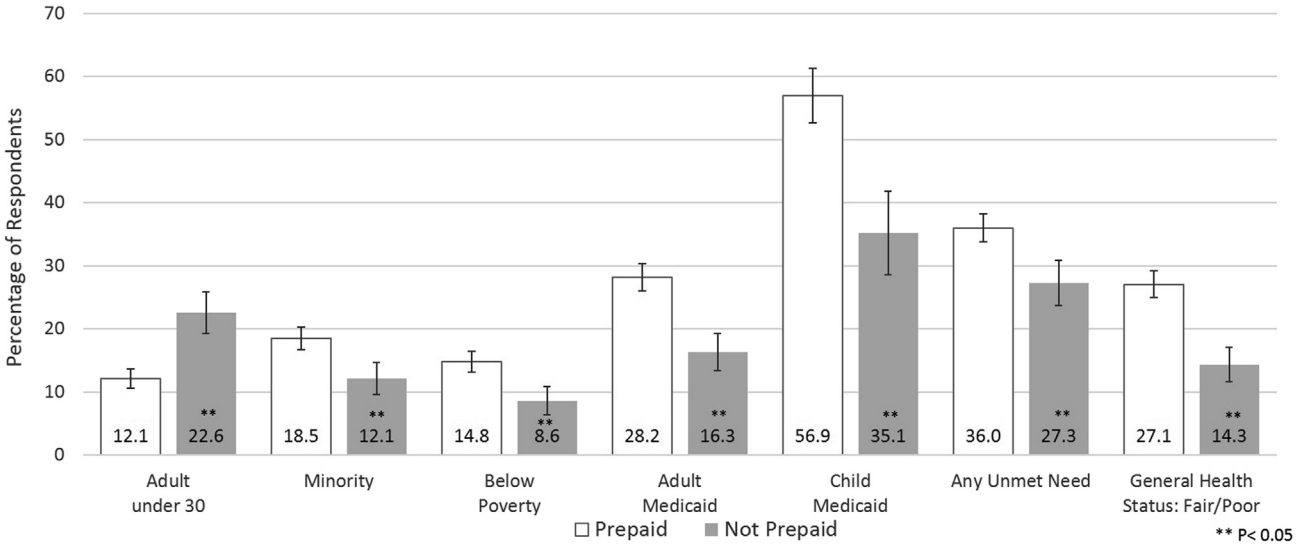

Fig. 1. Percentage of respondents by demographic and health care status and prepaid phone use.

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Noninferiority drug trials fail to report adequate methodological detail: an assessment of noninferiority trials from 2010 to 2015

1. Introduction

Noninferiority (NI) trials are prevalent in many therapeutic areas and are used to evaluate new drugs [1−4]. When reading NI trials, one must pay special attention to the justification for the NI margin [5,6]. With the NI margin being a key part of NI trial design, any questionable justification for the choice of the NI margin can lead to

Conflict of interest: The authors have no conflict of interest to report.

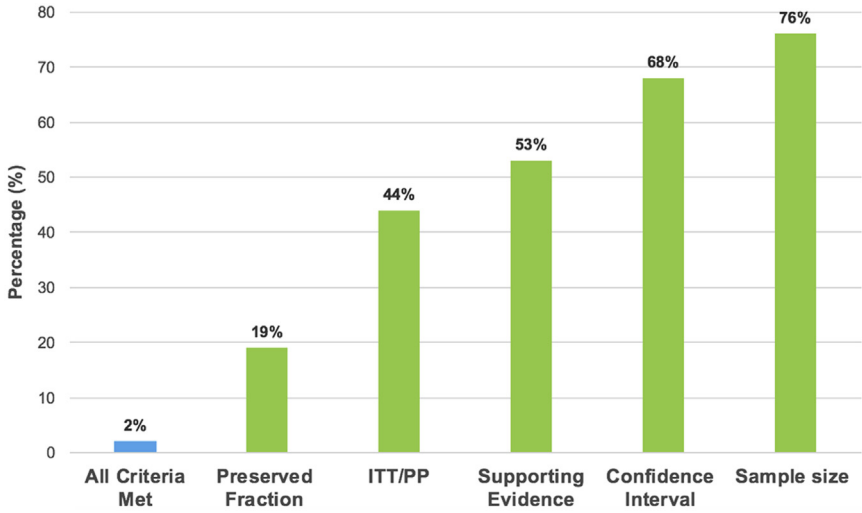

Fig. 1. Reporting of noninferiority margin details.

incorrectly declaring a new drug a reasonable alternative to the current standard therapy. Many comprehensive reviews have assessed the quality of reporting in NI trials and revealed considerable problems in reporting of the justification for NI margins [7−9].

2. Methods

The primary objective of our study was to describe the proportion of NI trials reporting 5 important details necessary for an average reader to interpret the NI margin. We performed a systematic search for NI trials in MEDLINE from January 1st, 2010 to August 17th, 2015. A sample of 225 trials was to be randomly selected from the search results. One investigator, J.H., conducted the search and screened the results to determine the studies for inclusion. J.H. extracted data on all included articles, with independent duplication extraction of the entire sample of 225 NI trials by one of three coinvestigators (A.T., A.K., A.M.T.). Any discrepancies between J.H. and the other investigator were resolved through discussion with a third investigator.

3. Results

Very few trials reported all important information we deemed necessary to appraise the NI margin (see Fig. 1; all 5 components of the primary outcome; 1.8% [range 0% to 7.1%]). Statistical details were reported frequently (e.g., sample size consideration of NI design and per protocol (PP) and intention-to-treat (ITT) analyses were done, correct end of confidence interval used in analysis). Although these details were reported, the methods were not always appropriate; 34.7% reported only an ITT analysis for NI, approximately 30% of trials did not use/report sample size calculations with reference to NI design and 27% did not make reference to which end of the confidence interval they used for their NI analysis. Information related to clinically relevant information was poorly reported (e.g., evidence used to justify the margin, retention of a clinically important effect). Most trials had a publicly available protocol/clinical trial registry. Of great concern was the fact that, of the studies that had protocols, only 45% mentioned the NI design in their protocol. Conversely, most trials (96%) in our cohort made mention of the NI design in their main publication. Almost half the articles reported assistance in writing their manuscript (46.8%). None of the trials described the reason or justification for an NI design. In a post hoc analysis, there was no statistical difference in the proportion of NI trials reporting on any one of the 5 components of the primary outcome when comparing industry-funded trials to publicly funded trials.

4. Conclusion

Very few NI trials reported sufficient information for assessment of NI margins. Less than half of the studies prespecified an NI design in their protocol.

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