

A landscape review of female-specific clinical outcome assessments (PROQOLID™), health agency recommendations (PROINSIGHT™) and drug label claims with COAs (PROLABELS™) related to women's health

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Objective

The FDA's 2015 Women's Health Research Roadmap² advocated outcomes research into **conditions solely or disproportionately affecting women** and conditions which **manifest differently in women compared to men**. As the Roadmap's 10th birthday approaches, the objective was to review the landscape of female-specific clinical outcome assessments (COAs) in terms of the number of instruments, health agency recommendation specific to the topic (FDA, EMA), and use of COAs in drug labels.

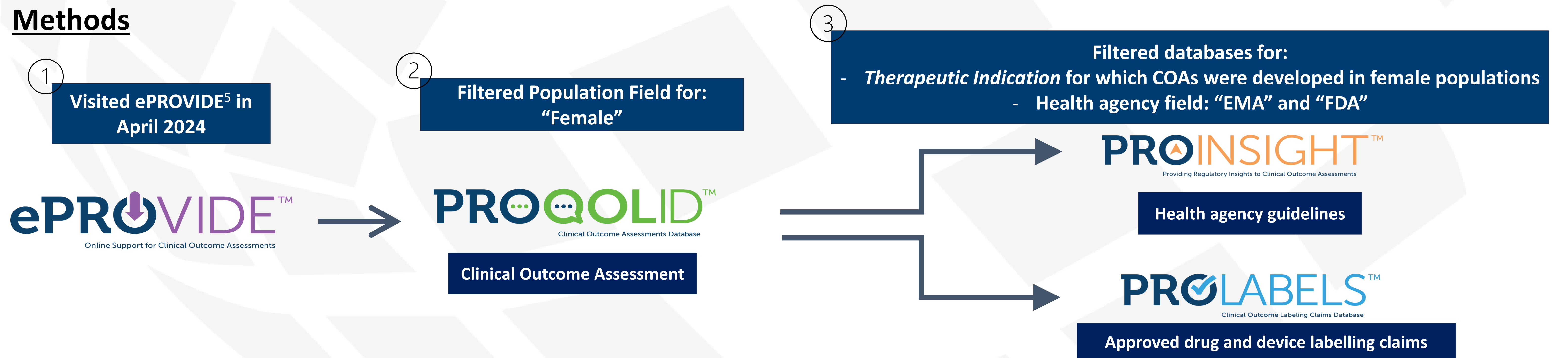
Main Outcomes

- **139 COAs** were identified in PROQOLID that were developed in an **all-female population**
- **All COAs** identified in PROQOLID except 3 were patient-reported outcomes (**PRO**), with **1 COA** also available as a clinical-reported outcome (**ClinRO**), and **3 COAs** were **composite** instruments
- **72 COAs** were developed in **all-female populations** for **female-specific conditions**
- **249 drug labels** were identified which were for **conditions related to females**. **69 COAs** were mentioned across these labels which were developed in an **all-female population** and **24 of them** were developed for conditions that **uniquely affect females**
- **Three EMA** and **1 FDA** guidelines featured **6 COAs** which were developed for **conditions related to females**
- **Nineteen** out of the **139 COAs** developed in an all-female population have been **developed since** the publication of the roadmap in **2015**. Whilst this represents a small proportion of the overall number of COAs identified in PROQOLID, this may reflect the trend to adapt existing COAs and revalidate them in a different population^{3,4} e.g., Functional Assessment of Cancer Therapy.

