Assessing the reporting quality of early phase dose-finding trials

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Background
Incomplete reporting of the design, conduct and analysis of early phase dose-finding trials can hinder interpretability and reproducibility, and lead to erroneous conclusions on tolerability and efficacy. This methodological review investigates the reporting quality of published trials using broadly the CONSORT 2010 checklist with added items unique to dose-finding trials.

Methods
MEDLINE (PubMed) was searched for articles published in 2011-2020. Phase I or I/II trials, with planned interim dosing decisions (de/escalate, stay at the current level or an early stop), which aim to find a recommended dosing regimen(s) for further testing, were included. Data were extracted for 476 randomly selected trials, stratified by cancer/non-cancer settings.

Results
The key items that are frequently not reported include:

	n (%) reported	
	cancer (n=238)	non-cancer (n=238)
Methods		
Planned/maximum sample size	69 (29%)	105 (44%)
with justification	35 (15%)	59 (25%)
Recruitment method	19 (8%)	51 (21%)
Oversight committees	39 (16%)	90 (38%)
roles and structure	17 (7%)	40 (17%)
Who makes dose decisions	10 (4%)	39 (16%)
Definition of analysis population:		
dose-determination	108 (45%)	111 (47%)
Safety	114 (48%)	129 (54%)
key outcomes	100 (42%)	131 (56%)
Rationale for starting dose	52 (22%)	42 (18%)
Results		
Baseline demographic and clinical characteristics by each dose level	70 (29%)	148 (62%)
Settings and locations where data were collected	86 (36%)	149 (63%)
Participant flow diagram/table	85 (36%)	144 (61%)
Losses/exclusions for each dose level	30 (13%)	85 (36%)

Only 1 (0.4%) cancer trial was randomised compared to 180 (75.6%) non-cancer trials. Notably, very few trials (6.3%) provided accessible protocols. Improvement in the reporting over time is evident in some items, including participant flow and sample size justification.

Conclusion
Important methodological features in design, conduct and analysis are frequently omitted. Overall, non-cancer trials appear to be better reported, as mainly randomised, they may have adopted CONSORT 2010 guidance. This review confirms the need for robust consensus-driven guidance for researchers and journals reporting dose-finding trials, to allow accurate assessment of their results to reduce research waste.