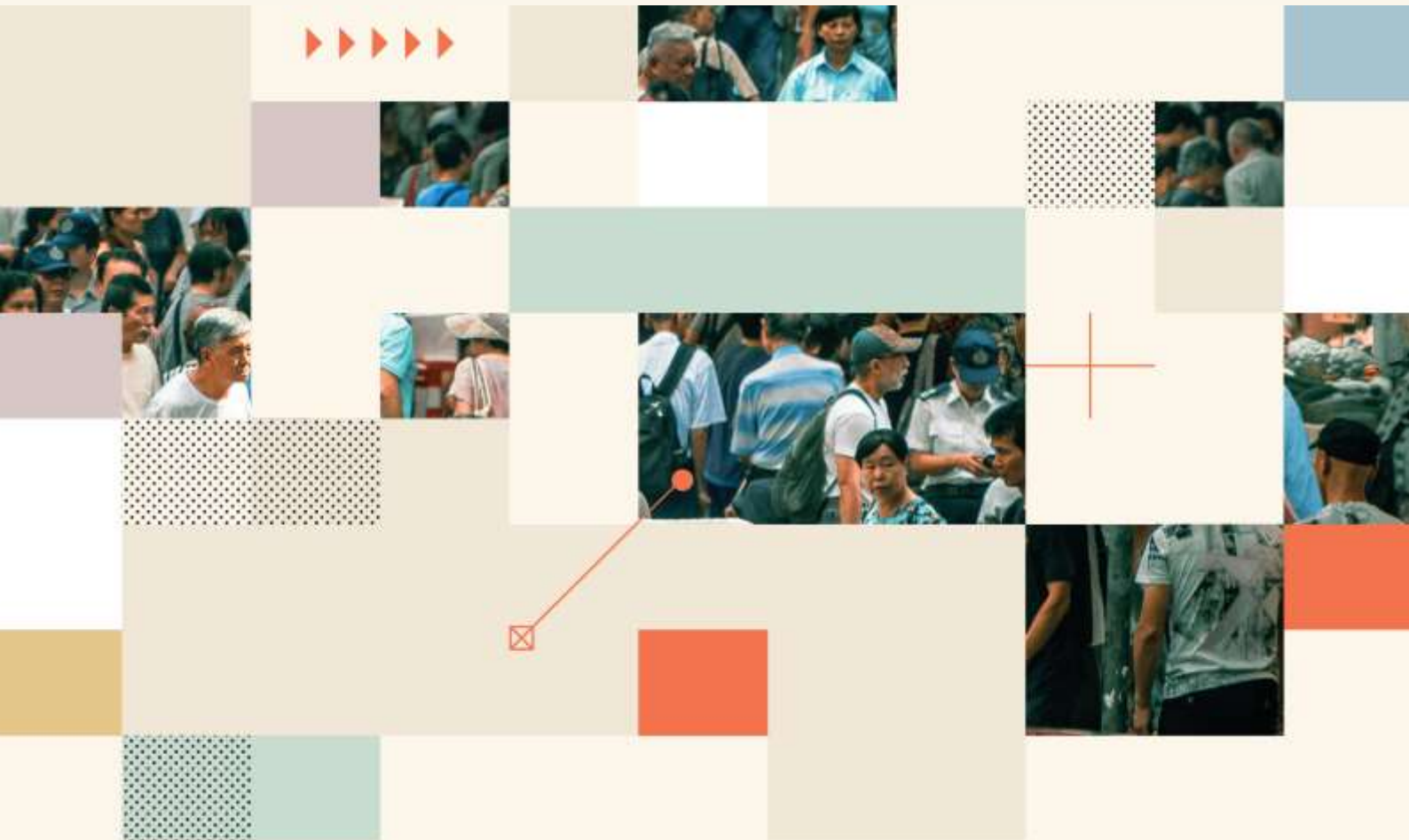


# Unveiling the hidden crisis in women's health

A deep dive into women's pain, endometriosis and uterine fibroids





# A bias against women's pain

Chronic pain is a leading cause of disability, affecting up to 30% of people worldwide.<sup>1,2</sup> Women\* disproportionately bear the brunt of this burden, reporting not only higher rates of pain but also more severe pain and greater functional impairment.<sup>3,4</sup> Yet, women's pain is frequently misdiagnosed, underestimated or dismissed altogether.

There are complex reasons why women have higher rates of chronic pain. Sex-dependent differences in hormones and immune system functioning may influence the processing of pain, and genetic variation can affect pain thresholds, inflammatory responses and the efficacy of pain medications.<sup>5-8</sup> Both biological and genetic differences also play a role in the higher prevalence of chronic pain conditions in women, including migraines, musculoskeletal pain, rheumatoid and osteoarthritis, and irritable bowel syndrome.<sup>9-12</sup> Moreover, there are chronic pain conditions which are exclusive to women: endometriosis and uterine fibroids are the most common, causing chronic pelvic pain alongside several other symptoms.

