific publications to two decades of Global Burden of Disease (GBD) data across 125 disease categories. We examined the distribution of research output by volume and type and compare it with disease burden disaggregated by YLL and YLD, and their composite measure, disability-adjusted life years (DALYs)[20,21] and eventually further disaggregated by sex/gender. To stratify results by development, we used the Socio-Demographic Index (SDI), the GBD's composite measure of income per capita, educational attainment, and fertility[5]. In this context, SDI offers a consistent way to compare locations across the same framework used for burden estimation while capturing broad variation in epidemiological profiles, including the balance between mortality- and disability-related burden[22]. We documented the historical misalignment between biomedical research and sex/gender-disaggregated health measures from 2000 to 2023, the most recent year available from the GBD. We used simulations to project how the alignment between research effort and the evolving disease burden for men and women is likely to develop through 2040.

Results

Sex/gender differences in mortality-focused vs morbidity-focused research

We began our analysis by examining whether research activity aligns differently with YLLs and YLDs. To do so, we extended our established approach that links research publications to broad disease categories and their associated burden[19] by applying a granular mapping to 125 disease categories from the GBD database (see Methods).

In Figure 1A, we first examined how YLLs and YLDs accumulate across diseases when ranked by research volume. The resulting cumulative distributions show that research is substantially more concentrated on diseases that primarily cause YLL than those that primarily cause YLD. The 10 most researched disease causes account for 59% of global YLLs compared to 14% of global YLDs, corresponding to a 4.2-fold difference in research coverage. Expanding to the 30 most researched diseases increases coverage to 79% of YLLs and 46% of YLDs.

To quantify divergence across the full distribution of diseases, we followed prior work using the Kullback–Leibler divergence (KLD) to measure the extent to which the distribution of research aligns with the distribution of disease burden across causes[19]. A KLD of zero indicates perfect alignment and higher values indicate greater divergence. As shown in Figure 1B, research exhibits lower divergence from YLLs (KLD = 0.67) than from YLDs (KLD = 1.23), corresponding to a 1.8-fold difference. Thus, across disease categories, global biomedical research is more aligned with mortality-related burden than with disability-related burden.

We next examined how YLLs, YLDs, and their composite measure, DALYs, differ between women and men and across countries. For each country, we calculated the ratio of total burden in women relative to men. Ratios below one indicate higher burden in men, ratios above one indicate higher burden in women, and ratios equal to one indicate approximate parity.

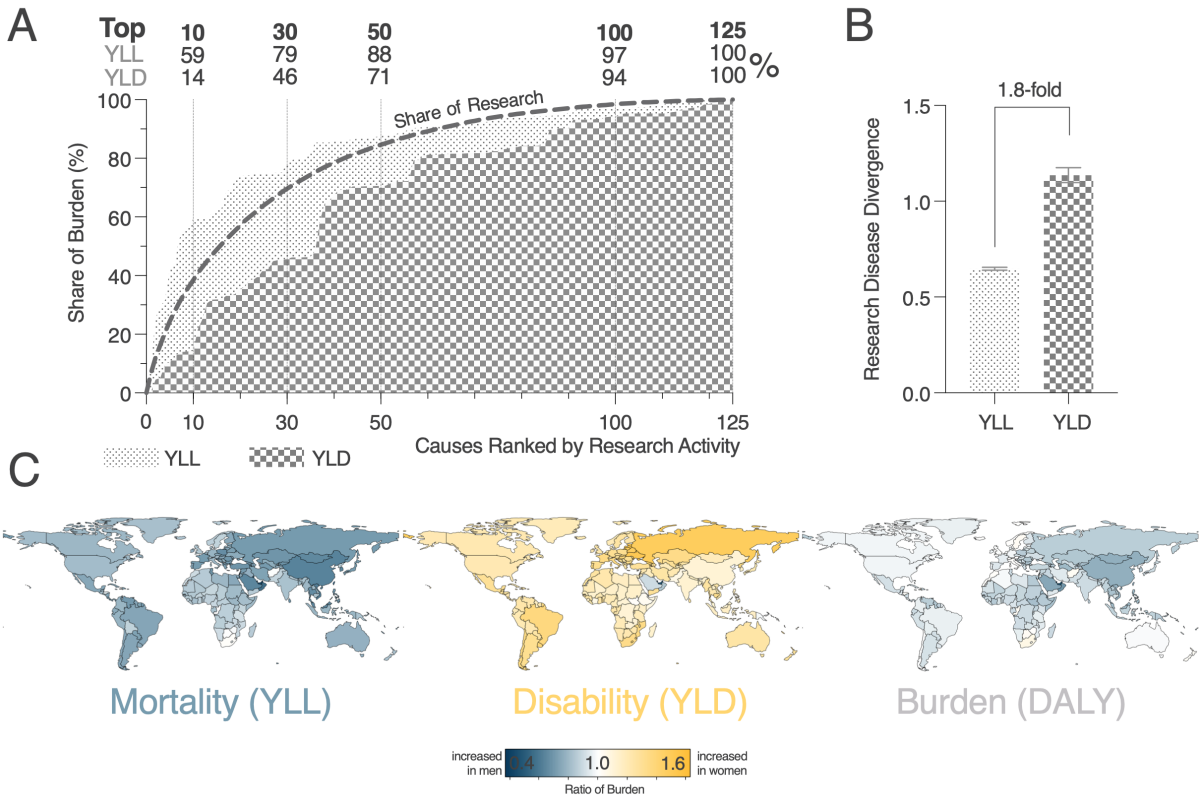

Fig. Alignment between research and disease burden, stratified by disease burden metric and sex/gender.
(A) Cumulative distribution of disease burden for years of life lost (YLLs, dotted area) and years lived with disability (YLDs, square-patterned area) across diseases ranked by research volume, illustrating the stronger alignment of research with mortality-related than with disability-related burden. (B) Divergence between research and disease burden across all diseases measured by the Kullback–Leibler divergence (KLD), showing stronger alignment of research activity with YLLs than with YLDs. (C) Ratio of disease burden carried by men versus women shown for YLLs and YLDs, and their composite measure, DALYs, averaged for the years 2000 to 2023 and stratified by country. Mortality-related burden (YLL) is higher in men, whereas disability-related burden (YLD) is higher in women.

Figure 1C shows that excess mortality among men and excess morbidity among women are global phenomena, across diverse geographic and sociodemographic contexts. In contrast, DALYs, combining YLLs and YLDs, often appear closer to parity because the composite excess mortality in men and excess disability in women partially offset one another. These patterns, however, are based on data pooled over 2000–2023. Over this period, the composition of global disease burden shifted substantially: YLDs increased by 44%, whereas YLLs declined by 14% (Extended Figure 1). Although these trends do not imply that research caused this shift, they indicate that disability represents a growing share of total burden and thus provide an important context for evaluating whether research priorities have kept pace with changing health needs. Importantly, this shift is not simply a consequence of people living longer and the disabilities associated with older age,

since YLDs are most pronounced among people aged 30 to 60 (Extended Figure 2). Consequently, a transition toward disability-related burden has important implications for sex/gender equity in the research portfolio.

Research-disease divergence for men and women across world regions

To quantify how this shift in disease burden influences the alignment between research and sex/gender-specific disease, we integrated sex/gender-disaggregated burden data with disease-specific publication data. For each burden metric (YLLs, YLDs, and DALYs), we computed a sex/gender-specific divergence between the global research distribution and the burden distribution for women and men separately. We then derived the *sex/gender research gap* as the absolute difference in the women and men specific research-disease divergence, relative to the average divergence across both groups. This metric offers a clear assessment: positive values indicate that research is less aligned with the burden profile of women; negative values indicate greater misalignment for men. The absolute magnitude reflects the extent of misalignment between research effort and the sex/gender-specific disease burden. As the denominator in this metric is the average divergence across women and men, and since diseases affecting only one sex/gender represent only a small fraction of overall burden, we offer a separate analysis of the eight diseases that affect either men or women (Extended Figure 3) and restrict the main analyses to the diseases affecting both.

Figure 2A shows that the sex/gender research gap is consistently larger for women across all burden metrics. The gap is most pronounced for YLDs, where research alignment for women deviates by about 18% from the mean divergence, reflecting both the stronger concentration of research on mortality and the higher disability burden borne by women. For YLLs, the gap remains positive at roughly 2% and statistically distinguishes from zero, i.e., from sex/gender-balanced research. Using DALYs as a composite measure yields a gap of about 10%, consistent with the continued (though declining) dominance of mortality within total burden.

