Supplementary Online Content

Kasenda B, von Elm E, You J, et al. Prevalence, characteristics, and publication of discontinued randomized trials. *JAMA*. doi:10.1001/jama.2014.1361

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Working Definitions

Variable	Working Definitions and Explanations
Planned total sample size	Planned total sample size or target sample size as documented in the protocol (in the regression models included as continuous variable in increments of 100)
Placebo/no active intervention *versus* Active intervention	If the control arm consisted of a placebo intervention or no active intervention, the trial was labelled as "placebo/no active intervention" trial. All others were considered active control intervention.
Single centre *versus* Multicentre	If the protocol mentioned planned recruitment of participants from more than one centre, the trial was labelled as "multicentre trial". If only one centre was mentioned, the trial was classified as "single centre trial". If it remained unclear from the protocol, the trial was labelled "unclear".
Parallel *versus* Cross-over/Factorial	If in a trial participants were randomized to parallel intervention groups, it was labelled as "parallel group" trial. Trials with a randomized cross-over design or factorial design were labelled as such. If it remained unclear from the protocol, the trial was labelled "unclear".
Methodological/ logistical support (reported *versus* not-reported)	If the trial protocol clearly mentioned that the trial was supported by a clinical trial unit, a contract research organization, or had paid staff at recruiting sites to manage the trial, we labelled a trial as "reported methodological/logistical support".
Recruitment projection (reported *versus* not reported)	If the protocol mentioned that the anticipated number of eligible participants to be included in the trial was estimated using retrospective chart reviews of participating centres, reviews of routine registry data, experiences from similar prospective studies conducted at the centres, or pilot trials, we labelled the trial protocol as "reported recruitment projection".
Sponsorship (industry *versus* investigator/not-for-profit)	The purpose of this variable was to describe the party "behind the trial" in terms of resources, organization, and commercial interest. We anticipated that at least in some instances it would be difficult to retrospectively judge who was the sponsor of the study. Consequently, when extracting information we assessed RCT protocols for industry- or investigator-sponsorship using the following criteria: The protocol clearly named the sponsor, displayed a company or institution logo prominently, mentioned affiliations of protocol authors, included statements about data ownership or publication rights, or statements about full funding by industry or public funding agencies. Data abstractors made an overall judgment based on these criteria

	and classified RCTs as “definitely industry-sponsored”, “probably industry-sponsored”, “definitely investigator-sponsored”, or “probably investigator-sponsored”. Disagreements were resolved by discussion and consensus. In over 95% of cases funding and other criteria being used for sponsorship classification were consistent. In some cases, RCT protocols that did not report full industry funding were classified as industry-sponsored, because they had unclear/absent funding statements but prominently displayed a company logo, listed only protocol authors with industry-affiliation, or made claims of data ownership and mentioned restricted publication rights. We collapsed the subgroups for 'definitely' and 'probably' for both categories (industry- and investigator-sponsorship) and compared the results in a sensitivity analysis with calculations based on the individual funding variable dichotomized as ‘fully industry-funded versus all others’. The results were very similar (data presented in eTable 3).
RCT discontinuation	In principle, an RCT can be discontinued during the phase of participant recruitment or during follow-up of participants. If investigators of an included RCT indicated in correspondence with the responsible REC, in a journal publication, or in a response to our survey questions that their trial was discontinued for a specific reason, we considered this RCT as discontinued and noted the reported reason independent of the proportion of the achieved sample size. Only if RCT investigators indicated the presence of slow participant recruitment in their trial or if we could not clarify the reason for trial discontinuation did we use our pre-specified threshold of 90% of sample size achieved in order to determine “discontinuation”. RCTs that did not achieve the pre-specified threshold proportion of achieved sample size and for which we could not clarify the reason are listed in a separate row in Table 2 without further specification. We classified discontinued RCTs as discontinued due to slow/poor recruitment only if indicated by trial investigators. When we defined the 90% threshold we had looked at other studies empirically examining recruitment in RCTs. Some used different thresholds for successful/unsuccessful recruitment without providing specific justification: Pich et al. Lancet 2003, Decullier et al. BMJ 2005, and Damen et al. J Med Ethics 2012 used 100% of planned target. McDonald et al. (STEPS study) Trials 2006 used two thresholds (100% and 80%), and Chan et al. BMJ 2008 considered 90% or more of the planned target sample size as “no discrepancy”. The definition for “abandoned trial” in Easterbrook et al. Lancet 1991 remained unclear. We discussed potential thresholds for our study with several experienced trialists and clinical epidemiologists and eventually decided to set the cut-off at 90% for our primary analysis and to use a threshold of 80% in a sensitivity analysis (Kasenda et al. BMC Med Res Methodol 2012). Here are the main points of our earlier deliberations: 1) The safety margins in terms of extra sample size in order to ensure adequate power are usually small and relatively

