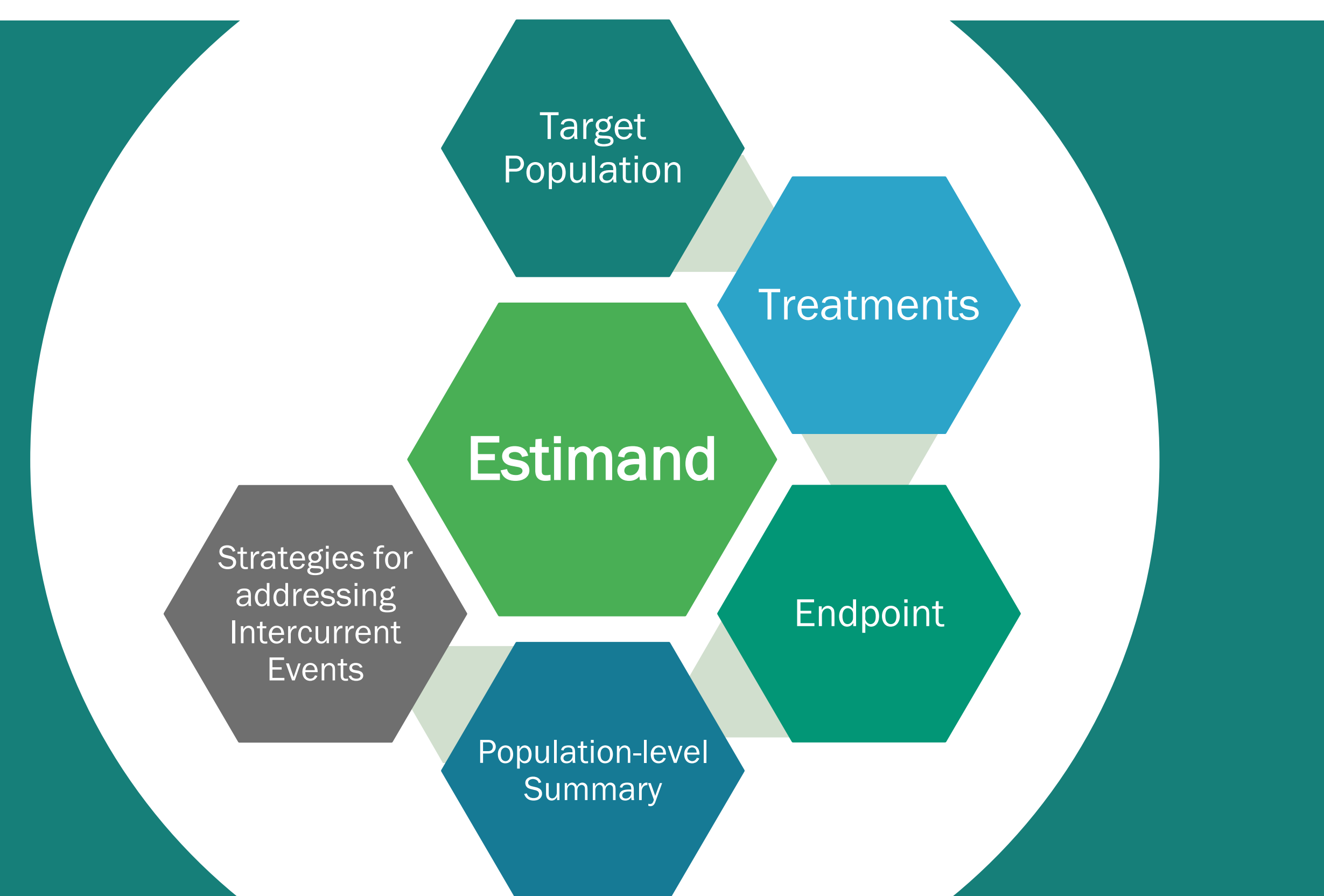


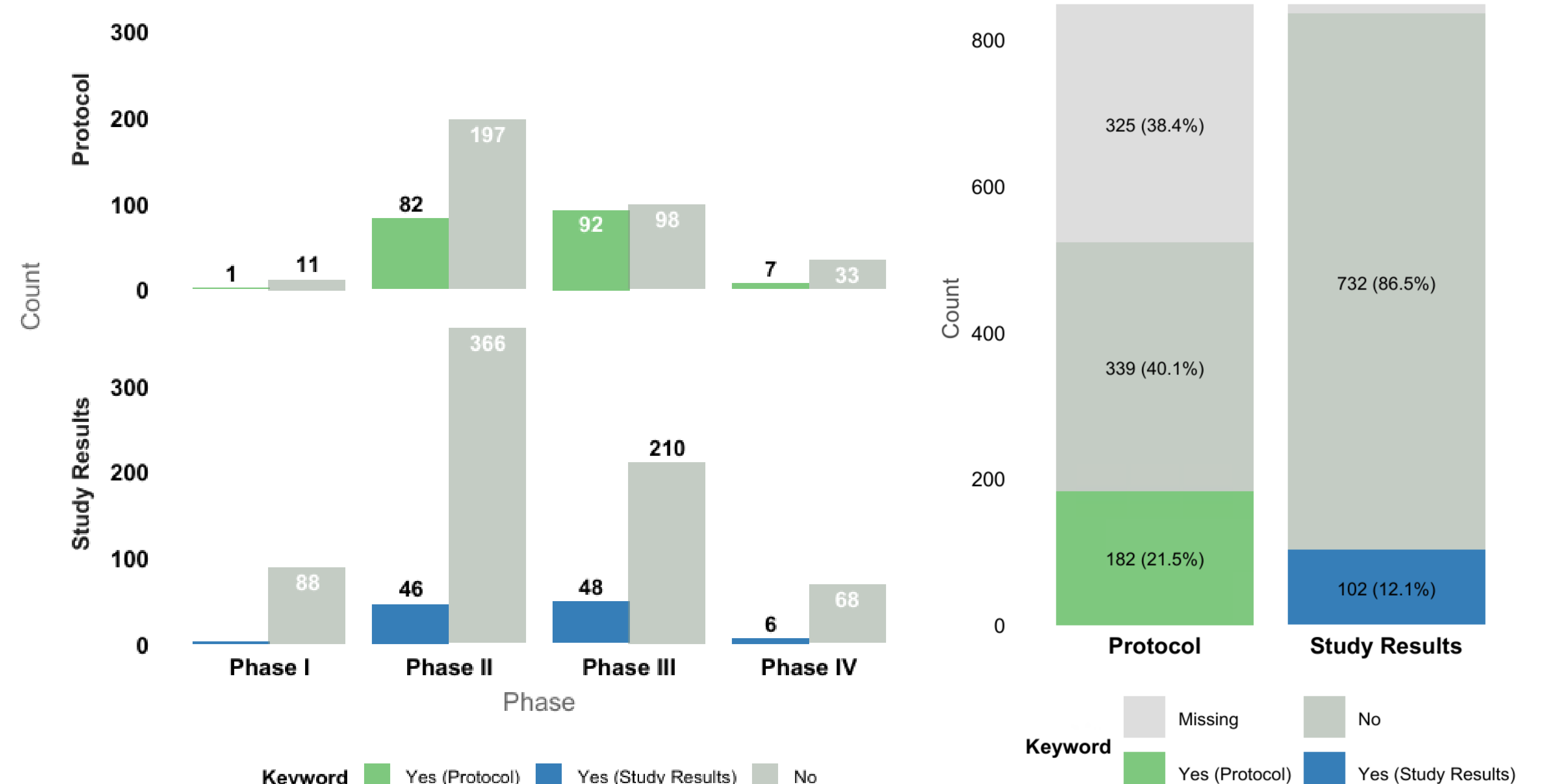
