

Background

Objective

Methods

*With COA

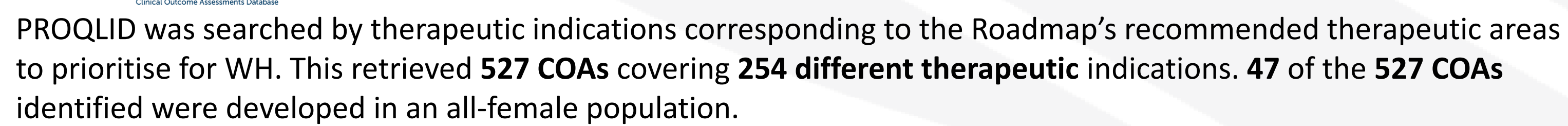
Main Outcomes

- **527 COAs** were identified which covered **254** different **therapeutic indications**. **9%** (n=47) were developed in an **all-female population**
- Lowest number of COAs for **cardiovascular diseases** (n=12 COAs, 2%), **psychological phenomena** (n=23 COAs, 4%), and **musculoskeletal diseases** (n=26 COAs, 5%)
- **21 guidelines** identified including **9 COAs** – **none** of which were developed in an **all-female population**
- **106 labels** encompassing **48 COAs** (**8** of which were developed in an **all-female population**)
- **FDA** have **approved more labels** in these therapeutic areas **since 2015** than the **EMA**, but there are **more COAs** in **EMA** approved labels than **FDA** labels

Future Direction

- Further research into **cardiovascular** and **musculoskeletal diseases**, and **psychological phenomena**
- Remains a need to **develop COAs** with women which are **specific for women's health needs**
- **Need for more guidance** on how to **capture women's health needs** in COA measurement
- More COAs **developed for women** to be used in **labels** targeting WH priority **therapeutic areas**

Results



Greatest Number of COAs	Least Number of COAs
Neoplasms (n=267 COAs, 51%) 11% (n=30) in an all-female development population 50% were (n=15) for breast neoplasms	Cardiovascular diseases (n=12 COAs, 2%) 0 in all-female development population
Diabetes (n=118 COAs, 22%) 0 in all-female development population	Psychological phenomena (n=23 COAs, 4%) 4% (n=1) in an all-female development population for body image in women with breast cancer
Substance-related disorders (n=53, 10%) 0 in all-female development population	Musculoskeletal diseases (n=26 COAs, 5%) 34% (n=9) in an all-female development population - All-female COAs were for osteoporosis with 4 specifically for post-menopausal osteoporosis

Discussion: These findings are in line with several reports showing that breast cancer research receives the greatest amount of funding compared to other cancers in the UK⁹ and USA¹⁰. Further, there is a shortage of COAs developed with a WH focus being used in key therapeutic areas. It is important to address this difference as research shows women have **different health experiences** to men and **disease can manifest differently** in men to women⁵.

Most common concept measured
(total n=227 COAs)

developed COAs: **42%** (n=201)

All-female developed COAs: **55%** (n=26)

Health-Related Quality of Life

The top **therapeutic areas** for which HRQoL was measured:

- Neoplasms (n=19)
- Osteoporosis (n=7)
- All-female population
- Neoplasms (n=133)
- Diabetes (n=45)
- Non-female specific population

One reason why there are slightly more COAs developed in an all-female population measuring HRQoL may be because some studies have found that women tend to report lower HRQoL compared to men⁸ and so it is important to ensure that COAs are fit-for-women.

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graph LR
    A["472 PROs 21 ClinRO 10 Composite 10 ObsRO"] --> B["developed in a female-specific population were PROs"]
    A --> C["All COAs developed in an all-female population were PROs."]
    A --> D["16 COAs were also available as different types of COAs, e.g. either a PRO or an ObsRO, PRO or a ClinRO"]
    B --> E["Researchers are currently developing COAs with an all-female population may be acutely aware of the importance of eliciting women's perspective when measuring health outcomes due to their historical absence from health research7."]
    C --> E
  