	rare. 2) The use of overoptimistically large treatment effects in sample size calculations are probably much more frequent in RCT protocols (with the intention to show feasibility) than the use of conservatively small treatment effects. 3) Participants lost to follow-up occur independently of participant recruitment, i.e. if an RCT has recruitment problems it often still has a 10-15% rate of loss to follow-up, so the extra number of participants to cover anticipated loss to follow-up usually does not compensate for the smaller number of recruited participants. 4) If we found protocol amendments among the archived REC documents that indicated a revised smaller target sample size based on fewer than expected participants lost to follow-up or a larger than expected event rate/smaller than expected standard deviation and the RCT managed to recruit at least 90% of the new target sample size, we did not consider this RCT as discontinued. Among included RCTs that were discontinued due to poor recruitment (as indicated by trial investigators, N=101) none recruited 90% or more of the target sample size and only 3 RCTs recruited more than 80% of the target.
Full journal publication	Any peer-reviewed journal publication that was not a conference abstract or research letter.
Additional Working Definition	
Poor Recruitment	We considered “poor recruitment” only in the context of reasons for RCT discontinuation and defined it as any statement about slow or insufficient recruitment of participants made by trial investigators in correspondence with the responsible Research Ethics Committee, in a corresponding publication, or in response to our survey.

eAppendix. Standardized Survey Questionnaire

Trial status

1. WAS THE TRIAL STARTED AT ALL?

YES ☐ **NO** ☐ **UNKNOWN** ☐

- If NO, check the appropriate box (← applies only to **multicenter** studies):
  - *Whole study* was not started ☐
  - Not started only in *your center* ☐

2. IS THE TRIAL STILL RUNNING?

YES ☐ **NO** ☐ **UNKNOWN** ☐

- IF **YES** (Check all that apply):
  - Recruitment not completed yet ☐
  - Recruitment completed ☐
  - Data collection completed ☐

If the **trial is <u>still running</u>**, the **questionnaire** is **completed** for you.

If the **trial <u>is NOT running anymore</u>**, **please proceed** with this questionnaire.

3. HAS THE TRIAL BEEN DISCONTINUED PREMATURELY?

YES ☐ **NO** ☐ **UNKNOWN** ☐

- If **YES** (Check all that apply):
  - Stopped because of slow recruitment ☐
  - Stopped for harm ☐
  - Stopped for benefit ☐
  - Stopped because of evidence from other trials ☐
  - Stopped for futility ☐
  - Other reason (please specify) ☐

Specification/comments:_____

Publication status of the trial

4. HAVE THE RESULTS OF THIS TRIAL BEEN PUBLISHED?

YES ☐ **NO** ☐ **UNKNOWN** ☐

If **YES,** what was the type of the publication (CHECK ALL THAT APPLY)

- Publication in **Journal** ☐
- **Abstract** presentation at conference ☐
- **Internet Report** ☐
- **Other form** (please specify below) ☐

PLEASE GIVE **ALL REFERENCES** OF THE PUBLICATION WITH **NAME OF THE FIRST AUTHOR**, **TITLE OF THE PUBLICATION**, **NAME OF THE JOURNAL/ CONFERENCE/OTHER FORM** AND **PUBLICATION YEAR**. FOR **INTERNET PUBLICATIONS** PLEASE PROVIDE THE WEBADRESS**:**