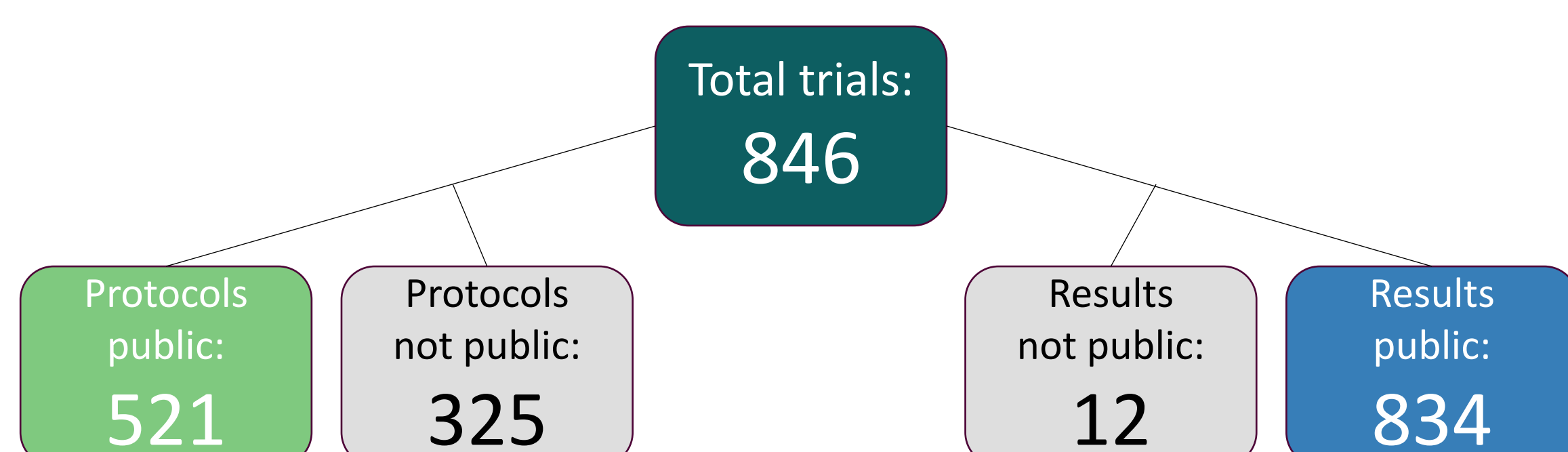
Estimand implementation in the EU Clinical Trial Register **CTIS**: Are we there yet?