## ENDOMETRIOSIS

Endometriosis occurs when tissue resembling the uterus lining (endometrium) grows outside the uterus.<sup>13</sup> Pain is one of the most common symptoms, with over 60% of those diagnosed reporting chronic pelvic pain.<sup>14</sup> Other symptoms include painful periods, pain with sex, pain with urination or bowel movements, and infertility.<sup>15</sup> These often start in adolescence, though there is often a significant delay in diagnosis, ranging from 4-11 years.<sup>16</sup> The gold standard of diagnosis is visual inspection via laparoscopy with or without biopsy.<sup>17</sup> During laparoscopy, endometriosis lesions may be excised or ablated, which may improve symptoms of pain and infertility. Beyond surgery, treatment of endometriosis may also involve medication, including pain relief and hormonal treatments.<sup>18</sup>

While estimates vary, endometriosis affects approximately 1 in 10 women of reproductive age.<sup>19</sup> Unresolved pain affects 70% of endometriosis patients, and the cumulative impact of symptoms leads endometriosis patients to report higher rates of chronic stress, anxiety and depression.<sup>19</sup> Many patients experience substantial interference with work and education, with one study finding that each patient with endometriosis, on average, loses six hours of work productivity each week.<sup>20</sup> Overall, the per person cost of endometriosis has been estimated at Int \$16,970 to \$20,899 per year, with most costs relating to loss of productivity due to chronic pain.<sup>21</sup>

## UTERINE FIBROIDS

Uterine fibroids are non-cancerous growths in the muscular layer of the uterus.<sup>22</sup> Uterine fibroids may be asymptomatic or present with symptoms, including pelvic pain, heavy menstrual bleeding, painful periods, bloating, lower back pain, pain with sex, increased urinary frequency and constipation.<sup>23</sup> Fibroids may also be associated with infertility, miscarriage, preterm labour, breech or caesarean birth, and postpartum haemorrhage.<sup>24,25</sup> Ultrasound, MRI and hysteroscopy may diagnose them.<sup>26</sup> Treatment may involve monitoring, medication including pain relief and intrauterine devices, MRI-guided ultrasound therapy, uterine artery embolisation or surgical procedures to remove fibroids.<sup>26</sup>

The reported incidence of uterine fibroids varies widely from 4.5%-68.6%, though the true prevalence of fibroids is likely underestimated.<sup>27,28</sup> Patients with fibroids have higher rates of depression, anxiety and self-directed violence, and one study reported that the negative impact on quality of life for uterine fibroids was similar to or exceeded a diagnosis of diabetes mellitus, heart disease or breast cancer.<sup>25,29</sup> A survey found that 28% of respondents reported missing work due to uterine fibroids symptoms, and 24% believed that their symptoms prevented them from reaching their career potential.<sup>30</sup> In 2012, the societal and financial cost of uterine fibroids was estimated to range from \$5.9 to \$34.4 billion in the United States annually.<sup>31</sup>

\*While we acknowledge that gender identity is complex and non-binary, we use the term 'women' and 'female' to refer to biological characteristics, such as having a uterus and being capable of pregnancy, that are usually correlated with being perceived as a woman. While not all women have these sex characteristics, and not all people with uteruses are women, the overlap between female sexual and reproductive organs and the social category of 'women' is meaningful to categorise how issues specific to this biological sex have been approached culturally and institutionally.



Despite the high incidence of chronic pain in women, their pain is frequently overlooked and inadequately managed. Gender stereotypes contribute to this systematic bias against women, promoting the belief that women dramatise, overemphasise, and even fabricate their pain relative to men.<sup>32</sup> Some medical professionals believe that female patients are more likely to benefit from psychotherapy, whereas men are deemed to benefit more from pain medicine.<sup>33</sup> This belief has been ingrained throughout the history of medicine. Hysteria was previously recognised as a diagnosis exclusive to females that stemmed from the uterus, with the name 'hysteria' even derived from the Greek word for uterus 'hystera'.<sup>34,35</sup> Today, as a consequence of this bias, female patients have reported feeling dismissed by their healthcare provider. A UK government survey of over 110,000 women found that 50% of women felt their pain was disregarded and ignored.<sup>3</sup>

In addition to the bias evident in clinical settings, medical research has historically been male-centric, with findings generalised to women without any real consideration of the inherent clinically meaningful differences between the sexes.<sup>45</sup> Most studies investigating pain mechanisms are conducted on the male population, and most drugs are tested on the 70-kilogram male, with recommended dosages often referring to this standard.<sup>46</sup> Several hypotheses for favouring males in research have been identified, including harm to fertility or pregnancy, researcher bias from predominantly male researchers, and the perception that males are representative of all humans.<sup>47</sup> This gender bias in research contributes to a lack of understanding surrounding women's pain, as well as inadequate strategies to address it.