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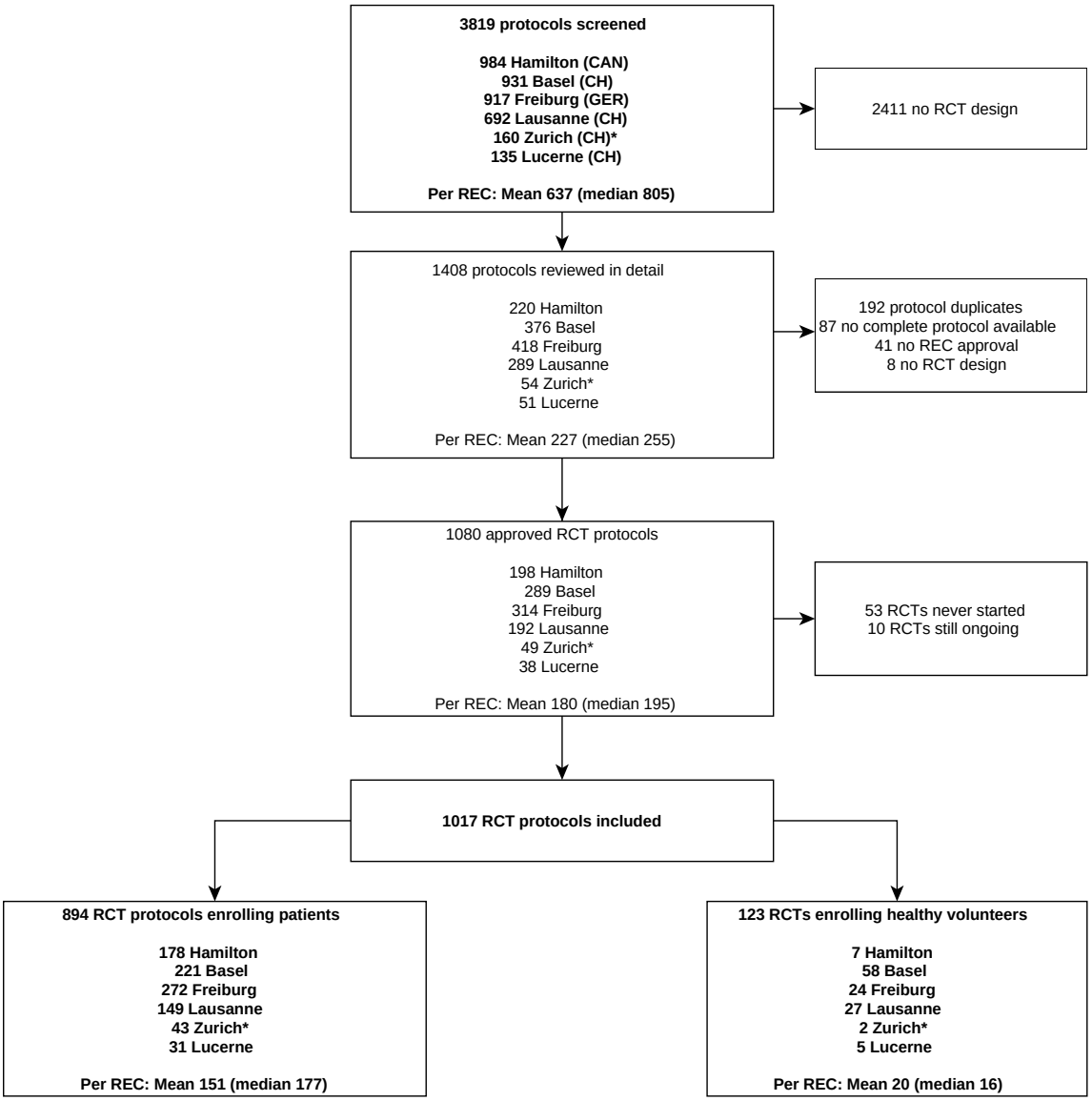
eFigure. Flow Diagram of RCT Protocols



*In Zurich, we screened only RCT protocols from the two subsidiary Research Ethics Committees responsible for paediatric and surgical RCTs.

