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Characteristics of antimicrobial studies registered in the USA through ClinicalTrials.Gov

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Abstract

Increasing rates of antimicrobial-resistant infections and the dwindling pipeline of new agents necessitate judicious, evidence-based antimicrobial prescribing. Clinical trials represent a vital resource for establishing evidence of safety and efficacy, which are crucial to guiding antimicrobial treatment decisions. The objective of this study was to comprehensively evaluate the characteristics of antimicrobial research studies registered in ClinicalTrials.gov. Primary outcome measures, funding sources, inclusion criteria and the reporting of study results were evaluated for 16 055 antimicrobial studies registered in ClinicalTrials.gov as of mid 2012. Interventional studies accounted for 93% of registered antimicrobial studies. Clinical trials of drugs (82%) and biologics (9%) were most common. Antibacterial, antiviral and antifungal studies accounted for 43%, 41% and 16% of drug trials, respectively. Among interventional drug trials, 73% featured randomised allocation to study arms and 71% included measures of safety and/or efficacy as primary endpoints. Children were eligible for enrolment in 26% of studies. Among the studies, 60% were sponsored primarily by non-profit organisations, 30% by industry and 10% by the federal government. Only 7% of studies reported results; however, 71% of these were sponsored primarily by industry. Antimicrobial studies commonly incorporated elements of high-quality trial design, including randomisation and safety/efficacy endpoints. Publication of study results and updating of ClinicalTrials.gov should be encouraged for all studies, with particular attention paid to research sponsored by non-profit organisations and governmental agencies. Leveraging the application of these data to guide the careful selection of antimicrobial agents will be essential to preserve their utility for years to come.

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1. Introduction

Antibiotic-resistant pathogens are on the rise globally and limit the effectiveness of existing antibiotics [1]. The economic burden associated with these infections has been estimated at $21–34 billion annually in the USA [2]. Although reports from the Infectious Diseases Society of America (IDSA) and the US Centers for Disease Control and Prevention (CDC) highlight the urgent need for new antimicrobial agents with novel mechanisms of action [3,4], few new anti-infective agents are currently under development. A recent study found nine new intravenous compounds active against Gram-negative bacilli that were in phase 2 or 3 trials and only two of them featured novel mechanisms of action [5]. In addition, the emergence of antiviral-resistant influenza, herpes simplex virus, varicella–zoster virus, human immunodeficiency virus and others provides a sobering reminder of the clinical and public health implications of antiviral resistance [6]. Collectively, these reports underscore the need to spur antimicrobial development and simultaneously enhance the dissemination of evidence-based antimicrobial prescribing with appropriate stewardship.

No studies to date have comprehensively evaluated the state of antimicrobial clinical research, largely owing to the difficulty in evaluating such a large and diverse number of studies. However, DiMasi et al. calculated the probability of achieving clinical approval for several classes of drugs in development from 1993–2009 and found that systemic anti-infective agents feature the highest clinical approval success rate (24%) [7]. Conversely, these drugs have the lowest likelihood of progressing beyond phase 1/2 trials (58%). This may reflect the availability of definitive endpoints in anti-infective trials, which can be used to abandon drugs with unfavourable safety and efficacy profiles.

Recognising the need to provide a central resource for identifying and tracking clinical trials conducted in the USA, Congress mandated the creation of a clinical trials registry in 1997 [8]. The ClinicalTrials.gov registry was created and released in 2000 by the National Institutes of Health (NIH) National Library of Medicine (NLM) with input from the US Food and Drug Administration (FDA) and others [9]. In 2005, the International Committee of Medical Journal Editors (ICMJE) required the registration of clinical trials in the ClinicalTrials.gov registry prior to publication [10]. More recently, in 2007 the FDA expanded the purview of ClinicalTrials.gov to include the registration of nearly all non-phase 1 drug and device trials [11]. The law also requires that study sponsors or their designees report key study design characteristics, basic results and adverse events [12].

In this study, we examined fundamental characteristics of observational and interventional studies of antimicrobial agents registered in the USA. The objective of this study was to report the extent to which antimicrobial trials have incorporated characteristics that are desirable for generating high-quality evidence, including randomisation, blinding, criteria for participation, primary endpoint selection, disclosure of study results and primary funding sources.