Furthermore, funding for research on women's health issues is often insufficient. An analysis of funding from the US National Institutes of Health (US NIH) found that in nearly three-quarters of cases where a disease primarily afflicted one gender, the funding patterns favoured males, in that either the disease affected more women and was underfunded with respect to burden, or the disease affected more males and was overfunded.<sup>48</sup> Given funding is integral to facilitating progress in biomedical product R&D, a lack of funding for conditions that predominantly affect women, including women-specific conditions like

### **A greater challenge in low-resource settings**

Epidemiological data is often sparse or unavailable in many low-resource settings where health services are limited. This makes it difficult to accurately estimate the true prevalence and associated burden of conditions responsible for women's pain, including endometriosis and uterine fibroids.<sup>36</sup> However, it is known that the prevalence of uterine fibroids, for example, is up to two- to three-fold higher in African women compared to women of other racial backgrounds.<sup>37</sup> While difficult to quantify, women's pain presents a significant burden in low- and middle-income countries (LMICs).

However, in these settings, women face even greater obstacles in addressing and managing their pain. Stigmatisation and cultural taboos surrounding reproductive health discourage health-seeking behaviour and hinder early diagnosis and treatment for women.<sup>38</sup> For those who do seek medical care, there is a lack of diagnostic infrastructure, including limited access to advanced diagnostic equipment and techniques.<sup>39-41</sup> This leads to a heavy reliance on basic diagnostic methods such as physical examination and ultrasonography, which augments pre-existing difficulties in accurately diagnosing causes of women's pain. Similarly, access to medications – including pain medications – remains poor. In 2021, over 80% of the morphine available was distributed to high-income countries (HICs).<sup>42</sup> In a 2023 WHO survey, 50% of respondents from low-income countries and 18% of respondents in lower-middle-income countries reported that 80% of people did not receive morphine or other strong opioids when needed.<sup>42</sup> Despite international efforts to enhance access to medications, barriers including financial constraints, supply chain issues and policy limitations continue to impede access for many.<sup>43,44</sup>



endometriosis and uterine fibroids, can severely impede the development of effective diagnostic and therapeutic tools that can improve women’s experiences of the condition.

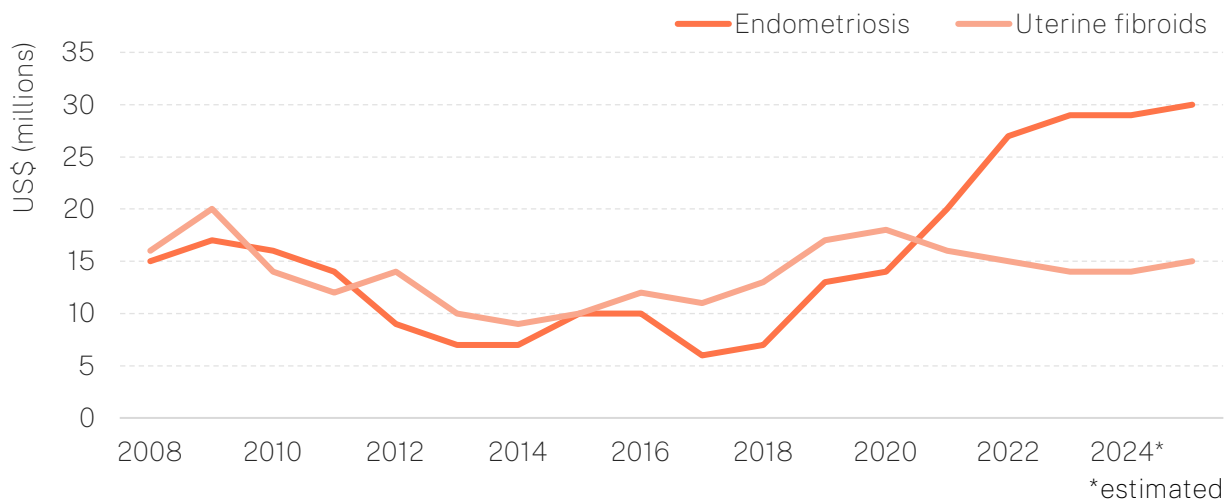
# US NIH funding for endometriosis and uterine fibroids expected to stagnate in the next couple of years

Mapping investment in R&D is critical in stimulating further funding as it identifies the gaps and opportunities for investment, which can inform budgets, priority-setting exercises and policy agendas. Given that the US NIH has consistently been the largest single funder of sexual & reproductive health R&D, assessing their funding can provide insight into the overall funding landscape.<sup>49</sup>

Focusing firstly on endometriosis, US NIH funding totalled \$29m in 2023. This represented its highest level of funding yet, rising for six consecutive years from a low of \$6m in 2017 and experiencing almost five-fold growth over this period. This rise, however, is not expected to continue, and funding is projected to plateau in the coming years. Funding is estimated to be at the same level in 2024 (\$29m) and only marginally higher in 2025 (\$30m).