- Most protocols and trial results posted on **CTIS** do not include estimands or intercurrent events
- Among trials whose protocols describe estimands and/or intercurrent events, 66 of 182 (36.3%) report estimands in their posted study results.



Methodology

Trials with publicly available **CTIS results** and with a start date between **01-09-2017 to 09-06-2026** were included. Using the R package 'ctrdata', trial variables, trial **protocol (pdf) and results (pdf) were extracted** from CTIS. Trial documents were searched for the **keywords**: 'estimand', 'intercurrent event', 'treatment policy', 'while on treatment', 'principal stratum' and 'hypothetical'.



Keyword hits per trial phase: The number of trials per phase with and without a hit for any estimand keyword in their public protocol or trial result documents posted on CTIS.

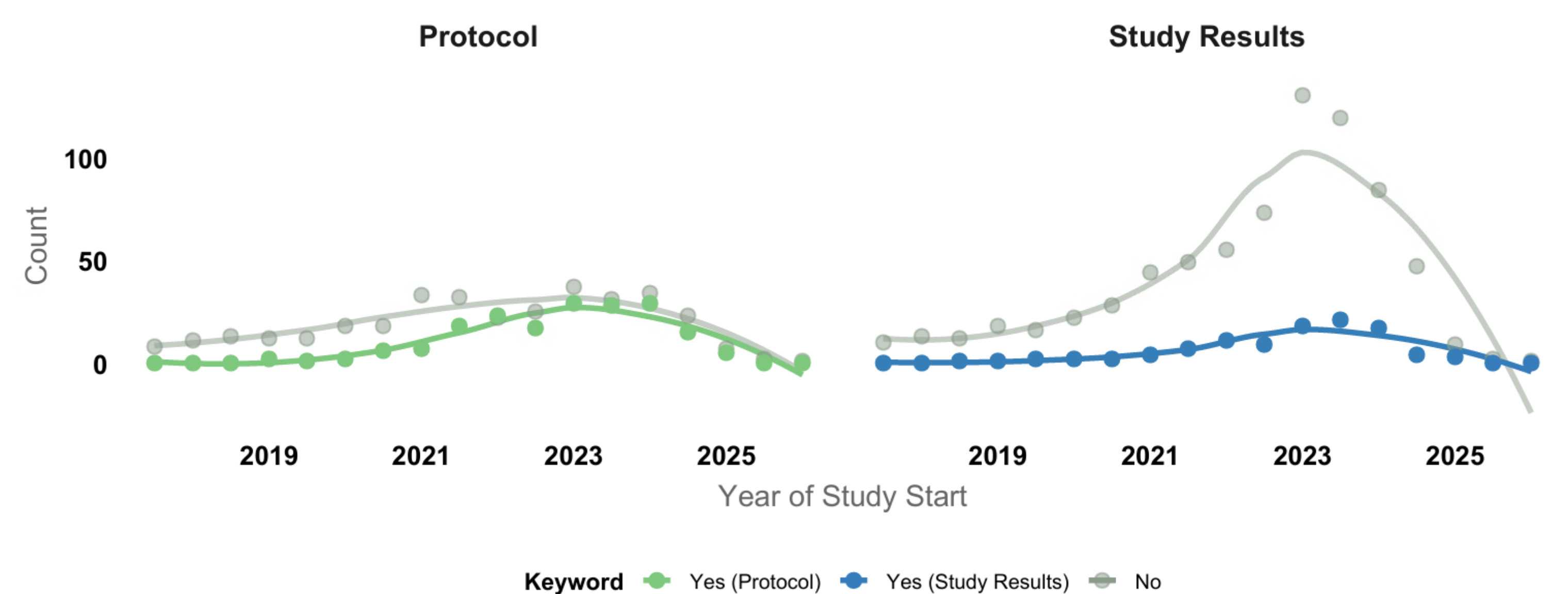
Distribution of trials with keyword hits: The percentage of trials which either had missing documents or had public documents on CTIS with or without a hit for any estimand keyword.

Results

Out of 846 trials with results posted on CTIS, 521 (61.6%) had publicly available protocols, whereas protocols were unavailable for 325 (38.4%) trials, likely because protocol publication could be deferred for up to 7 years until June 2024. Relevant keywords ('estimand' and/or 'intercurrent events') were described in 182 (35.5%) of the 513 trials with both protocols and results data available. However, only 66 (12.9%) of these trials described estimands in both public protocol and posted trial results.

Percentage wise, the use of estimands was highest in phase III trials and a slight increase can be seen from 2023 onwards.

Keywords	in trial results		
	No	Yes	
In protocols	No	322 (62.8%)	9 (1.8%)
	Yes	116 (22.6%)	66 (12.9%)