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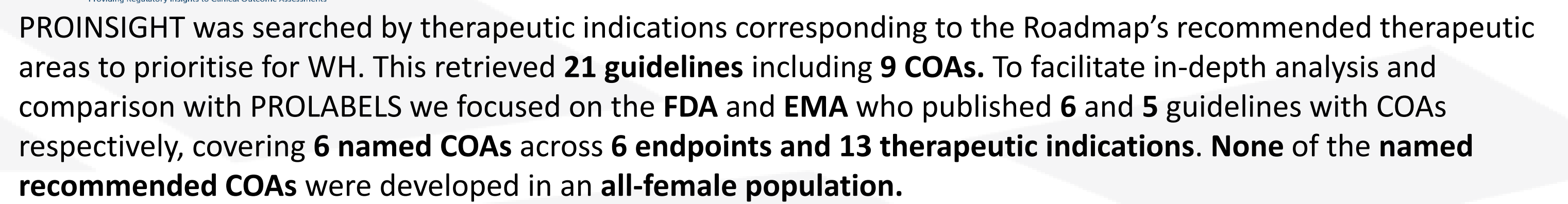
472 PROs 21 ClinRO 10 Composite 10 ObsRO

developed in a female-specific population were PROs

- All COAs developed in an all-female population were PROs.

16 COAs were also available as different types of COAs, e.g. either a PRO or an ObsRO, PRO or a ClinRO

Researchers are currently developing COAs with an all-female population may be acutely aware of the importance of eliciting women's perspective when measuring health outcomes due to their historical absence from health research⁷.



The EMA and FDA were fairly **aligned** on issuing guidelines in similar **therapeutic areas**. Most common therapeutic areas were **obesity** (EMA= 2; FDA= 1 guideline), **chemotherapy-induced nausea and vomiting** (CINV) (EMA=2; FDA=1 guideline), as well as two guidelines from the EMA on **diabetes**. Both agencies also aligned on therapeutic areas in which **specific COAs had been named for CINV** (EMA=2; FDA=5 named COAs) and **neoplasms** as well for the FDA (1 named COA). The focus on these therapeutic areas was also **reflected in COA and drug label data**.

There were **differences** between the agency in **endpoint positioning**. EMA recommended **more primary** and **secondary endpoints with COA** recommendations (n=3 and n=7 endpoints respectively) compared to FDA (n=3 and n=2 endpoints respectively). However, **FDA and EMA** recommended the same number of **not specified endpoints with COA** (n=9). Notably, **FDA specified named 5 COAs** for not specified endpoint use whereas the EMA only **named 1 COA** for a secondary endpoint, highlighting a **shortage of named COAs for endpoints with COA recommendations**.

Type of COA Recommended		
	EMA	FDA
PROs	n=17	n=9
ClinROs	n=1	n=0
Composite	n=0	n=2
PerfOs	n=1	n=0
ObsROs	n=0	n=0
Unspecified	n=0	n=3

Concept of Interest

HRQoL uniquely measured by PROs, **Fracture incidence** by ClinROs, **Exercise** by PerfO

FDA:

- PROMIS Item Bank v1.0 – Severity of Substance Use
- EORTC-QLQ-C30
- PRO-CTCAE
- NSCLC-SAQ
- FACIT

EMA:

- Functional Living Index - Emesis

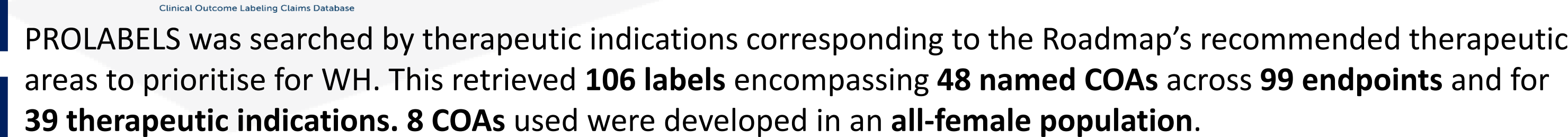
One **more guideline published** between **2015-2024** (n=6 guidelines) in comparison to **2005-2014** (n=5 guidelines):

- **2004-2014: EMA** issued **4 of 5** guidelines published in this period
- **2015-2024: FDA** issued **5 of 6** guidelines published in this period

This fits with the broader trend and may not be linked to the WH Roadmap:

- **2004-2014: EMA** (n=34 guidelines) **published more guidelines with COA** recommendations than the FDA (n=15 guidelines)
- **2015-2024: FDA** (n=91 guidelines) **published more guidelines with COA** recommendations than the EMA (n=36 guidelines)