In 2023, US NIH funding for uterine fibroids was less than half that of endometriosis, totalling \$14m. In contrast to endometriosis, funding for uterine fibroids has changed minimally over time, with its 2023 funding sitting slightly below its yearly average of \$15m over the past fifteen years. Furthermore, NIH funding for uterine fibroids is not expected to shift in 2024 and 2025, with funding projected to be \$14m and \$15m, respectively.

**Figure 1. US NIH funding of endometriosis and uterine fibroids 2008-2025\***



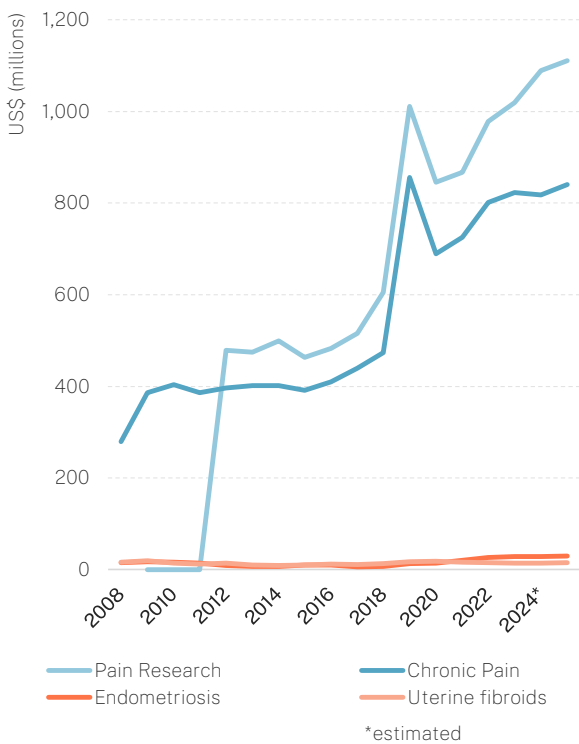
\*2009 and 2010 funding includes additional funding from the American Recovery and Reinvestment Act (ARRA). 2024 and 2025 funding is estimated.



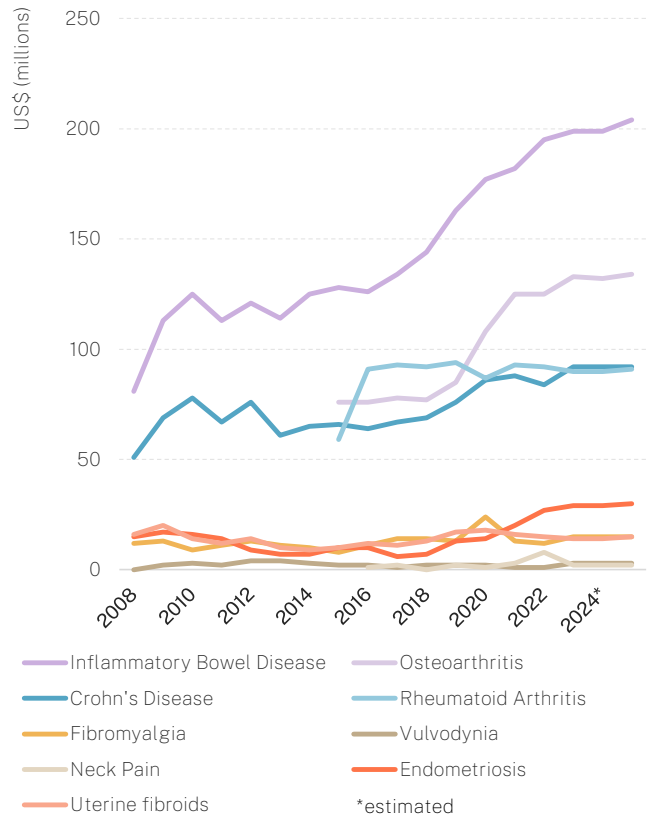
# Lack of accurate burden data and metrics designed for women makes comparing funding difficult

Despite the growth in endometriosis funding, the levels of US NIH funding for both endometriosis and uterine fibroids remain comparatively low. The NIH reports on its overall funding of pain and chronic pain research, totalling \$1,019m and \$823m in 2023, respectively. These categories of research, however, are broad, and comparing funding against other individual conditions can be more appropriate to contextualise funding levels.