Figure 2B illustrates the growing contribution of YLDs to DALYs with increasing levels of development across SDI regions (horizontal axis). Each shaded point represents the annual ratio of YLDs to DALYs for a given region (low SDI is represented by squares, middle SDI by diamonds, and high SDI by circles), while white symbols indicate the regional averages over the period 2000–2023. Within regions, the share of disability has increased steadily over time. Across regions, higher levels of sociodemographic development are associated with a larger contribution of YLDs to total DALYs, such that high SDI regions exhibit substantially greater morbidity shares than low SDI regions, where YLLs continue to dominate overall burden.

The sex/gender research gap increases with the share of YLDs in DALYs, exhibiting an almost perfectly linear relationship ($r = 0.97$, $p < 0.01$). In low SDI regions, where mortality accounts

for almost 90% of total burden, the research-disease gap remains close to parity. In contrast, in high SDI regions, where disability approaches half the total DALYs, the sex/gender research gap is largest, reflecting the interaction between a mortality-oriented research portfolio and the higher disability burden for women. This pattern further suggests that world regions may differ in the current need to rebalance research portfolios from a sex/gender equity perspective, while the pattern holds limited information about future needs for rebalancing.

Therefore, we analyzed the sex/gender research gap annually from 2000 to 2023 and projected trends through 2040, stratified by SDI region (Figure 2C). Between 2019 and 2023, the gap temporarily fluctuates, driven primarily by high SDI regions. This fluctuation reflects two concurrent dynamics: the mortality spike caused by COVID-19, which disproportionately increased premature mortality among men, and the even larger redirection of research toward COVID-related conditions[19]. Together, these dynamics demonstrate that the sex/gender research gap measure responds to shifts in both disease burden and research activity, while also highlighting the exceptional nature of the COVID-19 period that cannot be used to infer long-run trends. Looking ahead, the sex/gender research gap is projected to widen steadily through 2040 (Figure 2C). This trajectory follows directly from the interaction of two observed empirical regularities: biomedical research is expected to remain more closely aligned with mortality than morbidity in the steady-state, and disability-related burden will continue to rise and disproportionately affect women. By 2040, YLDs are projected to increase by 82% relative to 2000, whereas YLLs are projected to decline by 14% (Extended Figure 1). As the share of YLDs in total DALYs increases, misalignment in morbidity-focused conditions widens the sex/gender research gap to the disadvantage of women across all regions. This growth is projected to be fastest in low SDI regions, albeit from the lowest baseline.

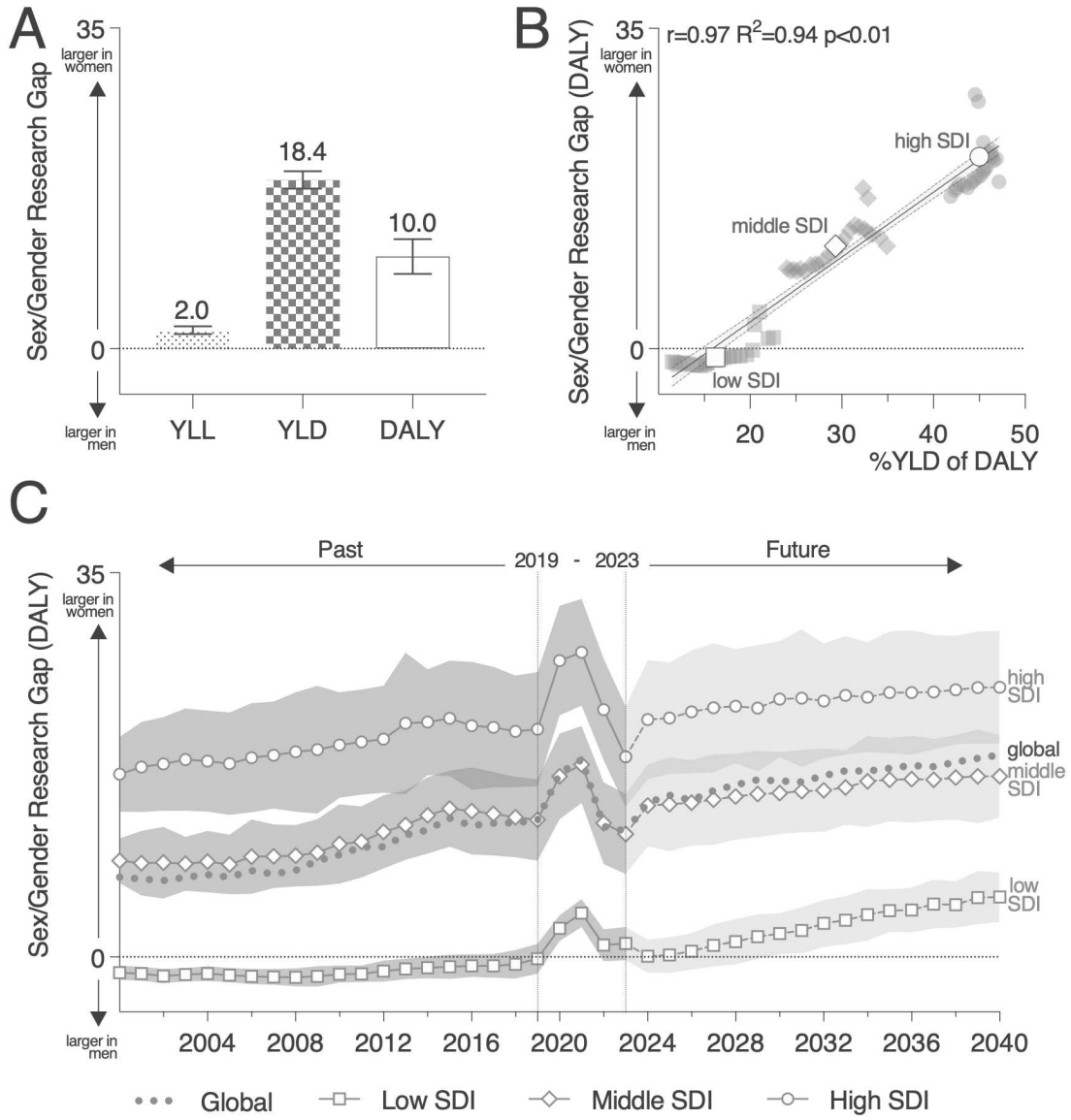

Fig. 2. Sex/gender research gap, stratified by disease burden and SDI (socio-demographic index) region.
(A) Sex/gender research gap for the global distribution of disease burden averaged over 2000–2023, shown separately for YLLs, YLDs, and DALYs. (B) Association between the sex/gender research gap for DALYs (y-axis) and the share of YLDs in total DALYs (x-axis), shown by SDI (socio-demographic index) region and over time. Shaded points represent annual observations by region (squares: low SDI, diamonds: middle SDI, circles: high SDI). White symbols indicate regional averages across 2000–2023. The fitted line shows the estimated linear relationship with dotted 95% confidence intervals. (C) Observed and projected sex/gender research gap from 2000 to 2040, stratified by SDI region and provided as global average (dots). Shaded areas indicate 95% confidence intervals. The period 2019–2023 is highlighted to denote the COVID-19 shock, which temporarily altered mortality patterns and research activity and is therefore excluded from the estimation of long-run projections from 2024 to 2040.

To highlight the geographic distribution of the sex/gender research gap, Figure 3 depicts country-level patterns inferred from SDI status and compares the earliest year in our dataset (2000) with projections for 2040. A gap to the disadvantage of women is already visible across most countries in 2000 (Figure 3A), indicating a greater misalignment between disease-specific research and the disease burden of women relative to men. The global sex/gender research gap is projected to more than double by 2040, increasing from 7.3% in 2000 to 18.4% (Figure 3B). The increase is observable across all levels of sociodemographic development but is most pronounced in high SDI

countries, where the gap rises from 17% in 2000 to 25% by 2040. Middle SDI countries show a slightly smaller increase, from 9% to 16%, while low SDI countries shift from near parity in 2000 (–1%) to a projected 5% gap by 2040. Thus, in contrast to many global health disparities that disproportionately affect less developed regions, the sex/gender research gap emerges most strongly in highly developed settings, spanning countries across North America, Europe, and Oceania. This analysis underscores that the disadvantage for women geographically coincides with areas where research capacity is also greatest.