2. Methods

2.1. Data source

ClinicalTrials.gov is a publicly accessible, national registry of research studies that is maintained by the NIH's NLM, in collaboration with the FDA. The registry includes data on federally and privately sponsored clinical studies of a wide range of diseases and conditions. As of mid 2012, ClinicalTrials.gov contained information on 131 072 studies [13]. These trials were conducted in all 50 states and in 179 countries.

2.2. Study selection

A query of ClinicalTrials.gov was performed using a registry search function with the following keywords: 'anti-infective', 'antimicrobial', 'antibiotic', 'antibacterial', 'antiviral' and 'antifungal'. No restrictions were applied on the basis of trial registration date, study inclusion/exclusion criteria or availability of study results. Separate databases were compiled to enable comparisons between antibacterial, antiviral and antifungal agents. All data were downloaded on 11 August 2012.

2.3. Data extraction

Data elements extracted from ClinicalTrials.gov included: a unique trial identifier; study title; recruitment status; condition(s) studied; primary purpose of the study; interventional or observational status; interventional type (if appropriate); primary funding source; age group and sex eligibility criteria; trial phase (0–4); anticipated enrolment size; study design; primary endpoint; blinding status; and the availability of study results. Primary funding sources were classified as government, industry or non-profit according to the methods described by Bourgeois et al. [14].

2.4. Statistical analyses

Descriptive statistics were used to characterise the antimicrobial studies extracted from the ClinicalTrials.gov registry. Comparisons between studies of antibacterial, antiviral and antifungal agents were conducted using the χ^2 test or Fisher's exact test, as appropriate. Continuous variables were compared using the non-parametric Wilcoxon rank-sum test. A *P*-value of <0.05 was considered to be significant. All statistical analyses were performed using Stata 11.2 (StataCorp LP, College Station, TX).

3. Results

3.1. Characteristics of all antimicrobial studies

A total of 16 055 antimicrobial studies have been registered in ClinicalTrials.gov since its inception in 2000. Overall, 47% have been completed, 25% are actively recruiting participants, and the majority of the remaining studies are not yet actively recruiting subjects. The most common primary purpose of these antimicrobial studies was research on treatment (77%), followed by prevention (8%), basic science investigations (2%), diagnostic investigations (1%) and supportive care studies (1%). Interventional studies accounted for 93% of all antimicrobial studies; observational study designs accounted for the remaining 7%. Among interventional trials, drugs and biologics dominated, accounting for a combined

91% of all interventional studies. Additional interventions and study characteristics are featured in Table 1.

3.2. Interventional drug trials

Interventional drug trials of antimicrobial agents accounted for 9% (n = 12 232) of the total number of clinical research studies registered in ClinicalTrials.gov among all medical specialties. The frequency of antimicrobial drug trials according to their stated primary purpose is presented in Table 2. Safety/efficacy were the primary endpoints in 63% of trials, followed by pharmacokinetics/pharmacodynamics (9%) and bioavailability/bioequivalence trials (2%). Allocation to intervention arms via randomisation was common (73%) among interventional antimicrobial drug trials. The most frequent allocation scheme was parallel group assignment (53%), followed by single group assignment (38%), cross-over assignment (8%) and factorial assignment (2%). Trials were evenly split between early phase 0–2 (25%), phase 2–3 studies (37%) and phase 3–4 studies (38%). The median estimated sample size was 66 participants (interquartile range 30–200 participants). Overall, 26% of interventional antimicrobial drug trials included children and adults. Only 5% enrolled children exclusively.

A comparison of trial characteristics among antibacterial, antiviral and antifungal agents is presented in Table 3. Double-blinded trials were far more frequent among studies of antifungal agents compared with studies of antibacterials or antivirals ($P < 0.001$). In contrast, randomisation status, interventional group assignment, trial phase and participant inclusion criteria were similar among all antimicrobial drug studies.

3.3. Primary funding sources

Overall, the primary funding sources of antimicrobial studies in the USA are non-profit organisations (60%), industry (30%) and the federal government (10%). Among interventional drug trials, 35% were funded primarily by industry sources. This was comparable with the funding provided by governmental sources (35%). Table 4 features a comparison of the study design characteristics of interventional antimicrobial drug trials according to their primary funding source. Studies of antibacterial agents were more commonly funded by non-profit organisations (64%) compared with antiviral (52%) and antifungal (56%) agents ($P < 0.001$). Thirteen percent of studies on antiviral agents were primarily funded by governmental agencies, which was slightly higher than the proportion of antibacterial (7%) and antifungal (8%) agents ($P < 0.001$).