**Figure 2a. US NIH funding of endometriosis and uterine fibroids compared with overall funding of pain and chronic pain research\***



**Figure 2b. US NIH funding of endometriosis and uterine fibroids compared with other chronic pain conditions\***



\*2009 and 2010 funding includes additional funding from the American Recovery and Reinvestment Act (ARRA). 2024 and 2025 funding is estimated.

In 2023, for example, inflammatory bowel disease received \$199m, osteoarthritis received \$133m and rheumatoid arthritis received \$90m. Levels of funding for these chronic pain conditions sit well above those of both endometriosis and uterine fibroids. This is not universally



true of chronic pain conditions, however, with fibromyalgia receiving similar amounts to uterine fibroids at \$15m and vulvodynia and neck pain receiving markedly less at \$3m and \$2m, respectively. Research on chronic pain conditions is known to be underfunded, though, and the general gap in funding widens when looking beyond chronic pain. For example, diabetes received \$1,187m, influenza received \$510m, and brain cancer received \$427m.

A range of factors influence investment and lead to differences in funding levels between conditions. Some conditions attract greater attention due to their commercial market. Immune disorders like rheumatoid arthritis and inflammatory bowel disease, for example, garner interest due to the size and profitability of the biologics and monoclonal antibody markets, with drugs like Humira costing more than \$80,000 per patient in the US and generating revenues of over \$200bn.<sup>50</sup> Without similar commercial incentives, conditions like endometriosis and uterine fibroids fail to enjoy similar publicity, which can influence even public government funding.

The degree of knowledge regarding the condition's pathophysiology and the presently available diagnostic and therapeutic options may also influence R&D investment. A foundational understanding of the condition is crucial to developing diagnostic and therapeutic products; if this is insufficient, R&D funding targeting product development may be disincentivised. If there is a lack of diagnostic tools that renders diagnosis difficult or inaccessible, as is seen with endometriosis, this can hamper the testing of therapeutics. This may again limit funding. Moreover, a dual focus on surgical and medical therapeutic options, which is the case for both endometriosis and uterine fibroids, may reduce the perceived requirement for and investment in the R&D of medicines, despite further need in this area.

Funding is also ideally influenced by the health and economic burden the condition exerts on the population. Robust comparisons of funding, therefore, need to be standardised by metrics of this burden. In a previous effort to do so, one study found that if endometriosis were funded at the same level as diabetes in relation to its annual economic burden in the US, its NIH funding would need to increase to \$298.8-\$455.3m.<sup>51</sup> More frequently, comparisons of investment are standardised using measures of health burden. However, this poses challenges for conditions like endometriosis and uterine fibroids, where the health burden is frequently underestimated. This critique was made of a recent study by the non-profit Women's Health Access Matters (WHAM), which found that endometriosis received less NIH funding than other conditions in proportion to its calculated disability-adjusted life years (DALYs). The correspondence argued that the calculated health burden of endometriosis was too low; therefore, the actual shortfall in funding was even greater.<sup>52,53</sup>

The incidence and prevalence of endometriosis and uterine fibroids are underestimated as these conditions go undiagnosed in a large proportion of affected women. There are several reasons for this, including varied symptom presentation, normalisation of symptoms, a lack of awareness of these conditions, the requirement for laparoscopic diagnosis in the case of endometriosis, and limited access to diagnostic tools.<sup>16,54-56</sup> The latter is particularly important in low- and middle-income countries, where conditions are more extensively underdiagnosed and epidemiological data is poor.<sup>53,57</sup> Moreover, the increased prevalence of uterine fibroids in



African-American populations means that underdiagnosis can also result from systemic racism and inequities in healthcare access, which can again reduce the accuracy of incidence and prevalence data.<sup>58,59</sup>

Beyond these concerns, there have also been questions raised about whether women are disfavoured in the calculation of DALYs, which is normally used as the summary measure for the burden of disease.<sup>60</sup> While DALYs address biological and genetic differences between men and women and gender-disaggregated data is available, only the physical burden is considered in the DALY calculation, with the social and emotional burden disregarded. If a condition imposes a greater social or emotional burden on women than men, this should be reflected in adjusted disability weight estimates which feed into the calculation of DALYs, to provide a more accurate measure of disease burden.

## Investment in endometriosis and uterine fibroids insufficient to meet R&D needs

Rather than benchmarking against other conditions to assess funding levels, it may be more feasible to determine whether funding is sufficient in magnitude to facilitate R&D progress and whether funding adequately covers areas of R&D need. For both endometriosis and uterine fibroids, further basic research is required on their aetiology, pathophysiology, and outcomes, all of which enable product development. In addition, there is a known need for novel therapeutics for both conditions and non-invasive diagnostic tools for endometriosis (see box-out).

