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Unlocking opportunities in women's healthcare

Advances in women's healthcare are accelerating, with implications for investors and stakeholders across the value chain and beyond.

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One half of the world's population is women. Women also account for 80 percent of consumer purchasing decisions in the healthcare industry.[1] Yet, remarkably, women's health has been considered a niche market and a mere subset of healthcare. Now, that's starting to shift, leading to better health outcomes for women and presenting new opportunities for investors, companies, employees, and other stakeholders across the healthcare ecosystem. In this article, we seek to provide a practicable definition of "women's health," to present a brief historical background of how men's physiology was often the default setting, and to identify value-creating opportunities for meeting women's healthcare needs. In a related article, "The dawn of the FemTech revolution," we take a deeper dive into FemTech specifically and explore the unique role that it plays.

Defining women's health

Men's and women's bodies are programmed differently from conception.[2] As the Institute of Medicine recognizes, "every cell has a sex," and sex-based differences influence all tissues, organs, and bodily functions.[3] These differences affect disease prevention, diagnoses, and treatments. Because women are often caretakers, better outcomes in women's health also have cascading benefits for groups such as children and the elderly. Women's health, in other words, contributes in a significant way to stronger, healthier societies.

Women's health encompasses much more than just reproduction. Our definition takes a broad approach. When we consider women's health, we incorporate both *female-specific* conditions, whether tied to women's reproduction or some other facet of women's biology, and *general health conditions* that may affect women differently or disproportionately (Exhibit 1).

Conditions that pertain generally to females include, of course, reproduction: contraception, fertility, and maternal health. Female conditions also include gynecology, gynecological infections, menopause, and women's oncology. General health conditions connected to women's health are those that affect women differently (for example, cardiovascular disease), disproportionately (such as autoimmune disease, migraines, and osteoporosis), or are characterized by gender-based discrepancies in care (for example, pain and mental health). Women's health also includes general health conditions for which sex differences are not precisely known or are not sufficiently studied, as is the case with Alzheimer's disease. Scientists and physicians increasingly recognize that multiple diseases and conditions affect women differently than men and that treatments and therapies can differ in both subtle and significant ways.

Tracing the transformation

The recognition of sex-based differences is long overdue but has been accelerating rapidly in recent years.

As highlighted in recent books such as *Invisible Women* (Penguin Random House, March 2019), *Doing Harm* (HarperOne, March 2019), and *Sex Matters* (Hachette Book Group, June 2021), modern medicine was developed with male physiology as the default. A predisposition to the male body type has long been reflected in medical training, diagnoses, and therapeutic development, which has influenced how physicians and scientists have come to understand human physiology. As a result, men and women historically can have very different health outcomes.

[1] "General facts on women and job based health," Employee Benefits Security Administration fact sheet, US Department of Labor.
[2] The authors acknowledge the importance of healthcare to the transgender, nonbinary, and gender-fluid communities and that not all people who identify as women are born biologically female and vice versa. The focus of this paper is on women's health support as related to a market segment specific to a certain biological sex. We recognize the need for future research into health issues that is inclusive of the transgender, nonbinary, and gender-fluid communities. Indeed, we intend to explore these needs in much greater detail in the months and years ahead.
[3] Mary-Lou Pardue and Theresa M. Wizemann, eds., *Exploring the Biological Contributions to Human Health: Does Sex Matter?*, Washington, DC: National Academies Press, 2001.

Exhibit 1

Defining women's health—broader than reproduction.

Diagnosis, prevention, and treatment (and related products) for:				Nonexhaustive examples
General health conditions	**Affect women differently** Cardiovascular disease		**Sex differences unknown or not sufficiently studied** Alzheimer's disease	
	Affect women disproportionately Autoimmune disease, migraines, osteoporosis			
	Gender bias in care delivery Pain, mental health			
Largely female-specific conditions	**Contraception** Oral contraceptive, IUD[1]	**Fertility** IVF,[2] egg freezing	**Maternal health** Prenatal care, breastfeeding	**Menopause** Peri- and post-menopausal symptoms
	Gynecology Endometriosis, pelvic floor, menstruation, sexual health			
	Gynecological infections Bacterial vaginosis, HPV[3]			
	Women's oncology Breast cancer, ovarian cancer, cervical cancer			

[1]Intrauterine device.
[2]In vitro fertilization.
[3]Human papillomavirus.