Trials that included children were substantially more likely to have been primarily funded by governmental agencies compared with industry sources (18% vs. 7%; $P < 0.001$). However, funding of paediatric and adult trials was evenly split among studies sponsored primarily by non-profit organisations.

3.4. Availability of study results

For all antimicrobial studies, only 7% have reported results in ClinicalTrials.gov. Among completed interventional drug trials of antimicrobial agents, 12% have made their results available. Fig. 1 shows the availability of study results for completed interventional drug

trials according to their primary funding source, trial phase, age groups eligible for enrolment and endpoint classification. The majority (71%) of trials with results available were funded primarily by industry sources. Only 3% of government and non-profit sponsored studies had reported results compared with 15% of industry sponsored studies ($P < 0.001$). There was no difference in the proportion of studies with results reported between paediatric and adult trials or among different antimicrobial types.

4. Discussion

More than 16 000 antimicrobial studies have been registered in ClinicalTrials.gov since 2000. Collectively, evaluation of antimicrobial agents accounts for nearly 1 in 10 of all registered clinical research studies. The vast majority were interventional trials of drugs and biologics. Primary endpoints frequently included markers of safety and efficacy. Nearly 75% of interventional drug trials were randomised and 26% recruited children in addition to adults. Funding for antimicrobial studies varied, with 60% of studies primarily sponsored by non-profit organisations, 30% from industry and 10% from the federal government. Across all completed interventional drug trials, only 12% have been updated with study results and/or publications and, notably, the vast majority of the studies with results available were sponsored primarily by industry sources.

Randomisation is appropriately regarded as a hallmark of a high-quality clinical trial [15]. The current study shows that nearly three-quarters of antimicrobial drug trials incorporated randomisation, more than one-quarter were double-blinded and the majority included a primary safety/efficacy endpoint. A further 28% of registered trials were double-blinded. These values are higher than have been reported among oncology trials and are comparable with cardiovascular and mental health studies [16]. The FDA requires that ‘pivotal’ trials include primary safety and efficacy endpoints, as these clinical studies ‘form the basis for FDA’s finding that a [drug or device] is safe and effective for its intended use’ [17]. On the other hand, consistent with previous reports, there were few pharmacokinetic/pharmacodynamic studies registered in ClinicalTrials.gov [14,18]. This is likely due to the fact that many safety and efficacy studies include a pharmacokinetic assessment or extrapolate from earlier studies [19]. Other possibilities, however, include a true deficiency of pharmacokinetic studies, a lack of registration of such trials or a combination of the above.

Paediatric trials are often regarded as challenging owing to scientific, ethical and practical considerations [20]. This perception stems from the physiological changes associated with growth and development, the vulnerable population status afforded to children by federal regulations, the low prevalence of many childhood diseases, and considerations of market size and profitability, among others [21]. Among all interventional trials registered in ClinicalTrials.gov, 17% included children <18 years of age from October 2007 through September 2010 [16]. In this study, 26% of interventional antimicrobial drug trials enrolled children and adults. Only 5% of studies recruited children exclusively. Although this compares favourably with drug trials in other disease states, additional work is needed to ensure that children are included in clinical trials of antimicrobials so that treatment

decisions may be based upon well controlled studies and not naïvely extrapolated from adults.

Funding for clinical research on antimicrobial agents is derived from a variety of sources, with non-profit organisations as the lead sponsor for three out of every five studies. Industry sponsors serve as the primary funding source for 30% of antimicrobial studies and governmental agencies sponsor the remaining 10%. When limited to interventional drug trials, the proportion of antimicrobial trials led by industry sources rose to 35%. Recent reports have claimed that industry has been reluctant to invest in research and development toward new antimicrobial agents owing to the size of the generic market, the short duration of many antimicrobial regimens, and the potential for the development of resistance, among other reasons [22]. Industrial sources were the primary sponsor of 36% of all interventional trials registered in ClinicalTrials.gov from 2000–2010 [16]. This indicates that industry funding of antimicrobial trials is on par with levels of support seen among studies in other disease states and conditions, including cardiology and oncology trials [16].

