Systematic Review of prospective pregnancy studies in Europe: Scope for improvement

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1 OBJECTIVES

Pregnant women are rarely enrolled in clinical trials and little or no data is available at the time of marketing approval. Regulatory agencies request post-approval studies (PASS) to evaluate adverse effects on pregnancy, birth and childhood development from exposure in pregnancy of newly approved drugs.

These studies are almost invariably observational and may involve primary data collection and/or secondary data sources.

Objective:
To describe the methodology and performance of primary data collection prospective studies in Europe and assess their quality.

2 METHODS

- Data source: A search of the EU PAS Register between January 2011 and November 2019.
- Information from EMA for studies with absent or partial results publicly available.

Inclusion criteria:
- Completed pregnancy studies conducted in ≥ 1 EU country with outcomes recorded.
- Studies with results in the full study report, abstract or manuscripts.

3 RESULTS

STUDY SELECTION PROCESS

1631 studies were identified in EU PAS Register, of which 30 were pregnancy studies. **Eight** were primary data collection studies with analysable data (Figure 1). Publicly available data were collected and analysed with descriptive statistics and data from EMA is awaited.

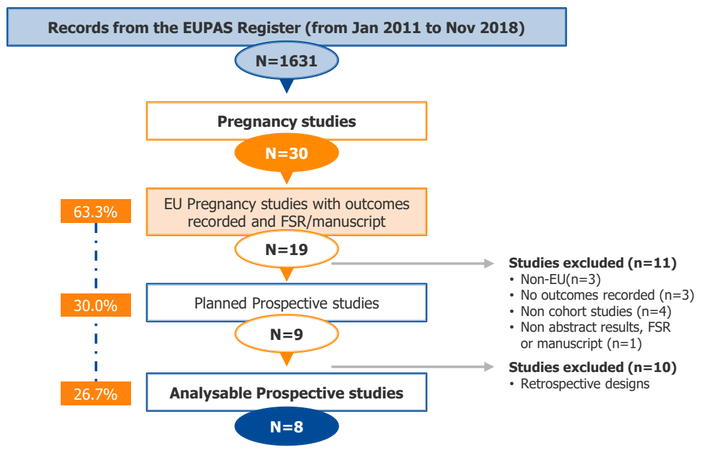

Figure 1 - Study selection process

PROSPECTIVE PREGNANCY STUDIES CHARACTERISTICS

1. Countries

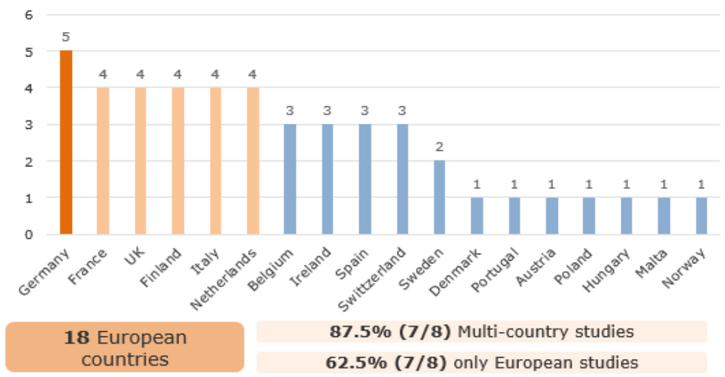

Figure 2 - Participating countries

2. Studies Design

- Half the studies (4/8) were conducted as active prospective data collection using a 'wide-net all comers' approach and half used an established registry database to recruit patients. Four studies (50%) reached the target number of patients and other four (50%) reported loss of follow up, ranging from 1% to 28.6% (Table 1).
- Six studies (75.0%) were conducted with a comparison group: three with a drug comparison and three with non-drug exposure groups.
- The median study duration was 36 months, with a range from 10 months to 89 months.
- The median number of patients in the studies was 1,186, with a range from 2 to 197,948 patients.

		No reached target	Loss of follow up
Active prospective data collection	4 (50%)	3 (75%)	3 (75%)
Established registry database	4 (50%)	1 (25%)	1 (25%)
	Total	**4 (50%)**	**4 (50%)**

Table 1 – Study methodology

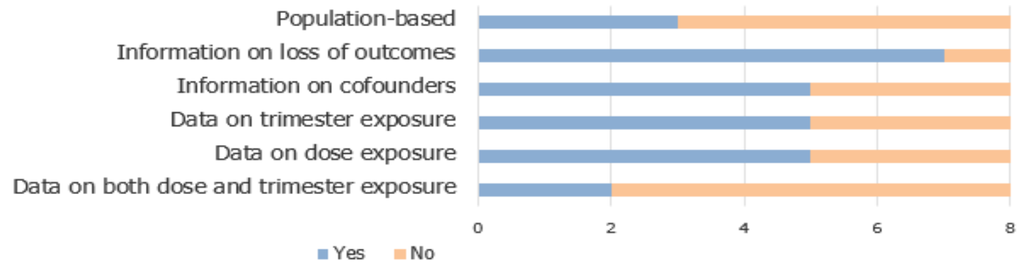

Figure 3 – Study results

3. Pregnancy outcomes collected

- All studies assessed birth outcomes (8/8), 87.5% (7/8) foetal outcomes and 75.0% (6/8) maternal outcomes.
- However, only two studies showed an association between drug exposed and foetal, birth or maternal outcomes.

4 CONCLUSIONS

- There were few prospective pregnancy studies involving European countries in the EU PAS Register.
- Many prospective cohort studies had **deficiencies** in information on dose and trimester exposure, confounders, loss to follow-up, population-base and target number reached.
- The conventional ´wide-net all registrants´ approach for prospective studies needs to be improved.
- **Novel methodologically robust and more efficient designs are needed**.