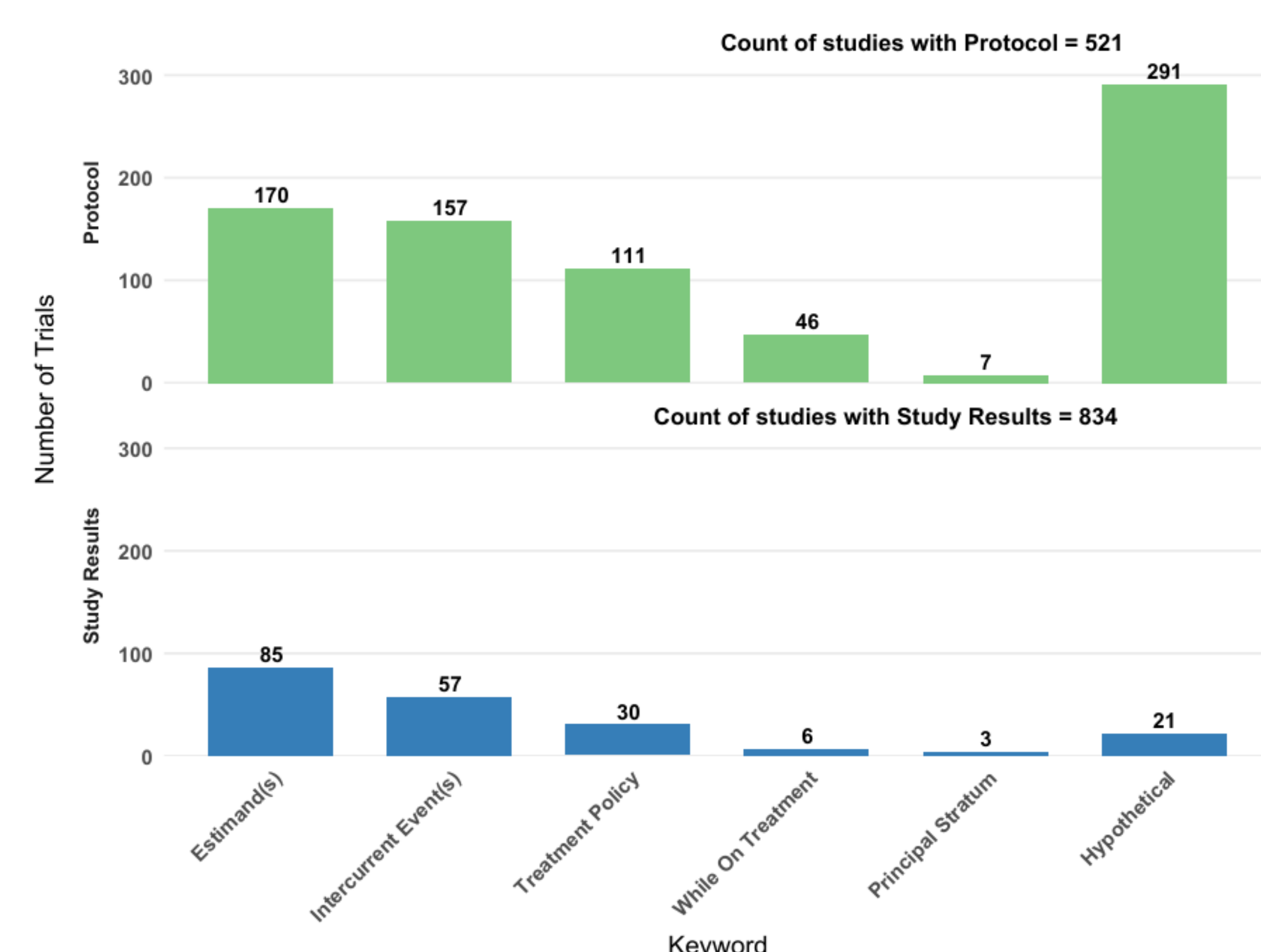


The number of trials with and without keyword hits: The number of trials by their study start date in 3-month buckets with and without a hit for any estimand keyword in their public protocol or trial results documents on CTIS.

Conclusion

Following EMA's adaption of the ICH E9 (R1) addendum only a minority of trials describe estimands in their protocols and an even lower number describes the trial results using estimand language in the required posting of results on CTIS.

Clear and consistent estimand reporting - and clear guidance - is key to realizing the full value of the estimand framework.



The number of trials with a keyword hit sorted by keyword: Total number of trials per keyword with a hit in their public trial documents on CTIS.

For the overall count of trials using estimands (above figures), the trials which only had a hit for the following keywords 'treatment policy', 'while on treatment', 'principal stratum' and 'hypothetical' were removed as these phrases were used in a different context.