Although industry-led studies accounted for only 30% of all clinical research on antimicrobials registered in ClinicalTrials.gov, 71% of the studies reporting results were sponsored primarily by industry. This finding may reflect an association demonstrated by previous studies between industry funding and favourable reporting of trial results [23–25]. This may indicate that industry sponsors benefit from study completion and the reporting of trial results. In this study, we could not assess whether trial outcomes were favourable or not. Although not all trials have completed recruitment or had the opportunity to prepare data for analysis and publish a manuscript, 15% of studies led by industry have reported their results within ClinicalTrials.gov. This compares with 3% of studies funded by non-profit and governmental sources. As noted by Zarin and Tse, this may reflect strategic study design, careful study co-ordination, selective publication, or biases in study conduct and data analyses [26]. Although all of these are possible explanations, Ross et al. reported that publication patterns are similar for publicly funded and industry-sponsored studies [18]. This suggests that reporting requirements for industry-led studies may lead to more comprehensive and accurate updating of study results in ClinicalTrials.gov. Regardless, there is an urgent need to improve the timely dissemination of study results among all antimicrobial studies, especially those funded by non-profit and governmental sources. The growth of online-only, open-access, peer-reviewed journals and encouragement from the ICMJE has reduced competition for limited print space and fostered the publication of trials with negative or inconclusive outcomes [27]. These data are essential for the development of new lines of scientific inquiry and the successful translation of research into clinical practice.

This study has several limitations. Notably, ClinicalTrials.gov does not capture all clinical research studies performed in the USA, as the legal requirement for registration does not extend to phase 0–1 trials or non-interventional studies. However, ClinicalTrials.gov accounts for >80% of all studies registered in the World Health Organization’s International Clinical Trials Registry Platform [16]. Second, the accuracy, validity and completeness of the data featured in ClinicalTrials.gov are dependent upon the quality of the information entered by the sponsor or their designee. ClinicalTrials.gov does, however, employ an

automated evaluation system to alert sponsors when data fields are missing or internally inconsistent [12]. Third, the evolution of federal regulations governing the registration and reporting of trial results within ClinicalTrials.gov may complicate the interpretation of this study's results, which evaluated all antimicrobial studies registered from 2000–2012. Fourth, it was not possible to evaluate the conditions or disease states evaluated in these antimicrobial studies. Consequently, it is unknown to what extent these studies are targeting the areas of greatest unmet need in infectious diseases research. Lastly, we did not manually review the publications associated with studies featured in ClinicalTrials.gov to assess their concordance with pre-specified trial endpoints, nor could we ascertain whether the study reported positive, negative or inconclusive results.

At a time of increasing antimicrobial resistance and a paucity of new drugs in the pipeline, it is more critical than ever that antimicrobial prescribing be based upon evidence of safety and efficacy from carefully conducted clinical trials. Here we show that since 2000 more than 16 000 antimicrobial studies have been registered in ClinicalTrials.gov. More than three-quarters of these studies have been registered with treatment designated as the primary purpose. Nearly all interventional drug trials featured a safety and/or efficacy primary endpoint and many featured randomised assignment to study arms. Unfortunately, few studies have been updated to include results and publications. Of those with results available, the majority were sponsored primarily by industry. Publication of study results and updating of ClinicalTrials.gov should be encouraged for all studies, with particular attention paid to research sponsored by non-profit organisations and governmental agencies. These studies will form the basis for evidence-based treatment recommendations and professional society guidelines for decades to come. Consequently, we must strive to bridge the gap between investigators and the public in order to further clinical research and medical progress.

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References

1. Hawkey PM. The growing burden of antimicrobial resistance. J Antimicrob Chemother. 2008; 62(Suppl 1):i1–9. [PubMed: 18684701]
2. Foster, S. The economic burden of antibiotic resistance—evidence from three recent studies. 2010 Annual Conference on Antimicrobial Resistance; 1–3 February 2010; Bethesda, MD.
3. Spellberg B, Guidos R, Gilbert D, Bradley J, Boucher HW, Scheld WM, et al. The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America. Clin Infect Dis. 2008; 46:155–64. [PubMed: 18171244]
4. Interagency Task Force of Antimicrobial Resistance. [accessed 29 April 2013] 2009–2010 Progress towards implementation of: A public health action plan to combat antimicrobial resistance. http://www.cdc.gov/drugresistance/pdf/PReport-2009-2010-final-june2011.pdf