Future Direction

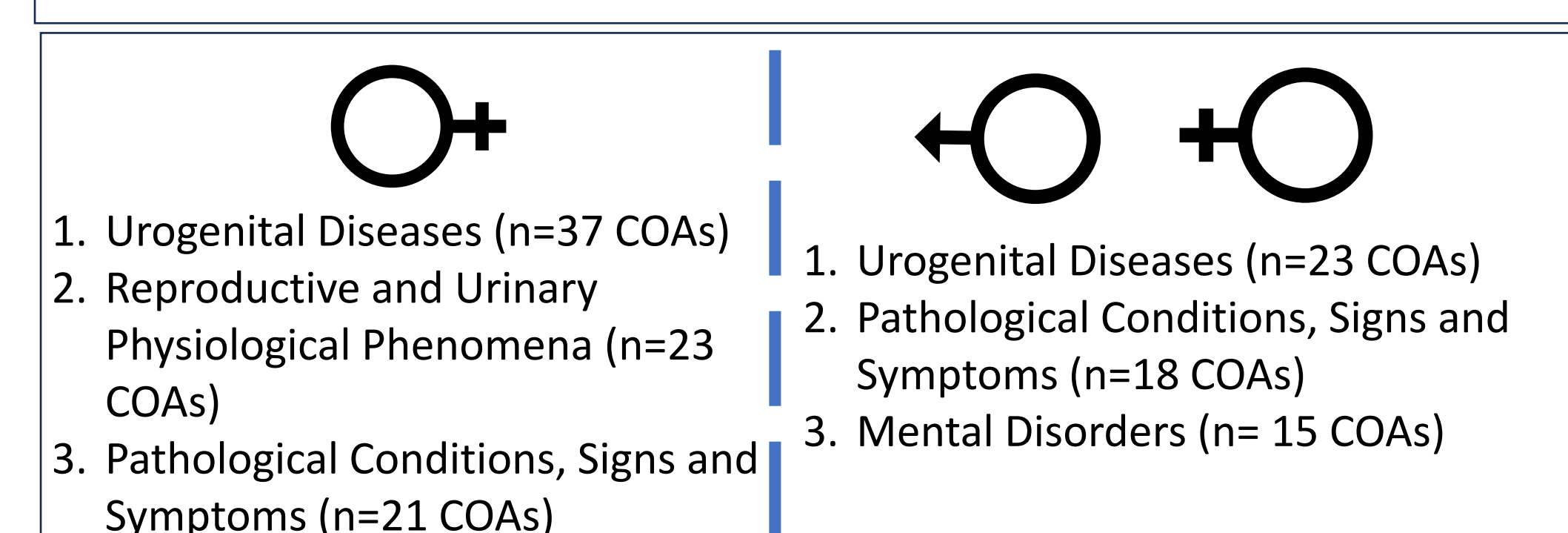
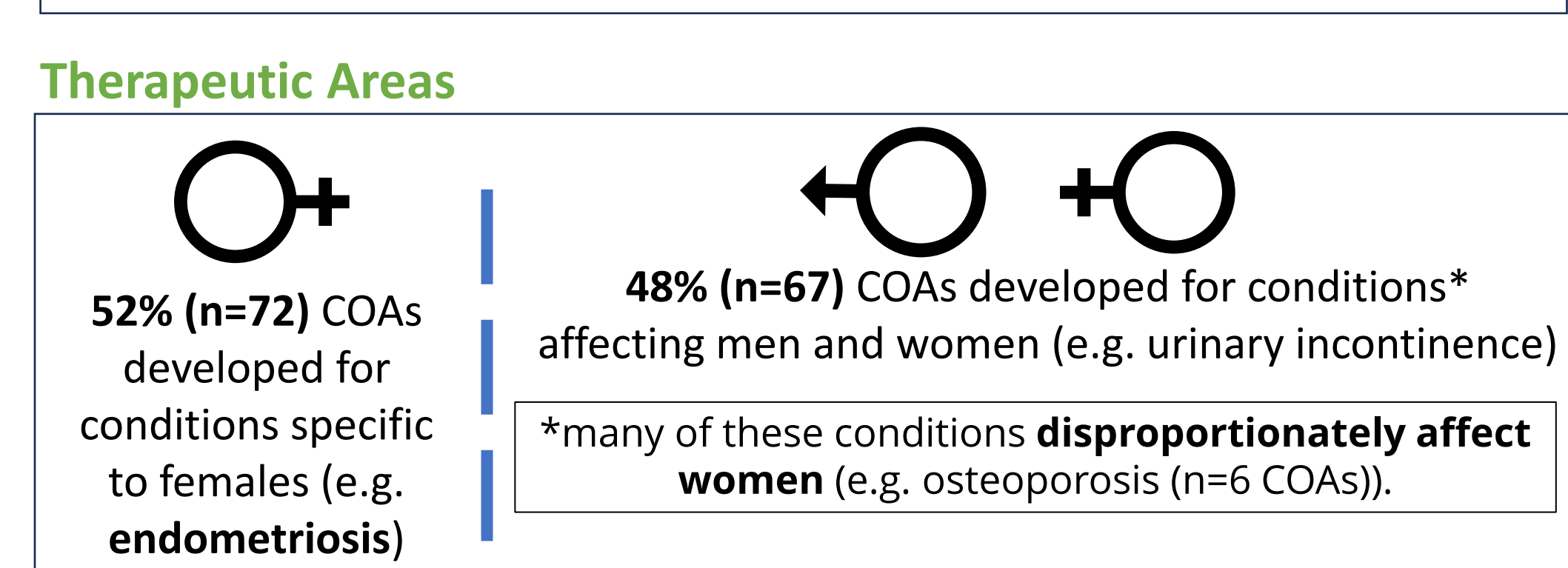
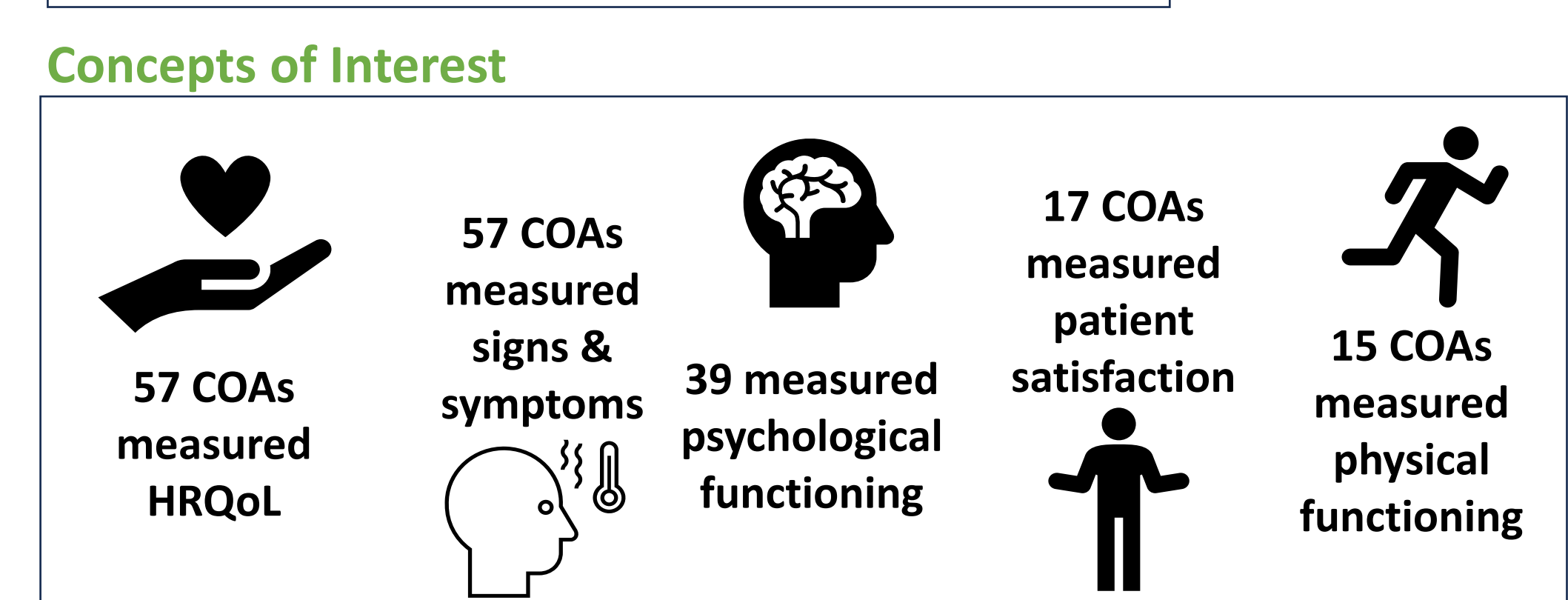