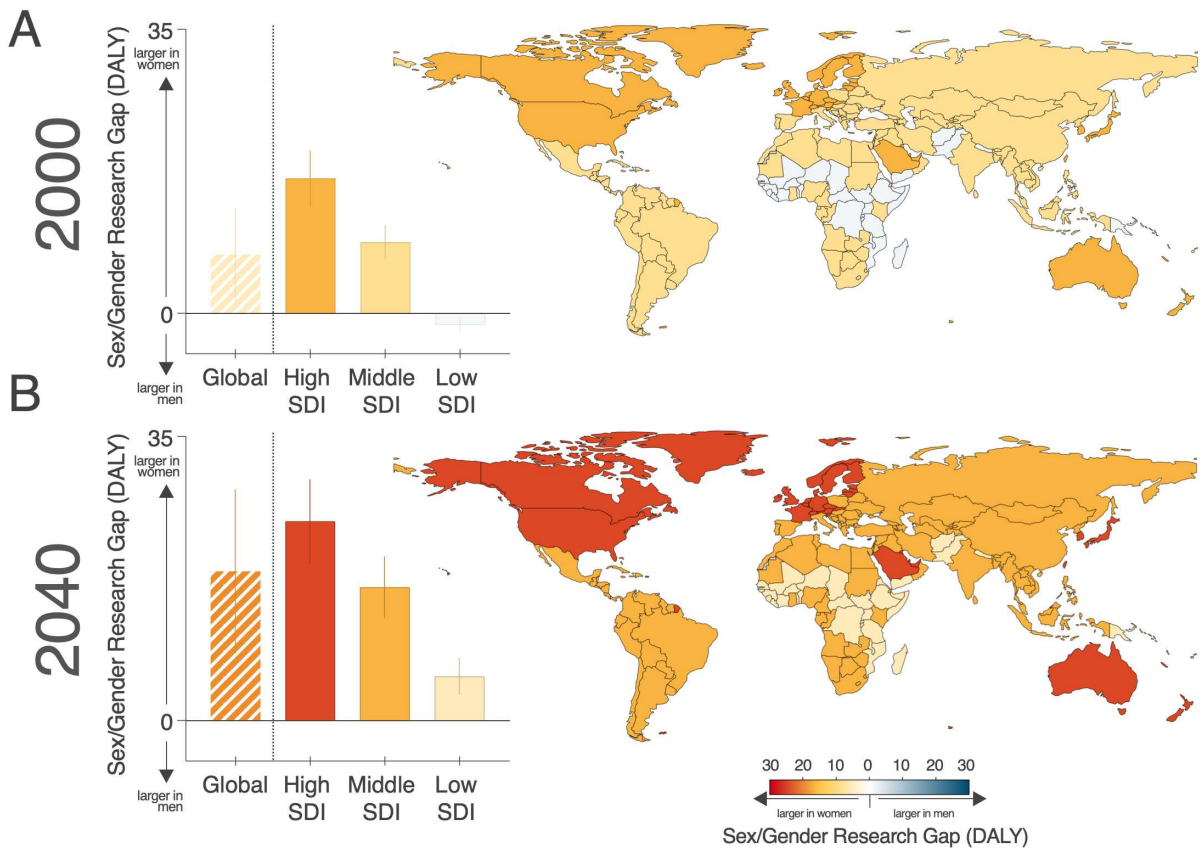

Fig. 3. Comparison of the sex/gender research gap in 2000 with the projected sex/gender research gap in 2040, stratified by SDI (socio-demographic index) region.

Sex/gender research gap across SDI regions, displayed as bar charts (left panels) and world maps (right panels) for the years 2000 (A) and 2040 (B). In the bar charts, vertical lines indicate 95% confidence intervals. In the world maps, coloring reflects the magnitude of the sex/gender research gap, with zero represented by a pale/white midpoint and increasing values indicating a larger gap to the disadvantage of women, shown along a gradient from yellow to orange to red. The respective color gradient for men is grey to dark blue. Across regions, the gap is projected to increase substantially by 2040 compared to 2000.

Contribution of disease causes to the sex/gender research gap, by region

To identify individual diseases that drive the sex/gender research gap, we analyzed disease-specific contributions. A given disease contributes to the sex/gender-specific gap depending on how strongly research activities diverge from the burden distribution for men and women, respectively. For each SDI region, we identified the ten disease causes with the largest contributions from 2000 to 2023 separately for women and men.

Figure 4 presents this breakdown by SDI region. The left panels show the 10 leading disease contributors for men by SDI region, while the right panels show those for women. Disease names in bold indicate conditions that rank among the top 10 contributors across all three SDI regions. For each region, the top horizontal bar displays the combined burden from these 10 contributors and the share for men (blue) and women (yellow). The middle bars indicate the proportions of that burden attributable to YLLs (dotted) and YLDs (squared), and the bottom bars compare the share of DALYs attributable to these diseases in the respective SDI region with the share of global research focused on the same causes.

Across all SDI regions, the top horizontal bars reveal a consistent pattern in the burden distribution of the ten leading contributors to the sex/gender research gap. Within each region, these diseases exhibit an approximately 60% to 40% split in burden between the more affected and the least affected sex/gender group. For example, in middle SDI regions, the identified diseases for men account for 59% of the burden of men, whereas the identified diseases for women account for 58% of the burden of women. In other words, the identified major disease contributors impose a roughly 50% higher burden on the associated sex/gender compared with the other group. This pattern holds symmetrically for men and women across regions, indicating that the identification of the major disease contributors effectively isolates conditions with substantial sex/gender imbalances.

The middle horizontal bars further show that the composition of this burden differs markedly by sex/gender. For men, the burden associated with these leading contributors is driven by YLLs, accounting for approximately 95% of total burden in low SDI regions and remaining dominant (82%) even in high SDI regions. In contrast, for women, mortality dominates only in low SDI regions, whereas in middle- and high-SDI regions the pattern reverses, with YLDs accounting for more than 70% of the burden. This gradient mirrors the broader patterns documented earlier, but here demonstrates that the divergence between mortality- and morbidity-driven burden is already fully reflected within the subset of diseases that most strongly drive the sex/gender research gap.

The bottom horizontal bars indicate that the diseases driving the gap for men are concentrated within a smaller set of conditions, particularly in low- and middle-SDI regions, where

they account for 50% and 41% of total regional DALYs, respectively. In high SDI regions, this concentration declines to 29%. By contrast, the corresponding contributors for women account for a smaller and more stable share of total burden across all regions, generally ranging between 20% and 30%. While conditions disadvantaging men are thus more concentrated, conditions disadvantaging women display greater cross-regional consistency. As indicated by the bolded disease labels, several conditions, dietary iron deficiency, low back pain, headache disorders, and neck pain, appear among the leading contributors in all SDI regions, pointing to a stable set of morbidity-driven conditions underlying the sex/gender research gap for women. These conditions largely fall within broader categories of musculoskeletal disorders, neurological and mental health conditions, and nutritional deficiencies, and their consistency across regions suggests opportunities for coordinated global research efforts. Finally, a rebalancing of research priorities appears warranted, as across regions the major diseases driving the sex/gender research gap remain under-researched relative to their burden for both men and women.