5. Boucher, H.; Gilbert, D.; Benjamin, D., et al. 10 × ‘20 progress: development of new drugs active against resistant Gram-negative bacilli. 49th Annual Meeting of the Infectious Diseases Society of America; 20–23 October 2011; Boston, MA. p. Abstract LB-27
6. Kimberlin DW, Whitley RJ. Antiviral resistance: mechanisms, clinical significance, and future implications. J Antimicrob Chemother. 1996; 37:403–21. [PubMed: 9182098]
7. DiMasi JA, Feldman L, Seckler A, Wilson A. Trends in risks associated with new drug development: success rates for investigational drugs. Clin Pharmacol Ther. 2010; 87:272–7. [PubMed: 20130567]
8. US Food and Drug Administration. [accessed 17 August 2012] Food and Drug Administration Modernization Act of 1997 (FDAMA): Public Law 105-15. http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FDAMA/FullTextofFDAMAlaw/default.htm
9. McCray AT, Ide NC. Design and implementation of a national clinical trials registry. J Am Med Inform Assoc. 2000; 7:313–23. [PubMed: 10833169]
10. International Committee of Medical Journal Editors. [accessed 13 August 2012] Uniform requirements for manuscripts submitted to biomedical journals: publishing and editorial issues related to publication in biomedical journals: obligation to register clinical trials. http://www.icmje.org/publishing_10register.html
11. US Food and Drug Administration. [accessed 13 August 2012] Food and Drug Administration Amendments Act of 2007: Public Law 110-85. http://www.gpo.gov/fdsys/pkg/PLAW-110publ85/pdf/PLAW-110publ85.pdf
12. Zarin DA, Tse T, Williams RJ, Califf RM, Ide NC. The ClinicalTrials. gov results database—update and key issues. N Engl J Med. 2011; 364:852–60. [PubMed: 21366476]
13. US National Institutes of Health. [accessed 16 August 2012] About ClinicalTrails.gov. http://clinicaltrials.gov/ct2/info/about
14. Bourgeois FT, Murthy S, Pinto C, Olson KL, Ioannidis JP, Mandl KD. Pediatric versus adult drug trials for conditions with high pediatric disease burden. Pediatrics. 2012; 130:285–92. [PubMed: 22826574]
15. Moher D. CONSORT: an evolving tool to help improve the quality of reports of randomized controlled trials. Consolidated Standards of Reporting Trials. JAMA. 1998; 279:1489–91. [PubMed: 9600488]
16. Califf RM, Zarin DA, Kramer JM, Sherman RE, Aberle LH, Tasneem A. Characteristics of clinical trials registered in ClinicalTrials. gov, 2007–2010. JAMA. 2012; 307:1838–47. [PubMed: 22550198]
17. US Food and Drug Administration Office of Device Evaluation. [accessed 17 August 2012] FDA summary of Safety and Effectiveness Data (SSED) Clinical Section Checklist. 2010. http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDRH/CDRHTransparency/UCM220929.pdf
18. Ross JS, Tse T, Zarin DA, Xu H, Zhou L, Krumholz HM. Publication of NIH funded trials registered in ClinicalTrials. gov: cross sectional analysis. BMJ. 2012; 344:d7292. [PubMed: 22214755]
19. Lee H, Yim DS, Zhou H, Peck CC. Evidence of effectiveness: how much can we extrapolate from existing studies? AAPS J. 2005; 7:E467–74. [PubMed: 16353924]
20. Steinbrook R. Testing medications in children. N Engl J Med. 2002; 347:1462–70. [PubMed: 12409558]
21. Smyth RL, Weindling AM. Research in children: ethical and scientific aspects. Lancet. 1999; 354(Suppl 2):SII21–4. [PubMed: 10507255]
22. Morel CM, Mossialos E. Stoking the antibiotic pipeline. BMJ. 2010; 340:c2115. [PubMed: 20483950]
23. Bourgeois FT, Murthy S, Mandl KD. Outcome reporting among drug trials registered in ClinicalTrials. gov. Ann Intern Med. 2010; 153:158–66. [PubMed: 20679560]
24. Bero L, Oostvogel F, Bacchetti P, Lee K. Factors associated with findings of published trials of drug–drug comparisons: why some statins appear more efficacious than others. PLoS Med. 2007; 4:e184. [PubMed: 17550302]

25. Lexchin J, Bero LA, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. BMJ. 2003; 326:1167–70. [PubMed: 12775614]

26. Zarin DA, Tse T. The effect of funding source on outcome reporting among drug trials. Ann Intern Med. 2011; 154:137–8. author reply 138. [PubMed: 21242372]