Bias is complicated. For example, nausea, ingestion, and general discomfort might typically suggest heartburn. Women, however, experience these symptoms in the event of a heart attack more commonly than men do. Early research in cardiovascular disease, a top killer among both men and women, largely involved male subjects, leading to the hallmark symptoms of heart attacks being taught as pain in the left arm and chest. Women, however, owing to different underlying biology and risk factors, are reported to be more likely to experience other symptoms, which are often labeled as "atypical." As a result, women have been found to be 50 percent more likely than men to be misdiagnosed following a heart attack and more likely than men to die from heart attacks.[4]

For years, women have been underrepresented in medical trials.[5] In 1977, following birth defects in the wake of fetal exposure to some medications, including thalidomide, the US Food and Drug Administration (FDA) recommended that "premenopausal female[s] capable of becoming pregnant" be excluded from Phase 1

[4] See Caroline Criado Perez, *Invisible Women: Data Bias in a World Designed for Men*, London: Penguin Random House, 2019, p. 218; Barbara Sadick, "Women die from heart attacks more often than men. Here's why—and what doctors are doing about it," *Time*, April 1, 2019; and Clare Arnott et al., "Sex differences in heart failure," *European Heart Journal*, December 2019, Volume 40, Number 47, pp. 3859–68c.

[5] Caroline Criado Perez, *Invisible Women: Data Bias in a World Designed for Men*, London: Penguin Random House, 2019, p. 200–205; Yasmin Anwar, "Lack of females in drug dose trials leads to overmedicated women," *Berkeley News*, August 12, 2020; drugtopics.com, accessed August 18, 2020; "Drug safety: Most drugs withdrawn in recent years had greater health risks for women," US Government Accountability Office, January 19, 2001.

and early Phase 2 clinical studies.[6] Protective in intent, the recommendation—which the FDA revised in 1993—had implications in researching differences in men's and women's health, including fundamental metabolic and hormonal differences that affect dosing.[7] Consider the case of Zolpidem, a medication primarily used for short-term treatment of sleeping problems. Decades after Zolpidem's approval and commercialization, the recommended dose for women was halved, in order to address the drug's slower metabolism in women.

Basing healthcare solutions on male physiology opens the door to suboptimal outcomes; among other consequences, women are twice as likely as men to experience adverse events from drugs.[8] Among medical devices, male-centric designs have also often been the default. Physiologic differences in load bearing, however, can result in up to double the failure rate of implants in women, as seen with certain hip implants.[9]

Women have also experienced differences in healthcare delivery.[10] Despite reporting more severe levels, frequency, and duration of pain, reports show that women are less likely to be treated for pain; their symptoms are at times expressed as "emotional" or "psychosomatic."[11] Disparities can also be found in some provider policies. One analysis of gender-specific procedures found that physician fees in Medicare led to a bias in procedure selection because fees for male procedures were higher than for female procedures, more than 80 percent of the time, and were 28 percent higher on average—even though male procedures were typically no more complex.[12] In another example, the associated physician's fee in Medicare for the removal of a penile lesion is currently three times as high as for the removal of a vaginal lesion.[13]