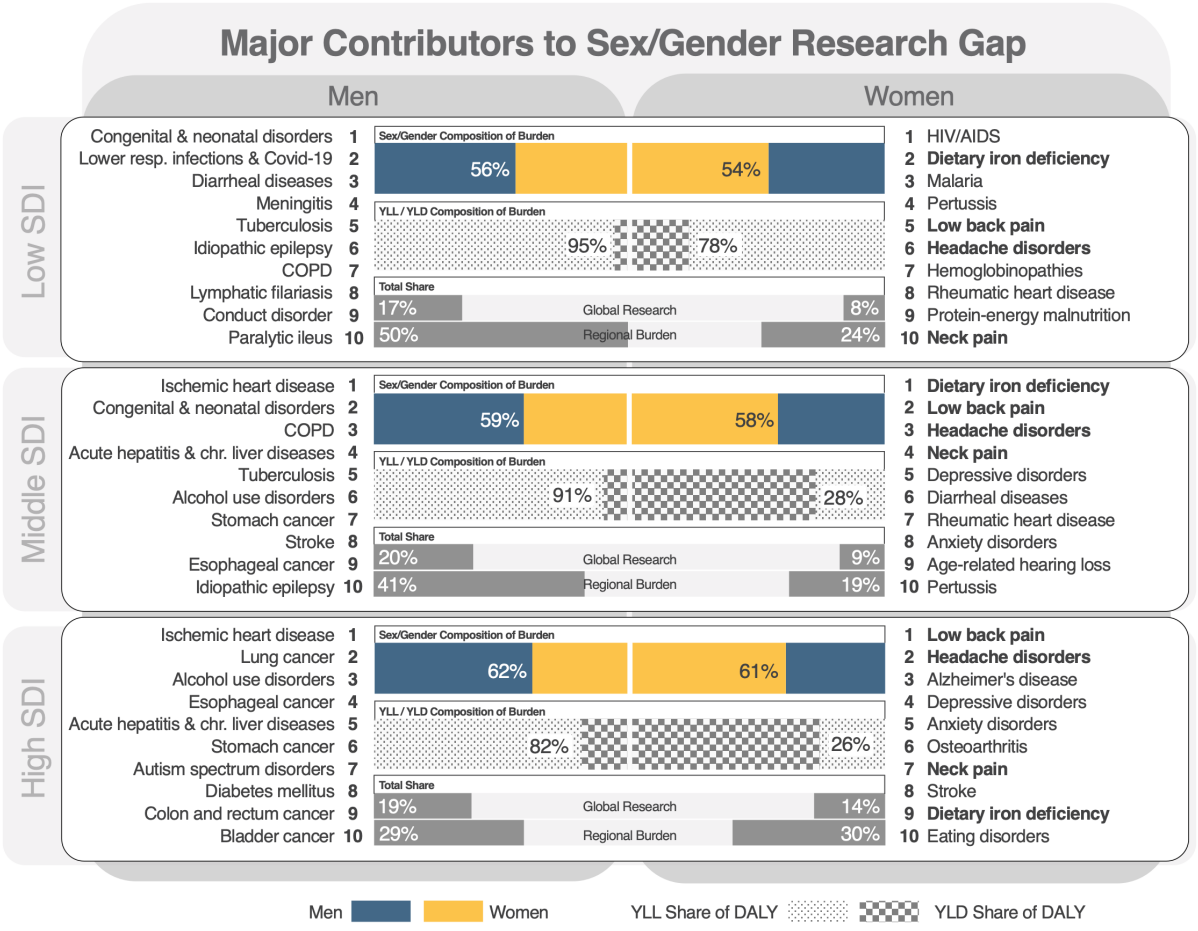

Fig. 4. Main contributors to the sex/gender research gap, by SDI region.

Disease causes contributing most strongly to research–disease divergence to the disadvantage of men (left panels) and women (right panels), shown by SDI region. The upper bars show the share of the total burden from these disease causes, measured in DALYs, borne by men (blue) and women (yellow). The middle bars show the share of that burden attributable to YLLs (dotted) and YLDs (squared). The lower bars compare the share of total regional disease burden attributable to these causes with the share of global research devoted to them. Disease names in bold indicate conditions that appear among the top ten contributors in all three SDI regions. Disease rankings, as well as the corresponding burden and research shares, are based on annual averages for 2000 to 2023.

Disease causes underlying the sex/gender research gap, by research type

We next examined whether the diseases contributing most strongly to the sex/gender research gap also differ in the types of research conducted. Publications were classified into three non-exclusive categories: basic research, clinical research, and health systems research. For each major contributing disease, we calculated the distribution of these research types across SDI regions. Across regions, the dominant research type differs by sex/gender (Figure 5A). Major diseases contributing to the research gap for men receive a 14% larger share of basic research (38% for men versus 33% for women). Clinical research shares are similar across the two groups (about 34% for men and for women). In contrast, diseases contributing to the research gap for women receive a 17% larger share of health systems research (33% versus 28%).

These broad differences in research types coexist with important disease- and region-specific dynamics (Figures 5B and 5C). The concentration of contributors differs visibly across sex/gender and SDI region, with fewer, but larger, blue bubbles for diseases contributing to the research gap for men, especially in low SDI regions, and a larger number of sizable yellow bubbles for major diseases driving the sex/gender research gap for women, especially in high SDI regions (consistent with Figure 4). Some contributors driving the sex/gender research gap for men lie squarely along the dominant basic/clinical axis, including congenital and neonatal disorders in low SDI regions and ischemic heart disease in middle- and high SDI regions. However, several conditions are also characterized by a stronger health systems research focus and depart from this pattern. Alcohol use and conduct disorders, for example, appear closer to the health systems vertex, reflecting the importance of prevention, behavioral interventions, and policy-oriented responses for certain diseases driving the gap for men.

Contributors to the sex/gender research gap for women also show notable variation around the overall clinical and health systems orientation. In high SDI settings, several conditions, including anxiety disorders, depressive disorders, and eating disorders, cluster toward the clinical and health systems side of the plots. At the same time, some contributors associated with women fall markedly outside this pattern. Alzheimer's disease, for example, appears closer to the basic research vertex, reflecting the strong molecular orientation of this field. In lower SDI settings, infectious diseases such as HIV/AIDS, malaria, and diarrheal diseases also contribute to sex/gender research gap for women and appear closer to the basic side of the plots. Although yellow bubbles tend to become larger toward higher SDI regions, consistent with the broader rise in YLD shares of total DALYs, these examples illustrate that the drivers of the sex/gender research gap vary across both diseases and regions.