27. International Committee of Medical Journal Editors. [accessed 17 August 2012] Uniform requirements for manuscripts submitted to biomedical journals: publishing and editorial issues related to publication in biomedical journals: obligation to publish negative studies. http://www.icmje.org/publishing_1negative.html

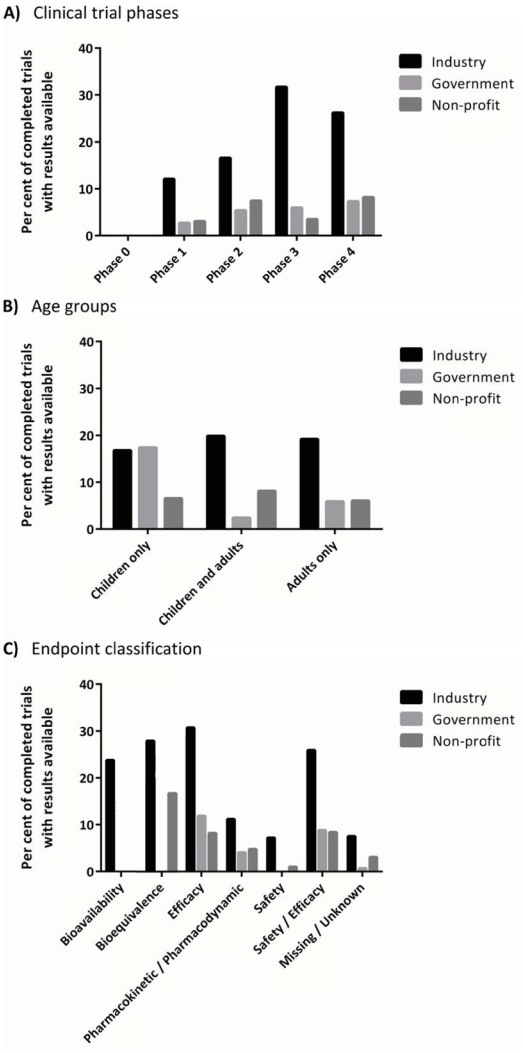

Fig. 1.

Availability of study results among completed interventional antimicrobial drug trials by (A) clinical trial phase, (B) age groups eligible for enrolment and (C) primary endpoint classification.

Table 1

Clinical trial attributes of antimicrobial studies registered in ClinicalTrials.gov

Characteristic	Category	Total (*N* = 16 055) [*n* (%)]
Overall status	Not yet recruiting	681 (4)
	Recruiting	3980 (25)
	Completed	7592 (47)
	Suspended	101 (1)
	Terminated	896 (6)
	Withdrawn	236 (1)
	Active, not recruiting	2398 (15)
	Enrolling by invitation	141 (1)
	Other	30 (<1)
Primary purpose	Treatment	12 382 (77)
	Prevention	1219 (8)
	Diagnostic	196 (1)
	Supportive care	182 (1)
	Screening	40 (<1)
	Health services research	69 (<1)
	Basic science	256 (2)
	Educational/counselling	18 (<1)
	Missing	1693 (11)
Study design	Interventional	14 936 (93)
	Observational	1089 (7)
	Expanded access	30 (<1)
Intervention [a]	Biologic	1403 (9)
	Drug	12 232 (82)
	Device	379 (3)
	Procedure	362 (2)
	Behavioural change	153 (1)
	Other	407 (3)

[a] Denominator reflects the number of interventional antimicrobial studies (*N* = 14 936).

Table 2

Primary purpose of interventional antimicrobial drug trials registered in ClinicalTrials.gov from 2000–2012

Primary purpose	*n* (%)			
	Industry (*N* = 4167)	NIH (*N* = 1039)	Non-profit [a] (*N* = 6869)	US federal [c] (*N* = 157)
Treatment	3512 (84)	937 (90)	5702 (83)	120 (76)
Prevention	183 (4)	81 (8)	651 (9)	23 (15)
Basic science	121 (3)	1 (<1)	111 (2)	3 (2)
Supportive care	15 (<1)	4 (<1)	106 (2)	0 (0)
Diagnostic	14 (<1)	5 (<1)	68 (1)	1 (1)
Health services research	6 (<1)	1 (<1)	20 (<1)	0 (0)
Screening	4 (<1)	0 (0)	12 (<1)	1 (1)
Education/counselling	2 (<1)	0 (0)	7 (<1)	2 (1)
Missing/unknown	310 (7)	10 (1)	192 (3)	7 (4)

NIH, US National Institutes of Health.