### R&D needs for endometriosis

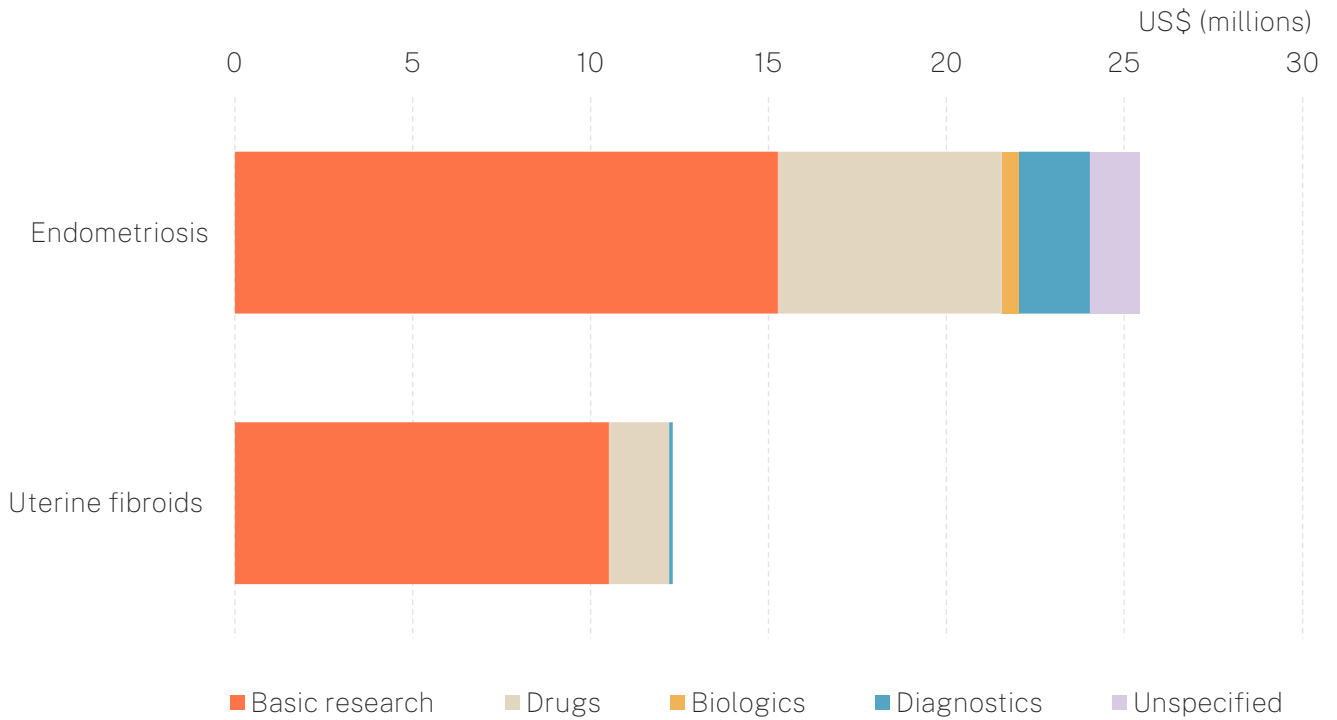
- **Non-invasive diagnostic tools:** Early diagnosis of endometriosis is hindered by its varied presentation of symptoms and the requirement for invasive laparoscopy for definitive diagnosis. There is an urgent need for non-invasive diagnostic tools, including biomarkers, that could facilitate earlier diagnosis and intervention.<sup>55,61</sup>
- **Novel therapeutics:** There is no curative treatment for endometriosis, and symptoms often remain unresolved with the presently available suite of treatments. Novel therapeutics are required to target this persistence of symptoms, particularly pain, which is the most significant contributor to loss of productivity. Non-hormonal treatments which do not impact fertility are also required.<sup>21,55</sup>

### R&D needs for uterine fibroids

- **Predictors of symptomatic and asymptomatic fibroids:** Fibroids can be easily diagnosed via imaging, however, no method exists to predict symptomatic fibroid development. Further research to understand the predictors and genetic markers of asymptomatic and symptomatic fibroids is required to ensure prevention or earlier treatment for patients with symptomatic fibroids.<sup>62</sup>
- **Non-hormonal therapeutics:** Current medical therapies for uterine fibroids target oestrogen and progesterone to inhibit fibroid growth. However, hormonal therapies impact fertility and are also required on an ongoing basis, which can be costly. Other therapeutic targets need to be explored, including vitamin D activity, the extracellular matrix and epitranscriptomics.<sup>62</sup>