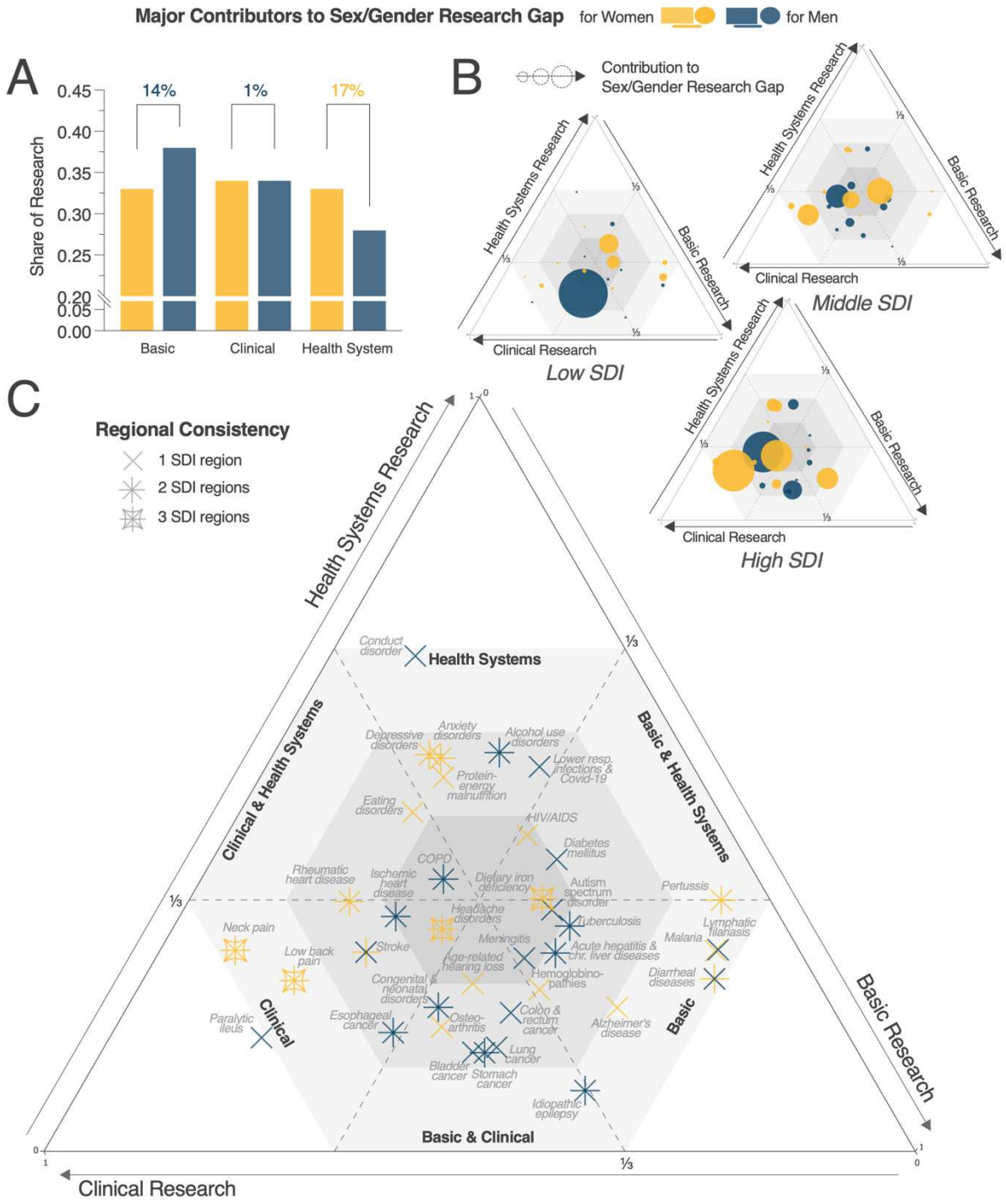

Fig. 5. Major contributors to the sex/gender research gap, by research type.
(A) Bar plot showing the distribution of research effort across basic, clinical and health systems research for the diseases contributing most to the sex/gender research gap for men and women. Percentages indicate the difference in research share between men and women within each research category. (B) Ternary plots illustrating the predominant research orientation for publications associated with each disease, stratified by SDI region (low, middle, high). Diseases near the center reflect a balanced distribution across research types, whereas proximity to a vertex indicates dominance of a single research type; positions along edges indicate combined emphasis on two research types. Bubble size represents the relative contribution of each disease to the sex/gender research gap within the respective SDI region. (C) Global ternary plot showing the distribution and regional consistency of major contributors to the sex/gender research gap. Labels indicate individual diseases and symbols denote whether a disease is a major contributor to the sex/gender research gap in one, two, or all three SDI regions.

Discussion

This study shows that global biomedical research aligns more closely with diseases that cause premature mortality than with those that drive morbidity. Because women experience a larger share of their disease burden through years lived with disability, this mortality-oriented research generates a persistent sex/gender research gap that disproportionately disadvantages women. Previous work has largely focused on how sex and gender should be incorporated into biomedical research practice[6,10,23]. In parallel, another body of work has documented sex/gender differences in global disease burden, particularly the greater contribution of disability over the life course of women[5,20]. By linking global research activity to standardized measures of mortality and morbidity across diseases, countries and time, our study brings these two strands together and provides the first global, longitudinal assessment of how research priorities align with sex/gender-based patterns of disease burden**.** Because research priorities shape the trajectory of medical knowledge, innovation, and clinical practice, gaps in research investment can create blind spots in diagnostics, therapeutics, and care delivery[15,24,25]. Our findings suggest that such gaps originate at least partially upstream, where global research focuses on mortality- over morbidity-causing diseases. This asymmetry results in gaps in understanding sex/gender differences and ultimately in failures to adequately protect women's health.

One possible explanation for this focus on mortality lies in the structural dynamics through which scientific research evolves. Research agendas often develop cumulatively, as existing infrastructures, expertise, and funding streams shape subsequent project selection and investment decisions. A growing literature in the economics and science of science shows that such dynamics can generate path dependence and risk-averse topic selection, with scientists often building on established areas of expertise and funding programs that reinforce existing trajectories[26,27]. These dynamics are consistent with our previous work showing that biomedical research activity has historically been only weakly adaptive to shifts in disease burden over time, creating inertia in the global allocation of biomedical research[19].

This structural inertia may be further amplified by the greater visibility of mortality relative to morbidity in public policy and funding priorities. Indicators such as life expectancy, driven solely by age-specific mortality, feature prominently than disability in cross-national comparisons of health attainment[28]. One founding motivation of the GBD was to move global comparisons of health attainment beyond mortality alone by incorporating non-fatal health outcomes into a common metric of population health.[29] The continued focus on mortality that we document here likely reflects the interaction of two related failings: the under-recognition of morbidity health outcomes, and the under-representation of women's diseases in biomedical research.

While the sex/gender research gap disadvantages women across all world regions, the magnitude of this gap varies systematically with sociodemographic development. In low SDI regions, where mortality still accounts for a large share of disease burden, the sex/gender research gap is relatively small. By contrast, in high SDI regions, where disability accounts for a much larger share of total health loss, the sex/gender research gap is substantially greater. This pattern differs from many global health disparities that disproportionately affect lower-income settings.[19,30-32] Paradoxically, the disadvantage for women emerges most strongly in highly developed research environments, where scientific capacity and investment are greatest.[33] These regional differences also point to an important temporal implication**.** Our longitudinal perspective suggests that the sex/gender-related research gap is likely to increase over time, although at different rates across SDI regions. Morbidity-driven conditions will represent a growing share of total disease burden worldwide,[19] and if research portfolios remain focused on mortality-dominated diseases, the resulting gap between research priorities and the health needs of women will widen across regions as lower SDI regions will likely develop toward higher SDI disease burden profiles.

Examining the region-specific disease drivers of the gap provides insight into where course correction may be most impactful. Conditions contributing to the sex/gender research gap for men are concentrated in a few high-burden diseases, including cancers, cardiovascular diseases and infectious diseases. These diseases account for a high share of overall disease burden for both men and women and thus remain important targets of biomedical research. Our findings should not be interpreted as a call to markedly reduce research in these areas. Rather, our findings point to the need for targeted efforts toward globally prevalent conditions, including musculoskeletal disorders, headache disorders, and nutritional deficiencies, which contribute disproportionally to women's disability burden.

Beyond the volume of research, differences in the types of research conducted may also contribute to the observed imbalance. Diseases contributing to the gap for men are more strongly represented in basic research, whereas many conditions contributing to the gap for women receive relatively greater attention in health systems research. This mirrors a wider funding pattern in biomedicine, in which basic science and early translation often enjoy greater institutional prestige and support, while later-phase, implementation, and health systems research are less well funded and less firmly embedded in evaluation systems[34-36]. Yet these later-stage forms of research are especially important for prevention, care delivery, and the long-term management of disability-dominated conditions[37,38]. These differences suggest that both the quantity and orientation of research may influence how scientific progress translates into improvements in health outcomes. For many conditions driving disability and affecting women, substantial gains may be achieved through economically efficient investments in clinical, implementation, and health systems

research aimed at improving symptom relief, access to effective care, rehabilitation, and long-term management.

Our study should be interpreted in light of its limitations. Although the GBD applies extensive methodological adjustments to address biases in epidemiological data, including those arising from self-reported health measures and diagnostic practices, systematic sources of bias cannot be fully eliminated.[39] In particular, estimated YLDs rely on self-reported symptoms, survey instruments, and model-derived disability weights, which may under-capture chronic, fluctuating and multi-morbid conditions.[39] If such conditions are underestimated in burden estimates, the contribution of disability to women's health loss may also be underestimated, rendering our estimates of the sex/gender research gap conservative. Also, while the advances in mapping research publications to GBD causes now allow large-scale analysis of disease-specific research activity, our approach cannot assess the extent to which individual studies adequately address sex/gender. In addition, for this study, we hold the egalitarian assumption that each research output is equally relevant to both women and men. However, in practice women remain underrepresented or insufficiently considered in many areas of biomedical research, including through inadequate inclusion, limited sex/gender-disaggregated analyses, and insufficient attention to sex/gender-specific mechanisms, presentation, diagnosis, treatment response, and outcomes[40,41]. A disease area may therefore appear well researched while still providing insufficient evidence for women's health, again implying that our estimates represent a conservative sex/gender research gap. Global health and development agendas, including authoritative commitments to gender equity and women's health (e.g. the Sustainable Development Goals), often adopt a prioritarian perspective in which historical and structural disadvantages justify targeted corrective action. Against this more demanding standard, the research-disease misalignment documented here would represent an even more pronounced inequity.

Addressing the large and growing sex/gender research gap identified in this study will require coordinated adaptation. Funding agencies, and research institutions, for example, could support adaptation through targeted long-term initiatives for under-researched, high-YLD conditions, particularly those that disproportionately affect women. Although the absolute sex/gender research gap is currently largest in high SDI regions, its projected growth in lower SDI settings suggests an opportunity to address existing disparities where research capacity is greatest while anticipating emerging needs where YLD-burden is increasing. Such initiatives would additionally help to build sustained expertise and infrastructure, which might include a shift towards broader, interdisciplinary, clinical, implementation, and health systems research. Progress is important not only for the health of women, but also for improving long-term management of chronic conditions across populations. The present study further underscores the need for systematic documentation and monitoring of sex/gender-disaggregated research and burden as a structural

dimension of health equity, so that persistent and emerging gaps can be identified, tracked over time, and addressed through targeted policy and funding responses – an effort that could be supported by global health organizations.