[a] Not-for-profit organisations.

[b] Other US federal agencies, excluding the NIH.

Table 3

Interventional therapeutic drug trial characteristics by antimicrobial type

Characteristic	Category	Antimicrobial type		
		Antibacterials (*N* = 5530) [a]	Antivirals (*N* = 5150) [a]	Antifungals (*N* = 2040) [a]
Allocation status	Randomised	2956 (53)	2346 (46)	929 (46)
	Non-randomised	1179 (21)	1147 (22)	502 (25)
	Unknown/missing	1395 (25)	1657 (32)	609 (30)
Blinding	Open	3618 (65)	3396 (66)	316 (15)
	Single-blind	209 (4)	69 (1)	59 (3)
	Double-blind	1202 (22)	941 (18)	1488 (73)
	Unknown/missing	501 (9)	744 (14)	177 (9)
Interventional group	Single group	1942 (35)	1661 (32)	810 (40)
	Parallel	2441 (44)	2057 (40)	813 (40)
	Cross-over	273 (5)	252 (5)	109 (5)
	Factorial	62 (1)	60 (1)	28 (1)
	Unknown/missing	812 (15)	1120 (22)	280 (14)
Endpoint classification	Bioavailability	17 (<1)	15 (<1)	8 (<1)
	Bioequivalence	114 (2)	43 (1)	21 (1)
	Efficacy	1085 (20)	874 (17)	298 (15)
	Pharmacokinetics and/or pharmacodynamics	326 (6)	469 (9)	191 (9)
	Safety	391 (7)	551 (11)	168 (8)
	Safety/efficacy	2481 (45)	2191 (43)	960 (47)
	Unknown/missing	1116 (20)	1007 (20)	394 (19)
Study phase	Phase 0, 1, 1/2	1220 (22)	1170 (23)	600 (29)
	Phase 2, 2/3	1754 (32)	1933 (38)	582 (29)
	Phase 3, 4	1972 (36)	1575 (31)	674 (33)
	Unknown/missing	584 (11)	472 (9)	184 (9)
Expected sample size [median (IQR)]		66 (32–201)	60 (30–60)	50 (25–145)
Sex	Female only	534 (10)	264 (5)	99 (5)
	Male only	147 (3)	97 (2)	104 (5)
	Both	4842 (88)	4785 (93)	1835 (90)
	Unknown/missing	7 (<1)	4 (<1)	2 (<1)
Age groups	Children only	294 (5)	176 (3)	107 (5)
	Children and adults	1158 (21)	942 (18)	479 (23)
	Adults only	4078 (74)	4032 (78)	1454 (71)
Lead funding source	Industry	1577 (29)	1801 (35)	717 (35)
	Government	406 (7)	671 (13)	161 (8)
	Non-profit [b]	3547 (64)	2678 (52)	1162 (57)

IQR, interquartile range.

[a] Data are *n* (%) unless otherwise stated.

[b] Not-for-profit organisations.

Table 4

Characteristics of interventional antimicrobial drug trials according to their primary funding source

Characteristic	Category	Industry (*N* = 4167) [b]	Non-profit [a] (*N* = 6869) [b]	Government (*N* = 1196) [b]
Allocation status	Randomised	2597 (62)	3534 (51)	405 (34)
	Non-randomised	819 (20)	1501 (22)	181 (15)
	Unknown/missing	751 (18)	1834 (27)	610 (51)
Blinding	Open	2321 (56)	4758 (69)	498 (42)
	Single-blind	152 (4)	242 (4)	11 (1)
	Double-blind	1387 (33)	1293 (19)	265 (22)
	Unknown/missing	307 (7)	576 (8)	422 (35)
Endpoint classification	Bioavailability	22 (1)	22 (0)	3 (<1)
	Bioequivalence	184 (4)	35 (1)	0 (0)
	Efficacy	391 (9)	1781 (26)	206 (17)
	Pharmacokinetics and/or pharmacodynamics	513 (12)	368 (5)	148 (12)
	Safety	594 (14)	301 (4)	170 (14)
	Safety/efficacy	1990 (48)	2865 (42)	327 (27)
	Unknown/missing	473 (11)	1497 (22)	342 (29)
Expected sample size, median (IQR)		90 (36–260)	60 (30–152)	60 (26–192)

IQR, interquartile range.

[a] Not-for-profit organisations.

[b] Data are *n* (%) unless otherwise stated.