Emerging opportunities

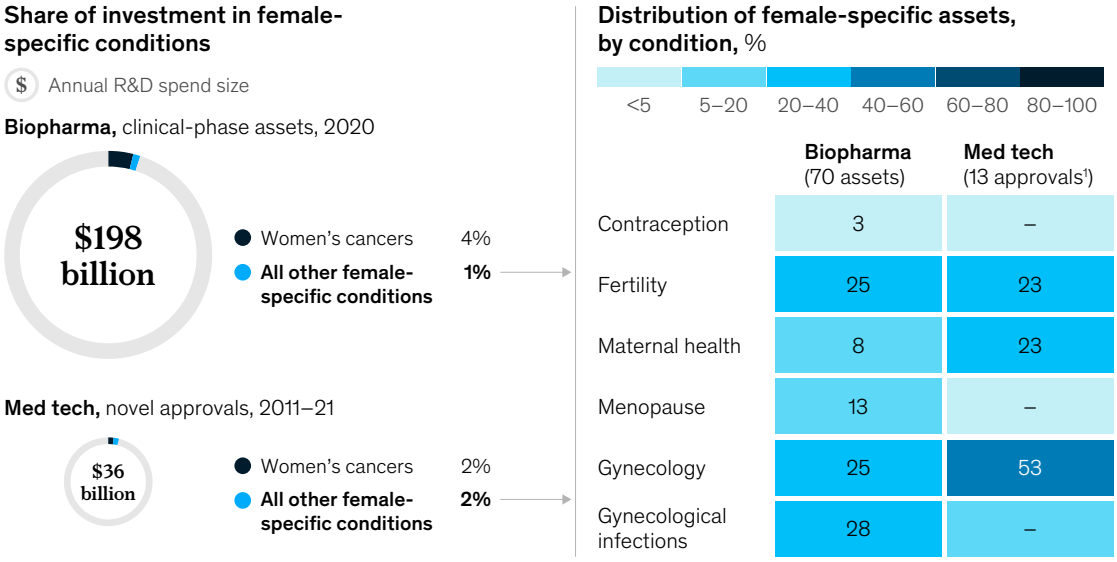
The current global innovation pipeline reveals mismatches between health investments and health needs. The gap highlights some remarkable opportunities for improving women's health within female-specific conditions (Exhibit 2).

In the aggregate, female conditions outside of oncology comprise less than 2 percent of the current healthcare pipeline,[14] even as women comprise half of the world's population. To contextualize and compare with disease burden, Hepatitis B, which afflicts twice as many men as women, has 41 times more biopharma assets relative to commensurate disability-adjusted life years.[15] The disparity between allocations to healthcare in general compared with women's health in particular is even more pronounced given that entire categories in female conditions are omitted from some health burden measures. For example, menopause and its associated symptoms are not captured in global disease burden databases, which look broadly at causes of death, diseases, injuries, and health risk factors.

[6] See "Gender studies in product development: Historical overview," US Food & Drug Administration, updated February 16, 2018.
[7] See "Timeline of FDA accomplishments in women's health: 1993 - present," US Food & Drug Administration, updated January 31, 2018; and Natalie A. DiPietro Mager and Katherine A. Liu, "Women's involvement in clinical trials: Historical perspective and future implications," *Pharmacy Practice*, January–March 2016, Volume 14, Number 1.
[8] Brian J. Prendergast and Irving Zucker, "Sex differences in pharmacokinetics predict adverse drug reactions in women," *Biology of Sex Differences*, December 2020, Volume 11, Number 1.
[9] Katrina Hutchison, "Gender bias in medical implant design and use: A type of moral aggregation problem?," *Hypatia*, Summer 2019, Volume 34, Number 3, pp. 570–91.
[10] Caroline Criado Perez, *Invisible Women: Data Bias in a World Designed for Men*, London: Penguin Random House, 2019, p. 223–26.
[11] Caroline Criado Perez, *Invisible Women: Data Bias in a World Designed for Men*, London: Penguin Random House, 2019, p. 226.
[12] Michelle F. Benoit et al., "Comparison of 2015 Medicare relative value units for gender-specific procedures: Gynecologic and gynecologic-oncologic versus urologic CPT coding. Has time healed gender-worth?," *Gynecologic Oncology*, February 2017, Volume 144, Number 2, pp. 336–42.
[13] Physician fee schedule from US Centers for Medicare & Medicaid Services; McKinsey analysis.
[14] McKinsey analysis of Phase 1–Phase 3 global pharmaceutical drugs in development; data sourced from Pharmaprojects as of June 2021.
[15] Fawad Khan et al., "Hepatitis B virus infection among different sex and age groups in Pakistani Punjab," *Virology Journal*, 2011, Volume 8, Article Number 225; McKinsey analysis.