In summary, our findings provide the first global, longitudinal assessment of how biomedical research priorities align with sex/gender-specific patterns of disease burden. By demonstrating that the global research portfolio remains substantially more aligned with mortality than with morbidity, and that this imbalance disproportionately disadvantages women, we highlight a structural misalignment between scientific investment and evolving global population health needs. Expanding research priorities more closely with disability-driven conditions will be essential to ensure that research reflects the full spectrum of disease burden and translates into meaningful health gains.

Table 1 | Policy summary table

Background	Men lose more years of life to premature mortality (Years of Life Lost, YLL), whereas women spend more years in poor health (Years Lived with Disability, YLD). We linked more than eight million disease-specific publications to sex/gender-disaggregated Global Burden of Disease (GBD) data across 125 causes. This allowed us to quantify research-disease alignment separately for women and men, across regions with different Socio-Demographic Indices (SDI), and over time. As disability-related conditions account for a growing share of total burden worldwide, understanding how research priorities align with sex/gender-stratified health needs are critical for ensuring an equitable and future-oriented global research agenda.
Main findings and limitations	Biomedical research is 1.8 times more aligned with YLL-related than with YLD-related burden. Because women bear a larger share of YLDs, this mortality orientation translates into a persistent sex/gender research gap to their disadvantage. The gap is present across all SDI regions and increases with socio-demographic development, with the largest misalignments observed in high SDI settings, where research capacity is greatest. Projections to 2040 suggest that, if research patterns persist while YLDs grow relative to YLLs, the global gap for women will more than double compared with the year 2000. Disease-level analyses show that conditions contributing to the sex/gender research gap for men are concentrated in a few high-burden diseases, including cancers, cardiovascular diseases, and infectious diseases. These diseases account for a high share of overall disease burden for both men and women. The sex/gender research gap for women is driven by a consistent group of high-prevalence, disability-dominated conditions that mostly burden women, such as musculoskeletal disorders, headache disorders, and dietary iron deficiency. These conditions are observed across all SDI regions and are more often situated in clinical and health systems research domains. Limitations: Our estimates rely on established YLL and YLD metrics, which may underestimate components of disability that disproportionately affect women, likely rendering the estimated sex/gender research gap conservative. In addition, linking research output to disease categories at a global scale cannot capture the extent to which studies adequately include women as subjects or generate sex/gender-sensitive evidence, which may further understate the true magnitude of the sex/gender research gap.
Policy implications	**Targeted funding toward disability burden.** Research funders could give greater priority to high-burden disability conditions and a burden-alignment criterion in grant review could be implemented. National research councils and philanthropic organizations could create dedicated multi-year programs for persistently under-researched, high-YLD conditions affecting women. **Reform incentives and strengthen downstream research**. Funders, publishers, and research administrators should reassess evaluation metrics, promotion standards, and prestige signals that anchor researchers in mortality-focused fields and introduce stronger incentives for work on high-burden, disability-dominated conditions. Policymakers should also expand health systems and implementation research, where underinvestment limits real-world gains from biomedical knowledge. **Prioritize shared disease drivers and act across regions**. Ministries of health and international agencies should prioritize conditions that contribute most to the sex/gender research gap and elevate them in national and global agendas to support coordinated research and shared infrastructure. While the largest gaps are currently in high SDI regions, faster growth in lower SDI settings calls for action where both capacity is highest and where future gaps are emerging. **Monitor the sex/gender research gap as a health equity issue.** Global health organizations should incorporate sex/gender-disaggregated research–burden alignment indicators into monitoring frameworks and recognize the sex/gender research gap as a structural determinant of health equity. Reducing this gap should be framed not only as a matter of fairness, but also as a strategy to improve productivity, labor force participation, and healthy longevity.

Methods

Terminology

The GBD framework provides estimates disaggregated by male and female. While these categories are labeled “sex,” the underlying data sources extend beyond strictly biological definitions, drawing on censuses, household surveys, hospital records, and registries that typically rely on self-report or administrative classification[1,42]. As a result, the GBD sex categories reflect a composite of biological sex (e.g., chromosomal, hormonal, and anatomical characteristics) and socially constructed gender (e.g., roles, norms, behaviors, and exposures), which shape health risks, access to care, and disease trajectories in distinct but interrelated ways.

Distinguishing between sex and gender is analytically important because biological mechanisms (such as pharmacokinetics or immune responses) and gendered social processes (such as occupational exposures, care-seeking behavior, or discrimination in health systems) can independently and jointly influence disease burden. At the same time, both dimensions are central to sex/gender-sensitive medicine, as effective prevention, diagnosis, and treatment require attention to biological differences as well as to socially patterned health determinants[3,41,43]. The available data, however, do not capture categories beyond the binary concepts of sex and/or gender, limiting more granular analyses of heterogeneity within and across groups[44].

In this manuscript, we therefore use the term sex/gender and refer to our analytical groups as men (man) and women (woman), acknowledging that these categories conflate biological and social dimensions and that not all individuals identify within these binaries. We encourage future data collection efforts to include more inclusive and specific measures across sex, gender, and other biological and sociocultural dimensions to support more nuanced analyses, which are crucial for understanding and improving global health outcomes.

Data sources

Our analysis rests on two core data foundations that together enable a comprehensive mapping of the global research enterprise to sex/gender-associated disease burden. First, we captured global biomedical research activity using PubMed XML records from a parsing of PubMed in January 2025[45]. PubMed is the largest repository of biomedical research worldwide, comprising nearly 40 million citations and abstracts[45]. A key feature of the PubMed data is that articles are indexed using Medical Subject Headings (MeSH terms), which are externally assigned keywords that represent the substantive content of each publication. These MeSH terms are central to our analysis, as they allowed us to map research articles to specific disease causes and to classify research into different research categories. In addition, PubMed provides rich metadata, including publication years, title, and abstracts[45].

As a second data source, we drew on the GBD Study provided by the Institute for Health Metrics and Evaluation (IHME). The GBD is the most comprehensive effort to quantify health outcomes across countries and over time, offering burden measures disaggregated by country, region, and sex/gender[46]. Central to our analysis are three indicators of health outcomes: years of life lost (YLLs), years lived with disability (YLDs), and the sum of the two, disability-adjusted life years (DALYs). We used the 2021 version of the GBD data, as it is the most recent release that provides both a historical account of disease burden through 2021 and forecasts of likely developments in disease burden in subsequent years[42,46,47].

GBD disease burden is reported at multiple levels of granularity, ranging from Level 1 (e.g., non-communicable diseases) to Level 2 (e.g., cardiovascular diseases), Level 3 (e.g., stroke), and Level 4 (e.g., ischemic stroke). Our analysis focuses on Level 3 causes, which strike a balance between clinical specificity and reliable linkage to research publications. This level allows meaningful assessments of sex/gender-related differences while ensuring comparability across diseases. Level 4 causes are available only for a subset of Level 3 categories; where present and medically meaningful, we aggregated them to their corresponding Level 3 cause. Following prior literature[48,49], we excluded disease groups that are overly broad or heterogeneous, such as residual "other" categories and umbrella groupings (e.g., "Endocrine, metabolic, blood, and immune disorders" or "Drug use disorders"), as well as external health threats and injuries. To address classification ambiguities, we combined "Congenital birth defects" with "Neonatal disorders,", "Lower respiratory infections" with "COVID-19", and "Acute hepatitis" with "Cirrhosis and other chronic liver diseases". Finally, we restricted the sample to causes with complete historical and forecast burden data, excluding Ebola and Zika virus that do not have forecast data.

In total, our study covers 133 Level 3 disease causes (see Supplementary Table 1 for an overview). Eight of these are sex/gender-specific, defined as conditions for which more than 95% of the disease burden occurs in one sex/gender.