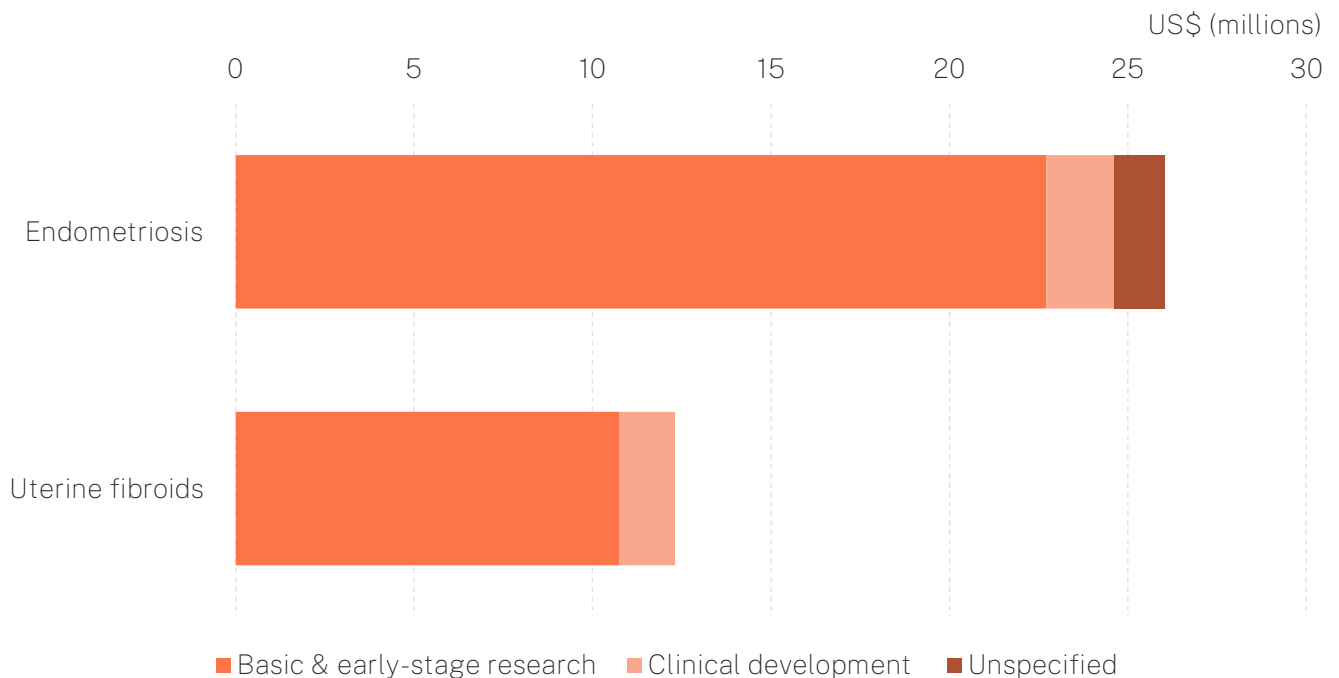


**Figure 3. US NIH funding for endometriosis and uterine fibroids by product 2023<sup>^</sup>**



In 2023, most of the US NIH’s endometriosis funding<sup>^</sup> went towards basic research (\$15m, 60%), followed by drugs (\$6.3m, 25%), diagnostics (\$2.0m, 7.8%) and biologics (\$0.5m, 1.9%). For uterine fibroids, basic research received an even greater majority of funding (\$11m, 85%), with the small remaining amount split between drugs (\$1.7m, 14%) and diagnostics (\$0.1m, 0.8%). Overall, despite the need, 2023 NIH funding for endometriosis therapeutics totalled just \$6.8m, uterine fibroids just \$1.7m and endometriosis diagnostics just \$2.0m. This level of funding is clearly not enough to facilitate the development of novel and effective therapeutics and diagnostics. Furthermore, just 7.5% (\$1.9m) of funding for endometriosis and 13% (\$1.6m) of funding for uterine fibroids was earmarked for clinical development. While the focus on basic and early-stage research reflects the needed push for fundamental research that informs product development, this research takes time and is not expeditious in helping women. Funding for basic research needs to be accompanied by concurrent investment in product development to accelerate the pace of innovation.

The NIH is evidently not the only funder of endometriosis and uterine fibroids R&D. Optimistically, the picture may change slightly when accounting for investment from other major funders. However, given the NIH’s outsized role in biomedical research, it is clear that accelerating progress in the development of biomedical products for these conditions will require further funding.


**Figure 4. US NIH funding of endometriosis and uterine fibroids by R&D stage 2023<sup>^</sup>**


<sup>^</sup>The 2023 US NIH funding totals referenced in the section 'Investment in endometriosis and uterine fibroids is insufficient to meet R&D needs' and Figures 3 and 4 only include funding for basic research and biomedical product R&D. The totals are therefore less than the 2023 US NIH funding totals previously referenced for endometriosis and uterine fibroids in Figures 1 and 2a/2b, which cover a broader scope of activities. More information is available in the methodology section at the end of the report.