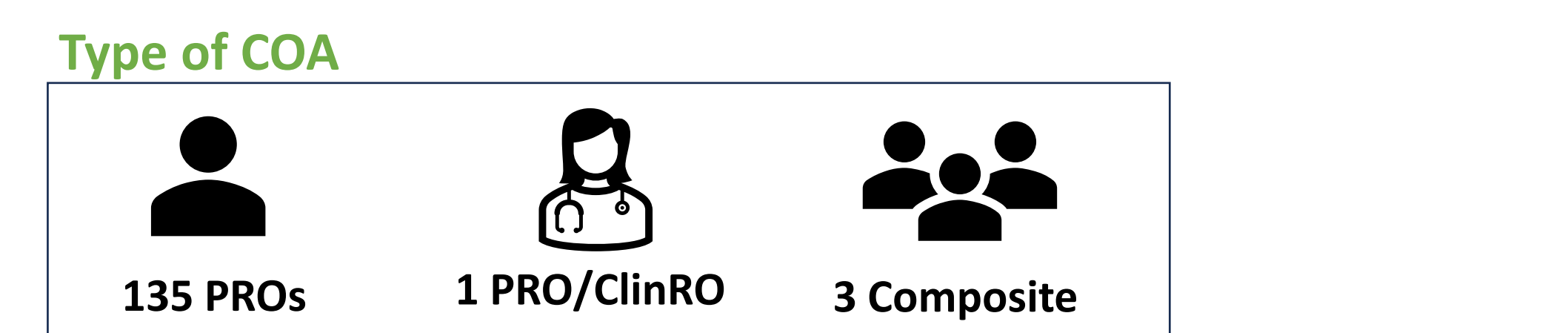
- Women's distinct experiences should be incorporated into **COA development** and **regulatory guidelines** for conditions that **uniquely impact women**
- The **FDA's 2015 Women's Health Research Roadmap** still provides key guidance for **COA development** and **endpoint strategy**²