Linking research with disease burden

A central challenge of our analysis is linking disease-specific burden data from the GBD to research data from PubMed[45,46]. To address this, we built on the approach developed and validated by our own group[19]. We used a large language model (LLM) to map disease causes recorded in the GBD database to MeSH terms and subsequently classified research articles based on these assignments. Compared to conventional approaches relying on crosswalks using *International Statistical Classification of Diseases and Related Health Problems* (ICD) codes, this method achieved substantially higher levels of recall, thereby identifying a broader set of relevant research outputs[19].

For the present study, we slightly adapted this method because the original approach was designed for Level 2 disease causes and additional refinement was required to ensure high recall and precision for the more granular Level 3 disease causes. Specifically, we implemented a three-step procedure: first, we identified relevant pairs of GBD causes and MeSH terms; second, we performed the matching between GBD causes and MeSH terms; and third, we refined these matches to ensure accuracy.

Step 1 – Identification

We began by defining the relevant sets on both sides of the mapping. On the disease side, we included 194 specific Level 3 and Level 4 causes corresponding to the 133 Level 3 causes retained for analysis. Where available and clinically more informative, we relied on Level 4 causes rather than their broader parent Level 3 categories to ensure greater medical specificity. On the MeSH side, we considered the 27,430 terms in branches A–G, the only branches containing disease-specific concepts. We then generated all possible pairwise combinations between these disease causes and MeSH terms, resulting in more than 5.3 million candidate pairs.

Because evaluating each pair individually is computationally inefficient, we applied a structured pre-screening step. Using GPT-4o mini, we screened all MeSH–disease combinations for plausible matches. Applying this lightweight LLM in this first step allowed to reduce the search space, preserving resources without compromising the solution. The prompt (see Supplementary Figure 1) was designed to prioritize recall (minimizing false negatives) while accepting a manageable number of false positives to be removed in later stages. This filtering reduced the search space by more than 95%, yielding 234,498 candidate matches involving 23,416 MeSH terms.

Step 2 – Matching

The filtered MeSH–GBD pairs from Step 1 were then evaluated for match accuracy. For each candidate pair, we first applied the original LLM-based matching prompt previously published,[19] using OpenAI's GPT-4o, to assess whether the pairing constituted a valid semantic match (see Supplementary Figure 2). In a subsequent step, we used ICD-10 codes to clinically validate and refine these matches. For each GBD disease cause, we compiled the full set of underlying ICD-10 codes provided by the GBD database. We collapsed codes to a first-level granularity that preserves their core medical meaning. We then verified with a second LLM-based prompt whether each matched MeSH term corresponded to at least one ICD-10 code within the respective GBD cause (see Supplementary Figure 3). MeSH terms that did not align with the ICD-defined disease profile were discarded. This procedure ensured that the medical definition of each disease cause, reflected in its associated ICD-10 codes, is consistent with the linked MeSH terms. Through this semantic and ICD-based validation, we retained 1,591 MeSH terms that are both conceptually related to and clinically aligned with the corresponding GBD causes.

To further increase recall, we complemented the LLM-based matches with additional mappings from the ICD–MeSH crosswalk provided in the MRCONSO table of the Unified Medical Language System (UMLS). The UMLS provides curated one-to-one links between MeSH terms and ICD codes[49]. As shown before,[19] these mappings are highly precise but incomplete. We therefore used them as a complement rather than a substitute, resulting in a 12% increase in MeSH–GBD matches and balancing precision with broader coverage.

Step 3 – Refinement

To resolve remaining ambiguities arising from overlapping matches and ICD-based aggregation, we implemented a final disambiguation and harmonization step. First, 68 MeSH terms were linked to more than one GBD Level 3 cause, creating a risk of double counting. To enforce an unambiguous mapping, we applied a rule-based disambiguation algorithm developed in collaboration with a medical expert. The rules prioritize clinically explicit matches, favor specific disease entities over broader categories, and assign complications to their underlying conditions (see Supplementary Figure 4). Second, we searched for exact matches between MeSH terms and GBD disease causes using exact string matching. This allowed us to identify clear 1:1 correspondences and reintroduce 21 relevant MeSH–GBD pairs that had been excluded in Step 2. In doing so, we ensured that no exact matches were omitted. In addition, all MRCONSO-based matches were reviewed by a medical expert, resulting in the exclusion of 24 unspecific MeSH terms. Finally, to ensure consistent disease granularity across the dataset, all matches involving GBD Level 4 causes were aggregated to their corresponding Level 3 causes.

This final harmonization step strengthened the clinical validity and internal consistency of the mapping. The resulting correspondence table links 133 GBD Level 3 causes to 1,818 MeSH terms (see Supplementary Table 1 for an overview), providing broad coverage while maintaining precise and clinically grounded assignments.

Creation of final sample

Building on the finalized MeSH to GBD mapping, we retrieved all PubMed publications linked to the matched MeSH terms and restricted the sample to the period 2000–2023. The year 2000 marks the beginning of our analytical window, as PubMed was substantially redesigned that year, introducing improved MeSH browsing, automated translation tables, and stronger integration with full-text archives, features that marked a transition toward more systematic and comprehensive biomedical indexing. The year 2023 is the most recent year with complete coverage in our January 2025 PubMed parse, given indexing lags. To reduce omissions due to missing or overly broad MeSH assignments (e.g., when a specific disease such as iodine deficiency is not precisely indexed), we complemented the MeSH-based linkage with a string-based search identifying exact

disease-name matches in article titles and abstracts. This step increases the number of publications in our dataset by 8%.

Because a single article can be associated with multiple MeSH terms, and thus multiple disease causes, we consolidated the data to unique paper–cause pairs. If several MeSH terms of an article map to the same disease cause, the link is counted only once. In total, the final sample comprises 6.9 million publications and 8.3 million unique paper–cause pairs. To avoid overstating research activity for diseases that frequently co-occur, we applied fractional counting across causes. For example, if an article maps to two distinct causes, each cause received a weight of 0.5. Most articles (82.8 %) map to exactly one cause (Supplementary Figure 5).

To measure disease burden, we used sex/gender-aggregated data on Disability-Adjusted Life Years (DALYs), Years Lived with Disability (YLDs), and Years of Life Lost (YLLs) from the Institute for Health Metrics and Evaluation (IHME). Countries are classified into high-, middle-, and low-Socio-demographic Index (SDI) groups, which capture income per capita, educational attainment, and fertility. Consistent with prior GBD practice[50,51],we applied established SDI thresholds to form these three categories, grouping all three middle categories together to ease interpretability (see Supplementary Table 2).

For projections beyond 2023, we extrapolated disease-specific publication trends based on linear pre-pandemic trajectories (through 2019), assuming that research activity returns to its pre-COVID trend following pandemic-related disruptions. Projections of future disease burden were obtained from the official GBD Foresight tool under the continued-past-progress scenario (from 2021 onward)[47].

Validation

A key requirement for the validity of our analysis is that the dataset accurately captures disease-related research activity. We therefore assessed both precision and recall of the final paper–cause assignments.

Precision, defined as the accuracy of assigned paper–cause links, was evaluated using a random sample of 200 paper–cause pairs. A medical expert reviewed each pair and assessed whether the assigned disease cause reflected the article's substantive focus. This validation resulted in a precision rate of 97.5%, with 195 of 200 pairs correctly classified. Among the few misclassified cases, one article, for example, was assigned to the GBD disease cause "Brain and central nervous system cancer" based on the MeSH term "brain neoplasms," likely reflecting metastatic cancer. However, no explicit mention of this cause was found in either the abstract or the full text.

Recall, defined as the comprehensiveness with which relevant articles are identified, was assessed searching for journals with exact GBD disease causes within their name. We found 11 disease-

specific journals. For each journal, we calculated the share of articles correctly mapped to the corresponding disease cause in our dataset. Recall rates were consistently high, averaging well above 90%. For example, 96.5% of articles published in Journal “The Journal of Asthma: Official Journal of the Association for the Care of Asthma” were correctly classified as research on Asthma (see Supplementary Table 3).

With both precision and recall exceeding 90% and performing consistently across disease causes, we concluded that our approach provides an accurate and reliable representation of research activity for the disease causes included in the analysis.