Abbreviations: RCT, randomized controlled trial; REC, research ethics committee

eTable 2. Frequencies of Specialties

1. Medical specialties of all 894 randomized trials involving patients.

Medical Field	Frequency	Percentage
oncology	155	17.3
cardiovascular	108	12.1
infectious disease	87	9.7
endocrinology	62	6.9
neurology	61	6.8
respiratory	58	6.5
Gastro-intestinal	50	5.6
psychiatry	42	4.7
hematology	36	4
rheumatology	29	3.2
dermatology	24	2.7
anaesthesia	20	2.2
intensive care	19	2.1
ophthalmology	17	1.9
obstetrics / gynecology	17	1.9
nephrology	17	1.9
cardiothoracic surgery	13	1.5
orthopedics	12	1.3
urology	9	1
radiology	7	0.8
immunology	7	0.8
general surgery	7	0.8
rehabilitation	6	0.7
neurosurgery	6	0.7
ear-nose-throat (ENT)	5	0.6
psychotherapy	3	0.3
transplantation	3	0.3
vascular surgery	2	0.2
traumatology	2	0.2
maxillofacial surgery	2	0.2
emergency medicine	2	0.2
sports medicine	1	0.1
plastic surgery	1	0.1
neonatology	1	0.1
dentistry	1	0.1
alternative medicine	1	0.1

2. Medical specialties of all 123 randomized trials involving healthy volunteers.

Medical Field	Frequency	Percentage
unspecified	21	17.1
endocrinology	16	13
infectious disease	14	11.4
gastroenterology	14	11.4
dermatology	13	10.6
cardiovascular disease	9	7.3
sports medicine	5	4.1
neurology	5	4.1
urology	3	2.4
pulmology	3	2.4
other	3	2.4
ophtamology	3	2.4
dentistry	3	2.4
immunology	2	1.6
gynecology	2	1.6
anaesthesia	2	1.6
radiology	1	0.8
pediatrics	1	0.8
oncology	1	0.8
nephrology	1	0.8
general medicine	1	0.8

eTable 3. Sensitivity Analyses

1: Prevalence of RCT discontinuation and reported reasons for discontinuation. *Use of 80% threshold to define discontinuation for RCTs with poor recruitment and RCTs for which we could not otherwise clarify discontinuation for a specific reason.* Values are frequencies (column percentages in brackets and corresponding 95% confidence interval in squared brackets).

