

Representation in Clinical Trials

- *data use-case from REPACT project at DKMA*

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Context: EU Regulatory basis for representation

EU

“Unless otherwise justified in the protocol, the subjects participating in a clinical trial should represent the population groups, for example gender and age groups, that are likely to use the medicinal product investigated in the clinical trial.”

EU Clinical Trial Regulation, recital 14

ICH General considerations & GCP guidelines

“involve participants who are representative of the diverse populations which will receive the intervention in clinical practice.

EMA

“Clinical trials need to involve neglected populations including the elderly and pregnant women so they too can benefit more directly from research.”

Regulatory science towards 2025 (March 2020)

Neglected populations in clinical trials

A pilot study of asthma medication use, comparing registered Real World populations with Phase III clinical trial populations

AUTHORS

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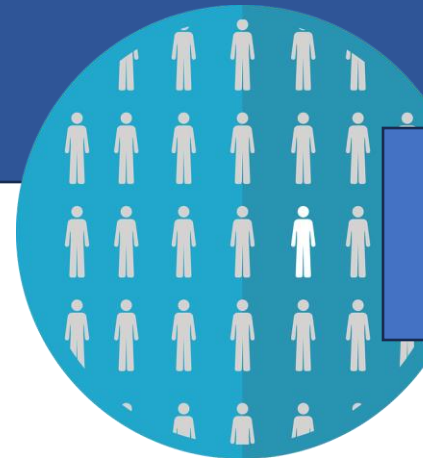
Objectives

Assess representation of sexes and age groups and prevalence of co-morbidities in clinical trials for asthma medication

Use population
RWD from DK LPR &
LSR



Trial population
Phase III CT in
EUDRACT



Use Population

- The National Patient Register (Landspatientregisteret-LPR)
- The Register of Pharmaceutical sales (Lægemedelstatistikregisteret-LSR)
- All Danish citizens
- 2 years of age or more
- At least 1 prescription of asthma medication (defined by ATC code)
- From 1. jan. 2015 to 31. dec 2022

Characteristics	Entire cohort (n = 1,057,418) n (%)	Females (n = 575,346) n (%)	Males (n = 482,072) n (%)
Age (years)			
2-11 (childhood)	129,445 (12.2%)	54,990 (9.6%)	74,455 (15.4%)
12-17 (adolescence)	58,330 (5.5%)	30,199 (5.2%)	28,131 (5.8%)
18-64 (adulthood)	551,403 (52.1%)	311,645 (54.2%)	239,758 (49.7%)
≥65 (middle-aged)	318,240 (30.1%)	178,512 (31.0%)	139,728 (29.0%)
Comorbidities			
Cardiovascular diseases	112,931 (9.8%)	53,974 (9.4%)	58,957 (12.2%)
Diabetes (Type 1 and Type 2)	39,862 (3.5%)	19,339 (3.4 %)	20,524 (4.3%)
Cancer	62,498 (5.4%)	41,956 (7.3%)	20,542 (4.3 %)

Trial Population

- EUDRACT
- Completed Phase III,
- Before 1. January 2015
- Selected with list of ATC codes for asthma medication

Table 1 Population characteristics of the persons enrolled in the 40* phase III clinical trial on asthma medication

Characteristics	Entire cohort (n=98.846)	Females (n=26.537)	Males (n=35.025)
Age (years)			
2-11 (childhood)	3354 (3,39%)		
12-17 (adolescence)	5432 (5,49%)	43%	57%
18-64 (adulthood)	64421 (65,17%)		
≥65a (middle-aged)	25639 (25,93%)		

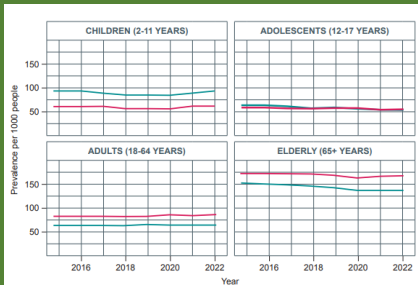
*only 30 trial reported representation of Sex.

Comorbidities

“Exclusion criteria (...) 7. Any **significant disease** or disorder (eg, **cardiovascular**, pulmonary other than asthma, gastrointestinal, hepatic, renal, neurological, musculoskeletal, endocrine, metabolic, malignant, psychiatric, major physical impairment) which, **in the opinion of the investigator**, either put the **patient at risk** because of participating in the study or may **influence the results of the study**, or the **patient’s ability to participate** in the study.”

Observations

Representation of SEX relative to AGE in EUDRACT



Reporting of SEX representation

- Are we good?

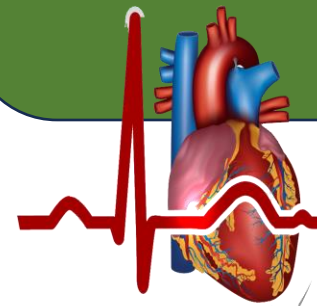


CO-MORBIDITIES

Transparency & Accountability

FDA criticism

Methods – NLP?



The Dog that didn't Bark...

Pregnant women
=> No ICD10 code

Ethnic minorities
=> Data & standards

=> the right use population?





Thank you
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