Overall, the framework represents a deliberate and transparent trade-off between coverage and specificity. By requiring unambiguous matches among MeSH terms, GBD causes, and ICD-10 codes, and by relying on structured MeSH indexing (supplemented with targeted title and abstract searches), the approach prioritizes clinically precise and reproducible disease attribution at scale. This inevitably excludes some non-indexed or broadly framed research, but it minimizes misclassification and ensures meaningful disease-level comparisons. While conceptual differences across GBD, MeSH, and ICD-10 cannot be fully eliminated, systematic harmonization and validation steps reduce their impact. The resulting dataset, publicly available (see Data Availability statement), thus provides a scalable and robust foundation for tracking the alignment of scientific research with global health priorities over time.

Analyses

Alignment between research activity and burden

Our main analysis focuses on 125 disease causes that affect both men and women. The eight sex/gender-specific causes, defined as those for which one sex/gender accounts for more than 95% of the total burden, were analyzed separately (Extended Figure 2), as they are not central to our research question. For this subset of diseases, research attention relative to disease burden is already comparatively high, suggesting no substantial research gap. Patterns are also consistent with the main analyses, with diseases specific for men showing a higher research-to-burden ratio than f/w-specific diseases.

For the 125 disease causes in focus of our study, we first examined how closely research activity aligns with the distribution of global disease burden measured in YLDs and YLLs. To that end, we ranked all 125 disease causes by the volume of research conducted on each between 2000 and 2023. Based on this ranking, we then computed the cumulative share of global YLDs and YLLs accounted for by diseases in descending order of research activity (Figure 1A).

Next, we quantified the degree of misalignment between research activity and disease burden, using the Kullback–Leibler divergence (KLD) as our central measure. The KLD is calculated as:

$$(1)\ \mathrm{KLD}(\mathrm{P}||\mathrm{Q}) = \sum_{x \epsilon X} P(x) \ln \frac{P(x)}{Q(x)}$$

P(x) = the burden of cause *x* in a given region, year, and sex/gender divided by the total burden in that region and year

Q(x) = the number of research publications on cause *x* worldwide in a given year, divided by the total number of global research publications in that year

Higher KLD values indicate greater divergence, while a value of zero would imply perfect alignment. We calculate the KLD for both YLDs and YLLs (Figure 1B).

Country-specific profiles of disease burden

Next, we examined the sex/gender distribution of disease burden at the country level. Specifically, we plotted the ratio of absolute disease burden for women relative to men across the three burden metrics used in this study, i.e., DALYs, YLLs, and YLDs. Note that DALYs are the sum of YLLs and YLDs. For this descriptive overview, we used values averaged over the entire sample period (Figure 1C).

Sex/gender research gap

Building on the use of KLD as a measure of research–disease divergence, we next examined sex/gender differences in divergence. Specifically, we computed a sex/gender research gap, defined as the difference between the research-disease measures for men and women. These divergence measures are calculated using sex/gender-specific disease burden distributions while holding global research activity constant:

$$(2)\ \text{Sex/gender Research Gap} = \frac{\mathrm{KLD}_{\mathrm{women}} - \mathrm{KLD}_{\mathrm{men}}}{\frac{\mathrm{KLD}_{\mathrm{women}} + \mathrm{KLD}_{\mathrm{men}}}{2}} * 100$$

This measure expresses the sex/gender research–disease gap relative to the average divergence across both groups, multiplied by 100, and represents the percentage deviation from the average research–disease divergence. Positive values indicate greater divergence for women, whereas negative values indicate greater divergence for men. Figure 2A displays the sex/gender research gap for the 3 burden metrics and subsequent analyses use sex/gender research gap as the central measure.

Sex/gender research gap across burden profiles, SDI regions, and time

For the remaining analysis, we focused on the sex/gender research gap in DALYs as it represents the most inclusive burden metrics, capturing both YLDs and YLLs. Figure 2B plots the sex/gender research gap (y-axis) against the share of DALYs attributable to YLDs (x-axis), providing insight into how the relative importance of non-fatal disease burden relates to research alignment across regions. To assess the strength and direction of this relationship, we computed Pearson correlation coefficients between the share of YLDs and the sex/gender research gap across all years in the

sample. Figure 2C illustrates the evolution of the sex/gender research gap over time for the three SDI regions, using region-specific disease burden distributions and the global research distribution. The plot highlights three time periods: pre-pandemic (2000-2018), pandemic (2019-2023), and forecast (2024-2040). Figure 3 contrasts the sex/gender research gap across SDI regions in 2000 with projections for 2040, presented as bar plots in the left panel and corresponding world maps in the right panel.

Diseases contributing to the sex/gender research gap

Figure 4 decomposes the overall sex/gender research gap into the contributions of individual diseases. For each disease, we calculated the difference between its contribution to research-burden divergence for women and its contribution for men, using the same relative-difference approach as for the overall sex/gender research gap, but applied at the disease level.

This decomposition identifies which diseases contribute to the gap to the disadvantage of women and which contribute to it to the disadvantage of men. For each SDI region, we show the ten largest contributors for each sex/gender, together with the sex/gender distribution of the underlying burden, the proportion of burden attributable to YLDs and YLLs, and the total shares of regional burden and global research attributable to these diseases.

Research type composition across diseases

To contextualize the types of research conducted for each disease cause, we classified all publications into three research categories: basic, clinical, and health systems research. The classification is based on indexed MeSH terms and follows the Translational Research Framework, grouping T0 as basic research, T1–T2 as clinical research, and T3–T4 as health systems research[52]. Using a large language model, we systematically mapped more than 31,112 MeSH terms across all branches to these three categories (see Supplementary Figure 6 for the customized LLM prompt). We then validated the classification and applied fractional counting when publications were linked to multiple research types. Basic or mechanistic research captures laboratory and preclinical studies focused on molecular, cellular, or physiological mechanisms. Clinical or translational research comprises human-centered studies addressing diagnosis, treatment, disease management, or the translation of laboratory findings into clinical practice, while explicitly excluding MeSH terms that refer only to diseases in general. Health systems or population research encompasses work at the population level, including research on disease distribution, determinants, prevention, epidemiology, health systems, and policy interventions. As an external validation, we compared our classifications with journal categories defined by Clarivate's *Journal Citation Reports* and observed substantial overlap between the expected and observed research types (see Supplementary Figure 7 and Supplementary Table 4 for details)[53].

Figure 5A shows the average distribution of research across the three research types for the main contributors to the sex/gender research gap for women and men. Figure 5B maps these disease causes in separate ternary plots for each SDI region, with bubble size indicating their overall contribution to the gap in the respective region. Figure 5C combines all contributors into a single ternary plot, adds disease names, and indicates whether each disease is among the main contributors in one, two, or all three SDI regions. Together, these visualizations highlight the dominant research orientation of each disease.

Uncertainty measurements and sensitivity analyses

GBD estimates are subject to uncertainty arising from measurement error and data limitations, which should be reflected in downstream analyses. To account for this uncertainty, we incorporated the uncertainty intervals from GBD directly into our analytical framework. Specifically, for each country–year–cause observation, we sampled total DALYs from a log-normal distribution constrained by the reported upper and lower bounds of the uncertainty intervals. The sampled totals were then deterministically decomposed into sex/gender-specific DALYs as well as into YLLs and YLDs, using the observed proportional splits in the original data. In total, we generated 250 simulated datasets of cause–year–country–specific DALYs. All subsequent calculations and aggregations were performed separately for each simulation. In the final step, we applied the central limit theorem: point estimates are reported as the mean across simulations, and uncertainty intervals are constructed as the mean plus or minus 1.96 times the standard deviation of the simulated DALY values.

Data availability

The data assembled for this study are available on figshare and can be accessed at (currently for review purposes only: https://figshare.com/s/72b1326b1a1be8aad463). Source data are provided with this paper.

Code availability

The computer code used to perform the analyses in this study is available on figshare and can be accessed via the following link: (currently for review purposes only: https://figshare.com/s/72b1326b1a1be8aad463).

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Competing interests

M.J.L. is a co-founder and shareholder of AaviGen, a cardiovascular gene therapy company. The present study is not related to the company. The other authors declare no competing interests.

Author Contributions

C.L. and M.J.L. devised the original idea. C.L. and M.J.L. conceptualized and supervised the study. L.S. and M.B. led analyses. L.S., M.B. and L.M. assembled and analyzed the data. L.S., C.L., M.B. and M.J.L. drafted and wrote the final manuscript. C.R.S. and T.W.B. provided critical access to data sources and feedback on methods, results and interpretations at every stage of development. L.L.S. provided critical expertise on sex/gender in research frameworks. All authors edited the manuscript.

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