Methods

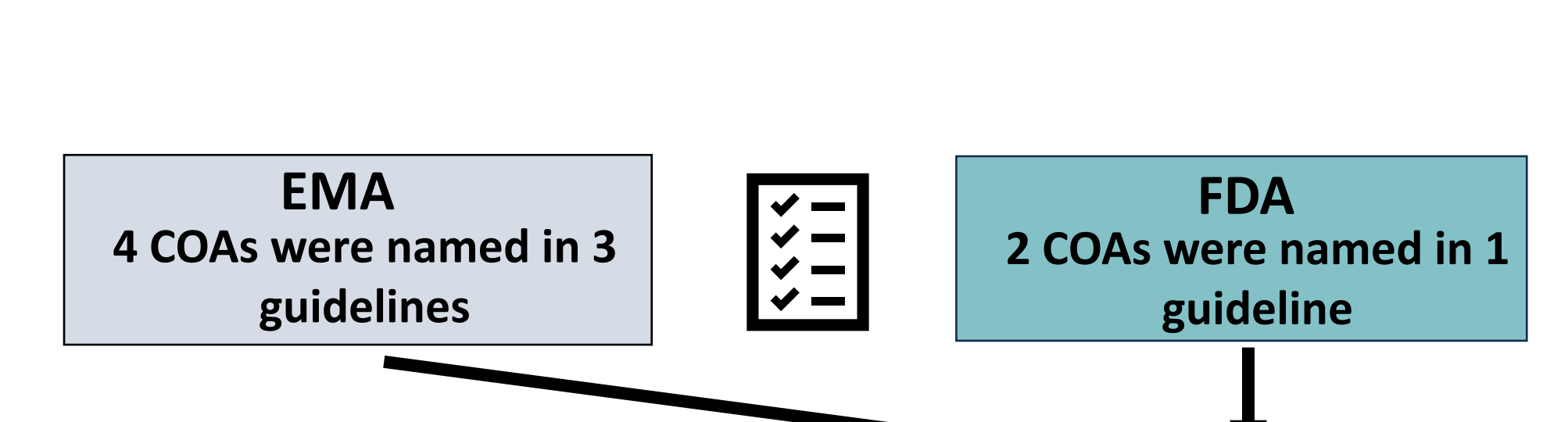


Results

PROQOLID was searched by **population (female)**. **139 COAs** were identified in PROQOLID that were developed with an **all-female population**. The majority of these COAs were **PROs**, measured **health-related quality of life (HRQoL)** or **signs and symptoms**, and just over half were developed for conditions specific to females (n=72, 52%). **Nineteen** out of **139 COAs** developed in an all-female population have been **developed since** the publication of the roadmap in **2015**.



PROINSIGHT was searched by **therapeutic indications** for which a COA had been developed with an **all female-population** in PROQOLID. From these results, **4 guidelines** were found in which a **COA was named that had been developed in an all-female population** (total = **6 named COAs**). **All but 1** of these COAs were suggested for use with a **primary endpoint**.



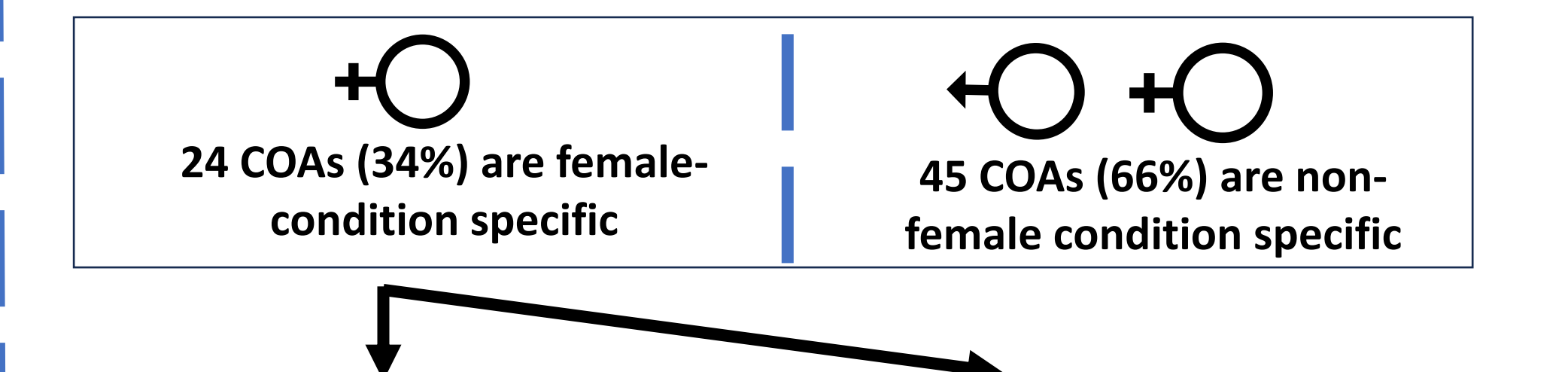
| Endpoint positioning | Concept area | COA instrument |
|----------------------|---------------------------|--|
| Primary endpoint | Signs and symptoms | Daily Record of Severity of Problems (DRSP) ⁺ |
| | | Kupperman Index (KI) |
| | HRQoL | Incontinence Stress Index (ISI) |
| | Psychological functioning | Female Sexual Function Index (FSFI) ⁺ |
| Secondary endpoint | Physical functioning | Incontinence Impact Questionnaire-Short Form (IIQ-7) |
| | Psychological functioning | Female Sexual Distress Scale (FSDS) ⁺ |