Limited consideration of how prevalence of these therapeutic areas and/or how they may manifest differently in women was seen in the guidelines. Fits with broader literature highlighting the lack of specific guidance on women's unique health needs with a consideration of how experiences may differ from men¹¹.	• Cardiovascular: women are at high-risk of CINV and recommended this be reflected in clinical trial populations • Osteoporosis: discussion of how the disease manifests differently in women – explicit focus on postmenopausal women	• CINV: suggested that future 'sex' to be adjusted for in statistical analysis as this can impact efficacy outcomes. • HIV: consideration for trials in pregnant and/or high-risk women because determination because of the variable historical evidence of HIV prevention efficacy in at-risk women.
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Most Common Therapeutic Areas	Least Common Therapeutic Areas
Osteoporosis (n=30 labels; FDA=17/EMA=13)	Cardiovascular disease (n=1 label FDA)
Breast neoplasms (n=25 labels; FDA=12/EMA=13)	Autoimmune diseases (n=1 label EMA)
Diabetes (n=24 labels; FDA=15/EMA=9)	HIV Infections (n=1 label FDA)
COAs developed in a female-specific population: 1 for postmenopausal osteoporosis and 3 for breast neoplasms	

The diagram illustrates the distribution of endpoint positioning with COAs and the measurement of endpoints. It is divided into two main sections: 'Distribution of endpoint positioning with COAs' and 'EMA only had one label with a named COA used to measure a primary endpoint: Severity Weighted Assessment Tool (complete response)'. The 'Distribution of endpoint positioning with COAs' section lists three categories of endpoints: Primary endpoints (n=77 COAs), Secondary endpoints (n=113 COAs), and Tertiary/Exploratory endpoints (n=4 COAs). A blue oval highlights that 5 COAs were developed in a female-specific population, with 1 being exploratory and 4 not specified. The 'EMA only had one label...' section lists two endpoints: Memorial Pain Assessment Card (pain intensity) (n=4 endpoints) and Karnofsky Performance Status (performance status) (n=4 endpoints). A blue oval highlights that endpoints were largely measured by PROs (n=104) compared to ClinROs (n=72) or composite (n=48).

Distribution of endpoint positioning with COAs:

- Primary endpoints: n=77 COAs
- Secondary endpoints: n=113 COAs
- Tertiary/Exploratory endpoints: n=4 COAs

5 COAs developed in a female-specific population were for secondary endpoints, 1 was exploratory, 4 were not specified

EMA only had one label with a named COA used to measure a primary endpoint: *Severity Weighted Assessment Tool* (complete response)

- *Memorial Pain Assessment Card* (pain intensity) (n=4 endpoints)
- *Karnofsky Performance Status* (performance status) (n=4 endpoints)

Endpoints were largely measured by PROs (n=104) compared to ClinROs (n=72) or composite (n=48)

The diagram illustrates the relationship between COAs, Pain, and HRQoL. On the left, a vertical bar labeled 'COAs' is shown. To its right, two boxes are connected by arrows. The top box, labeled 'Pain', contains the text 'Most common concepts measured by specific COAs' and lists two endpoints: 'EMA: EORTC QLQ-C30 (2 endpoints)' and 'FDA: Memorial Pain Assessment Card (n=4 endpoints)'. The bottom box, labeled 'Health-Related Quality of Life', contains the text 'HRQoL most frequently measured by:' and lists two endpoints: 'EMA: EORTC-QLQ-C30 (n=9 endpoints)' and 'FDA: SF-36 Health Survey (n=5 endpoints)'. A blue circle on the right side of the diagram contains the text '6 of the 8 COAs developed in a female-specific population measured HRQoL'.

↑ Slightly more labels were approved between **2015-2024 (n=42 labels)** than **2005-2014 (n=38 labels)**

↑ Since 2015, a slightly more labels have been approved by the **FDA (n=22 labels)** than the **EMA (n=20 labels)**

↑ More COAs have been used in **2015-2024 (n=48 COAs)** versus **2005-2014 (n=32)**. This increase in COA use is mainly due to **EMA labels (n=29 COAs)** than **FDA (n=19 COAs)**. However, only **3 female-specific COAs** have been used since **2015 vs 9 pre-2015**.

References

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- 4 FDA Office of Women's Health (OWH). (2024) "Woman's Health Research Roadmap". FDA. Available at: <https://www.fda.gov/consumers/about-owh/research/womens-health-research-roadmap> [Accessed on 27-11-2024].
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