Completion status and reasons for discontinuation	**RCTs involving patients**				**RCTs involving healthy volunteers**				**All**	
	Industry sponsor (N=551)	Investigator sponsor (N=343)	All (N=894)	Full journal publication (N=530)	Industry sponsor (N=86)	Investigator sponsor (N=37)	All (N=123)	Full journal publication (N=37)	All (N=1017)	Full journal publication (N=567)
Completed	395 (71.7) [67.7-75.4]	191 (55.7) [50.3-61.0]	586 (65.5) [62.3-68.6]	428 (80.1) [77.1-84.0]	81 (94.2) [86.3-97.8]	28 (75.7) [58.4-87.6]	109 (89.0) [81.3-93.4]	37 (100.0) [88-100]	695 (68.3) [65.4-71.1]	465 (82.0) [78.5-85.]
Discontinued	118 (21.4) [18.1-25.1]	120 (35) [30.0-40.3]	238 (26.6) [23.8-29.7]	102 (19.2) [16.0-23.0]	1 (1.2) [0.0-7.2]	3 (8.1) [2.1-23.0]	4 (3.3) [1.0-8.6]	0 (0.0) [0.0-11.7]	242 (23.8) [21.2-26.8]	102 (18.0) [15.0-21.5]
Poor recruitment *	40 (7.3) [5.3-9.8]	57 (16.6) [12.9-21.1]	97 (10.9) [8.9-13.1]	37 (7.0) [5.0-9.6]	0 (0.0) [0.0-5.3]	1 (2.7) [0.1-15.8]	1 (0.8) [0.04-5.1]	0 (0.0) [0.0-11.7]	98 (9.6) [7.9-11.7]	37 (6.5) [4.7-9.0]
Futility †	25 (4.5) [3.0-6.7]	12 (3.5) [1.9-6.2]	37 (4.1) [3.0-5.7]	18 (3.4) [2.1-5.4]	0 (0.0) [0.0-5.3]	0 (0.0) [0.0-11.7]	0 (0.0) [0.0-3.8]	0 (0.0) [0.0-11.7]	37 (3.6) [2.7-5.0]	18 (3.2) [1.9-5.1]
Administrative reasons ‡	20 (3.6) [2.3-5.7]	16 (4.7) [2.8-7.6]	36 (4.0) [2.9-5.6]	8 (1.5) [0.7-3.1]	1 (1.2) [0.0-7.2]	2 (5.4) [0.9-19.5]	3 (2.4) [0.6-7.5]	0 (0.0) [0.0-11.7]	39 (3.8) [2.8-5.3]	8 (1.4) [0.7-2.9]
Harm	17 (3.1) [2.0-5.0]	7 (2.0) [1.0-4.3]	24 (2.7) [1.8-4.0]	12 (2.3) [1.2-4.0]	0 (0.0) [0.0-5.3]	0 (0.0) [0.0-11.7]	0 (0.0) [0.0-3.8]	0 (0.0) [0.0-11.7]	24 (2.4) [1.6-3.5]	12 (2.1) [1.2-3.8]
Unknown reason[#]	5 (0.9) [0.3-2.3]	11 (3.1) [1.6-5.6]	16 (1.8) [1.1-3.0]	14 (2.6) [1.5-4.5]	0 (0.0) [0.0-5.3]	0 (0.0) [0.0-11.7]	0 (0.0) [0.0-3.8]	0 (0.0) [0.0-11.7]	16 (1.6) [0.9-2.6]	14 (2.5) [1.4-4.2]
Benefit	2 (0.4) [0.1-1.5]	7 (2.0) [1.0-4.3]	9 (1.0) [0.5-1.9]	9 (1.7) [0.8-3.3]	0 (0.0) [0.0-5.3]	0 (0.0) [0.0-11.7]	0 (0.0) [0.0-3.8]	0 (0.0) [0.0-11.7]	9 (0.9) [0.5-1.7]	9 (1.6) [0.8-3.1]

1 continued

Completion status and reasons for discontinuation	RCTs recruiting patients				RCTs recruiting healthy volunteers				All	
	Industry sponsor (N=551)	Investigator sponsor (N=343)	All (N=894)	Full journal publication (N=530)	Industry sponsor (N=86)	Investigator sponsor (N=37)	All (N=123)	Full journal publication (N=37)	All (N=1017)	Full journal publication (N=567)
External evidence	6 (1.1) [0.5-2.5]	2 (0.6) [0.1-2.2]	8 (0.9) [0.4-1.8]	1 (0.2) [0.0-1.1]	0 (0.0) [0.0-5.3]	0 (0.0) [0.0-11.7]	0 (0.0) [0.0-3.8]	0 (0.0) [0.0-11.7]	8 (0.7) [0.4-1.6]	1 (0.2) [0.0-0.6]
Lack of funding	1 (0.2) [0.0-1.2]	4 (1.2) [0.4-3.2]	5 (0.6) [0.2-1.4]	0 (0.0) [0.0-0.9]	0 (0.0) [0.0-5.3]	0 (0.0) [0.0-11.7]	0 (0.0) [0.0-3.8]	0 (0.0) [0.0-11.7]	5 (0.5) [0.2-1.2]	0 (0.0) [0.0-0.4]
Other	2 (0.4) [0.1-1.5]	4 (1.2) [0.4-3.2]	6 (0.7) [0.3-1.5]	3 (0.6) [0.1-1.8]	0 (0.0) [0.0-5.3]	0 (0.0) [0.0-11.7]	0 (0.0) [0.0-3.8]	0 (0.0) [0.0-11.7]	6 (0.6) [0.2-1.3]	3 (0.5) [0.1-1.7]
Unclear	38 (6.9) [5.0-9.4]	32 (9.3) [6.6-13.0]	70 (7.8) [6.2-9.8]	0 (0.0) [0.0-0.9]	4 (4.7) [1.5-12.1]	6 (16.2) [6.8-32.7]	10 (8.1) [4.2-14.8]	0 (0.0) [0.0-11.7]	80 (7.7) [6.3-9.7]	0 (0.0) [0.0-0.4]