⁺ COAs included in drug labels approved by the FDA

Therapeutic indication for COA instrument

- Premenstrual Dysphoric Disorder (DRSP, n=1)
- Menopause (KI, n=1)
- Urinary Incontinence (ISI, n=1 & IIQ-7, n=1)
- Sexual Dysfunctions, Psychological (FSFI, n=1 & FSDS n=1)

PROLABELS was searched by **therapeutic indications** for which a COA had been developed with an **all female-population** in PROQOLID. **Sixty-nine COAs** developed in an all-female population were mentioned in **249 drug labels**. **Twenty-four COAs** were developed for conditions that **uniquely affect females**. These were in drug labels approved by the FDA and EMA. The top mentioned COA in the labels measured concepts related to **HRQoL** and **signs and symptoms**.



Count of labels per indication containing any of the female specific COAs

| | EMA | FDA |
|---|---|---|
| Sexual Dysfunctions, Psychological (n=3 COAs) | Sexual Dysfunctions, Psychological (n=4 COAs) | Sexual Dysfunctions, Psychological (n=4 COAs) |
| Leiomyoma (n=3 COAs) | Endometriosis (n=2 COAs) | Endometriosis (n=2 COAs) |
| Breast Neoplasms (n=2 COAs) | Leiomyoma (n=2 COAs) | Leiomyoma (n=2 COAs) |
| Ovarian Neoplasms (n=2 COAs) | Menstruation Disturbances (n=2 COAs) | Menstruation Disturbances (n=2 COAs) |
| Endometriosis (n=1 COA) | Nausea Vomiting (n=1 COA) | Nausea Vomiting (n=1 COA) |
| Urinary Incontinence, Stress (n=1 COA) | Urinary Incontinence, Stress (n=1 COA) | Urinary Incontinence, Stress (n=1 COA) |

Top 3 - Count of Indications in which the COA was mentioned - EMA

| Endpoint positioning | Concept area | COA instrument |
|----------------------|--------------------|--|
| Secondary endpoint | HRQoL | Functional Assessment of Cancer Therapy - Breast Cancer (n=3 COAs) |
| | | Pictorial Blood-loss Assessment Chart (n=2 COAs) |
| Secondary endpoint | Signs and symptoms | Endometriosis Health Profile-30 (n=2 COAs) |

Top 3 - Count of Indications in which the COA was mentioned - FDA

| Endpoint positioning | Concept area | COA instrument |
|----------------------|--------------------|---|
| Secondary endpoint | HRQoL | Uterine Fibroid Symptom and Health-Related Quality of Life Questionnaire (n=2 COAs) |
| | | Pictorial Blood-loss Assessment Chart (n=2 COAs) |
| Secondary endpoint | Signs and symptoms | Urinary Incontinence-Specific Quality of Life (n=2 COAs) |

References:
²Food and Drug Administration (FDA). (2015) *Women's Health Research Roadmap 2015*. [Accessed on: 10-03-2024]. Note: The Women's Health Research Roadmap 2015 was updated in October 2024, the updated version is available here: <https://www.fda.gov/consumers/about-owh-research/womens-health-research-roadmap-2015>. [Accessed on: 22-10-2024].
³Centers for Medicare & Medicaid Services (CMS). (2023) "Patient-Reported Outcome Measures: Supplemental Material". The Measures Management System Hub. Available at: <https://mmshub.cms.gov/> [Accessed on: 22-10-2024].
⁴Alrubaiy L, Hutchings HA, Hughes SE, Dobbs T. (2022) "Saving time and effort: Best practice for adapting existing patient-reported outcome measures in hepatology". *World J Hepatol*. 27;14(5):896-910.
⁵Access ePROVIDE™ at: <https://eprovide.mapi-trust.org/>