## A pathway forward to improving women's experiences of pain

Women's pain has been overlooked for too long. Endometriosis and uterine fibroids are just two underlying causes of this pain, yet their levels of R&D funding reflect a broader minimisation and deprioritisation of women's pain, health and experiences. A problematic legacy of gender bias persists across the spectrum of medical research and healthcare and as a result, women continue to experience heightened physical, psychological and social impacts of pain, without receiving appropriate care and relief.

While long overdue, the crisis of women's pain is gradually being unveiled at the global level. The Lancet recently published an editorial titled 'Gendered pain: a call for recognition and equity' and in the past year, the Victorian government of Australia launched an enquiry that seeks to address the challenges women face in seeking care for their pain.<sup>3,63</sup> Capitalising on this momentum and tackling women's pain presents a prime opportunity to advance equity and quality of life for women, while furthering economic growth. The pathway forward demands a fresh approach that recognises the complexity of women's pain and the extent of ingrained gender bias, addressing it at multiple levels from research to clinical care.



## **Rethinking how we fund women's health research**

Funding of women's health research, including research targeting women's pain, needs to increase. Using endometriosis and uterine fibroids as examples, investment is currently insufficient to drive breakthrough products forward. While building fundamental knowledge through basic research is integral, research on therapeutics and diagnostics cannot afford to wait until we have all the answers. Funding needs to target therapeutics and diagnostics in parallel to basic research to accelerate the pace at which products reach women.

## **Including women in research that affects them**

The lack of research and clinical development for female-specific conditions like endometriosis and uterine fibroids is connected to a traditional reluctance to include women in clinical trials. This institutional bias in clinical research needs to be addressed. Women need to be included in clinical trials and sex-disaggregated data should be routinely collected to generate insights specific to women, including in the field of pain management. By making this a standard practice, products can be developed and designed to meet the needs of women rather than relying on a one-size-fits-all approach that doesn't actually fit all.

## **Designing disease burden metrics that cater to women and improving accuracy of burden data**

The burden a condition exerts on a population can rightly influence the attention and investment it garners. Burden of disease metrics like DALYs therefore need to better consider women and the different social and emotional burden a condition may exert on them in comparison to men, to provide a more accurate measure of disease burden for women. These efforts need leadership and sector-wide coordination to ensure uptake. Moreover, focus needs to be placed on obtaining accurate epidemiological data on women's health, so that the prevalence of conditions is not under-reported and the women's health burden not undervalued.

## **Breaking down gender bias in healthcare**

Women's pain has often been dismissed or downplayed by healthcare providers. This leads to inadequate management and a lack of proper diagnosis, including for conditions like endometriosis and uterine fibroids. We need to create healthcare systems that are more attuned to the realities of women's pain. This means training doctors and other healthcare providers, from the primary care level to tertiary levels of care, to recognise and address gender differences in pain management, as well as creating and implementing gender-sensitive clinical guidelines to ensure that women's pain is taken seriously and treated appropriately.

## **Ensuring everyone has access to care**

Women in low- and middle-income countries cannot be left behind. In these settings, women's pain, including conditions like endometriosis and uterine fibroids, go more extensively



underdiagnosed and undertreated. Removing barriers to healthcare access, strengthening diagnostic infrastructure and increasing access to medicines are crucial. We must ensure that diagnostics and treatments aren't just available but affordable and accessible to all women, regardless of where they live.

## A shared responsibility and call to action

A cohesive sector-wide approach will be required to improve women's pain experience. Funders need to commit a specific amount of funding to address women's pain, including its underlying conditions, to stimulate grant proposals and further research. A coalition-based approach to funding could help de-risk investment. This is particularly true where underpinning basic research is lacking to accelerate the concurrent development of biomedical products.

Alongside investment, governments, multilateral organisations, healthcare and research institutions need to prioritise women's health in policy frameworks and take action to address bias across the health sector, from medical research to clinical care. Women need to be included in clinical trials, and new disease burden metrics that consider women need to be formulated. Similarly, better burden data for women needs to be gathered, healthcare systems need to address ingrained gender bias in the provision of clinical care, and all action needs to consider women in low- and middle-income countries. This needs to be coupled with continued advocacy driven by patient groups and allied organisations to ensure women's pain continues to be spotlighted and that the momentum is maintained. The solutions are within reach, but only if definitive and coordinated actions are taken.



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# Methodology

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Almost all figures for US NIH funding have been taken from their estimates of funding for various [Research, Condition, and Disease Categories \(RCDC\)](#). In the section 'Investment in endometriosis and uterine fibroids insufficient to meet R&D needs', the US NIH database RePORTER was used to identify relevant funding, as part of the [G-FINDER survey](#). Funding in this section only includes funding for basic research and biomedical product R&D.



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