* Some trials had an additional reason for discontinuation: benefit (N=1), futility (N=2), and other reasons (N=3).

† Includes randomized trials with adaptive designs that have been stopped after the 1st (N=5) or 2nd stage (N=1).

‡ Includes strategic decisions from companies, consequence of new requirements from regulatory bodies, and change of workplace of principal investigators.

Reason for not achieving 80% of target sample size remained unclear

2: Factors associated with discontinuation of RCTs due to poor recruitment in RCTs involving patients. *Only RCTs that achieved less than 80% of the planned sample size were considered discontinued due to poor recruitment.*

Characteristics	RCTs discontinued for poor recruitment N=87	Completed RCTs N=536	Univariable			Multivariable		
			OR	95% CI	p-value	OR	95% CI	p-value
Planned total sample size (IQR)	180 (80-320)*	360 (150-800)*	0.95†	0.91 -0.99	0.012	0.96†	0.92 – 1.00	0.046
Control (placebo/no-active intervention *vs* active intervention)	52 (59.8)	328 (61.2)	0.91	0.59 - 1.41	0.671	0.85	0.52 - 1.38	0.510
Single centre status (*vs* multi-centre)	19 (21.8)	57 (10.6)	2.14	1.27 - 3.60	0.004	0.70	0.34 - 1.46	0.347
Design (cross-over *vs* parallel)	8 (9.2)	21 (3.9)	1.88	0.82 - 4.22	0.139	2.17	0.82 - 5.71	0.117
Methodological/logistical support (reported *vs* not reported)	26 (29.9)	246 (45.9)	0.45	0.28 - 0.73	0.001	0.65	0.38 - 1.12	0.119
Recruitment projection (reported *vs* not reported)	12 (13.8)	40 (7.5)	2.10	1.10 - 3.96	0.026	1.23	0.58 - 2.60	0.588
Sponsor (industry *vs* investigator)	34 (39.1)	371 (69.2)	0.29	0.18 -0.46	<0.001	0.30	0.17 - 0.51	<0.001

RCTs discontinued for reasons other than poor recruitment (N=141), RCTs with unclear completion status (N=70), cluster RCTs (N=9), and pilot RCTs (N=51) were excluded. Logistic regression was based on complete cases including 618 RCTs; in 5 RCTs information about target sample size was missing (*). All listed characteristics were included in the model as fixed effects and research ethics committees as random intercept.

IQR, interquartile range; OR, odds ratio; RCT, randomized controlled trial; CI, confidence interval.

† In increments of 100

3: Factors associated with discontinuation of RCTs due to poor recruitment in RCTs involving patients. *Logistic regression was based on all cases (N=616). Five missing target sample size values were imputed using multiple imputations.*