Exhibit 2

Approximately 1 percent of healthcare research and innovation is invested in female-specific conditions beyond oncology.



[1]Excludes 4 breast implant assets.
Source: Evaluate Medtech (accessed July 2021); *Global Burden of Disease Study 2019*, Institute for Health Metrics and Evaluation, 2021; Pharmaprojects (accessed July 2021); *Report of the Advisory Committee on Research on Women's Health, Fiscal Years 2017–2018: Office of Research on Women's Health and NIH Support for Research on Women's Health*, National Institutes of Health, Office of Research on Women's Health, October 2019

There are significant opportunities for healthcare providers to consider reallocating resources to female conditions, including the following:

— *Maternal health:* More than 800 women die globally every day from pregnancy- and childbirth-related causes, including hemorrhages and infections.[16] The tragedies are not confined to emerging economies; even before the outbreak of COVID-19, the maternal mortality rate in the United States doubled between 2002 and 2018, with Black women disproportionately affected.[17]

— *Endometriosis:* One in ten women of reproductive age is estimated to have endometriosis (growth of endometrial tissue outside of the uterus), which can cause debilitating pelvic pain and infertility. The underlying pathophysiology is poorly understood, diagnosis takes ten years on average, and there is currently no cure.[18]

— *Menopause:* Women spend more than a third of their lives in peri- or post-menopause, and trends indicate that 1.2 billion women globally will be in these life stages by 2030.[19] The

[16] See "Maternal mortality ratio," United Nations Population Fund, accessed February 16, 2020; and Hannah Ritchie and Max Roser, "Maternal mortality," Our World in Data, 2013.
[17] Eugene Declercq and Laurie Zephyrin, "Maternal mortality in the United States: A primer," Commonwealth Fund, December 16, 2020.
[18] "Endometriosis: Key facts," World Health Organization, March 31, 2021.
[19] Craig Best et al., "Prevalence of menopausal symptoms among mid-life women: Findings from electronic medical records," *BMC Women's Health*, December 2015, Volume 15, Number 1.

vast majority of women find that menopausal symptoms such as hot flashes, night sweats, and sleep disturbances interfere with their lives, yet only a quarter obtain treatment.[20] The economic impact is significant, with one study estimating nearly $1,400 in health costs and $770 in lost productivity per person per year for untreated hot flashes alone.[21]

There is great potential to begin addressing these conditions in new ways. A suite of scientific advances can now be harnessed in women's health. Recent advances in genomics, tissue engineering, and cell and gene therapy are ushering in a new wave of healthcare innovations that can be applied to underserved female-specific conditions. For example, researchers are studying transcriptomics (the study of all RNA molecules in a cell) for treating otherwise elusive conditions such as preeclampsia or preterm birth. Others are now using tissue engineering to create uterine organoids in order to push the knowledge frontier on endometriosis. The potential is vast to redefine a host of conditions, including endometriosis, preeclampsia, and unexplained infertility, and to achieve advances to the degree that researchers are already achieving with oncology and immunology. Investors, researchers, and companies alike have an opportunity to participate in this rising wave of innovation and to deliver a new era in women's health.

Women's health is not a niche market, and it includes much more than just maternal or reproductive care. Indeed, women's healthcare presents enormous opportunities for value creation and for improving the lives and livelihoods of women, with positive effects that redound across society. The first waves of major change are already on the rise.

[20] Deb Gordon, "73% of women don't treat their menopause symptoms, new survey shows," *Forbes*, July 13, 2021.
[21] Peter M. Aupperle et al., "Incremental direct and indirect costs of untreated vasomotor symptoms," *Menopause*, March 2015, Volume 22, Number 3, pp. 260–66.

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