10 years on from the FDA's Women's Health Research Roadmap

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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 Roadmap**[2] 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

1. **Visited ePROVIDE[5] in April 2024**
2. **Filtered Population Field for: "Female"**
3. **Filtered databases for:**
   - ***Therapeutic Indication*** **for which COAs were developed in female populations**
   - **Health agency field: "EMA" and "FDA"**

ePROVIDE™ Online Support for Clinical Outcome Assessments → PROQOLID™ Clinical Outcome Assessments Database → **Clinical Outcome Assessment**

→ PROINSIGHT™ Providing Regulatory Insights to Clinical Outcome Assessments → **Health agency guidelines**

→ PROLABELS™ Clinical Outcome Labeling Claims Database → **Approved drug and device labelling claims**

Results

PROQOLID™ Clinical Outcome Assessments Database

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.**

Type of COA

- **135 PROs**
- **1 PRO/ClinRO**
- **3 Composite**

Concepts of Interest

- **57 COAs measured HRQoL**
- **57 COAs measured signs & symptoms**
- **39 measured psychological functioning**
- **17 COAs measured patient satisfaction**
- **15 COAs measured physical functioning**

Therapeutic Areas

52% (n=72) COAs developed for conditions specific to females (e.g. **endometriosis**)

48% (n=67) COAs developed for conditions* affecting men and women (e.g. urinary incontinence)

*many of these conditions **disproportionately affect women** (e.g. osteoporosis (n=6 COAs)).

1. Urogenital Diseases (n=37 COAs)
2. Reproductive and Urinary Physiological Phenomena (n=23 COAs)
3. Pathological Conditions, Signs and Symptoms (n=21 COAs)

1. Urogenital Diseases (n=23 COAs)
2. Pathological Conditions, Signs and Symptoms (n=18 COAs)
3. Mental Disorders (n= 15 COAs)

PROINSIGHT™ Providing Regulatory Insights to Clinical Outcome Assessments

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**.

EMA 4 COAs were named in 3 guidelines — **FDA** 2 COAs were named in 1 guideline

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)⁺
	Physical functioning	Incontinence Impact Questionnaire-Short Form (IIQ-7)
Secondary endpoint	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™ Clinical Outcome Labeling Claims Database

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**.

24 COAs (34%) are female-condition specific | **45 COAs (66%) are non-female condition specific**

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)
Leiomyoma (n=3 COAs)	Endometriosis (n=2 COAs)
Breast Neoplasms (n=2 COAs)	Leiomyoma (n=2 COAs)
Ovarian Neoplasms (n=2 COAs)	Menstruation Disturbances (n=2 COAs)
Endometriosis (n=1 COA)	Nausea | Vomiting (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)
	Signs and symptoms	Pictorial Blood-loss Assessment Chart (n=2 COAs)
		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)
	Signs and symptoms	Pictorial Blood-loss Assessment Chart (n=2 COAs)
		Urinary Incontinence-Specific Quality of Life (n=2 COAs)

References:
[2]Food 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?utm_medium=email&utm_source=govdelivery [Accessed on: 22-10-2024].
[3]Centers 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].
[4]Alrubaiy 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.
[5]Access ePROVIDE™ at: https://eprovide.mapi-trust.org/