Characteristics	RCTs discontinued for poor recruitment N=90	Completed RCTs N=526	Univariable			Multivariable		
			OR	95% CI	p-value	OR	95% CI	p-value
Planned total sample size (IQR)	180 (80-320)	368 (154-800)	0.95*	0.91 – 0.99	0.012	0.96*	0.92 – 1.00	0.059
Control (placebo/no-active intervention *vs* active intervention)	53 (58.9)	321 (61.1)	0.89	0.56 - 1.41	0.628	0.86	0.53 – 1.39	0.531
Single centre status (*vs* multi-centre)	19 (21.1)	53 (10.1)	2.41	1.35 – 4.32	0.003	0.76	0.37 – 1.57	0.462
Design (cross-over *vs* parallel)	8 (8.9)	21 (4.0)	2.37	1.01 – 5.53	0.046	1.64	0.62 – 4.34	0.316
Methodological/logistical support (reported *vs* not reported)	27 (30.0)	245 (46.7)	0.50	0.31 - 0.81	0.005	0.63	0.37 – 1.07	0.086
Recruitment projection (reported *vs* not reported)	12 (13.3)	40 (7.6)	1.71	0.84 - 3.47	0.138	1.10	0.51 – 2.27	0.842
Sponsor (industry *vs* investigator)	34 (37.8)	371 (70.5)	0.25	0.16 -0.40	<0.001	0.27	0.16 – 0.46	<0.001

RCTs discontinued for reasons other than poor recruitment (N=148), RCTs with unclear completion status (N=70), cluster RCT (N=9), and pilot RCTs (N=51) were excluded. All listed characteristics were included in the model as fixed effects and research ethics committees as random intercept.

IQR, interquartile range; OR, odds ratio; RCT, randomized controlled trial; CI, confidence interval.

* In increments of 100

4: Factors associated with discontinuation of RCTs due to poor recruitment in RCTs only recruiting patients. *Country was included as a categorical variable. All listed variables were included as fixed effects in the logistic regression model.*

Characteristics	**Univariable**			**Multivariable ***		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Centre						
Switzerland	Reference	-	-	-	-	-
Germany	1.24	0.70 - 2.20	0.461	0.75	0.43 -1.31	0.323
Canada	0.92	0.54 - 1.56	0.747	0.96	0.51 - 1.81	0.889
Planned total sample size	0.94†	0.90 - 0.99	0.010	0.96†	0.92 – 1.00	0.037
Control (placebo/no-active intervention *vs* active intervention)	0.91	0.58 - 1.43	0.686	0.81	0.50 - 1.31	0.395
Single centre status (*vs* multi-centre)	2.38	1.33 – 4.26	0.003	0.66	0.32 - 1.38	0.268
Design (cross-over *vs* parallel)	2.34	1.00 – 5.46	0.049	1.96	0.74 - 5.23	0.178
Methodological/logistical support (reported *vs* not reported)	0.49	0.30 – 0.79	0.004	0.62	0.36 - 1.06	0.078
Recruitment projection (reported *vs* not reported)	1.87	0.94 – 3.72	0.076	1.01	0.46 - 2.19	0.991
Sponsor (industry *vs* investigator)	0.23	0.16 – 0.40	< 0.001	0.25	0.15 - 0.42	<0.001

RCTs discontinued for reasons other than poor recruitment (N=148), RCTs with unclear completion status (N=70), cluster RCT (N=9), and pilot RCTs (N=51) were excluded. Logistic regression was based on complete cases including 611 RCTs; in 5 RCTs information about target sample size was missing.

OR, odds ratio; RCT, randomized controlled trial; CI, confidence interval.

† In increments of 100

5: Factors associated with discontinuation of RCTs due to poor recruitment in RCTs only recruiting patients. *Discontinued RCTs with unknown reason for not achieving 90% of target sample size were considered as being discontinued due to poor recruitment.*

Characteristics	Univariable			Multivariable		
	OR	95% CI	p-value	OR	95% CI	p-value
Planned total sample size	0.95†	0.91 - 0.99	0.012	0.96†	0.92 – 1.00	0.045
Control (placebo/no-active intervention *vs* active intervention)	0.91	0.58 - 1.44	0.691	0.85	0.52 - 1.38	0.518
Single centre status (*vs* multi-centre)	2.01	1.14 - 3.55	0.016	0.63	0.30 - 1.28	0.201
Design (cross-over *vs* parallel)	2.43	1.04 - 5.68	0.040	2.41	0.92 - 6.27	0.073
Methodological/logistical support (reported *vs* not reported)	0.52	0.32 - 0.84	0.008	0.67	0.39 - 1.14	0.142
Recruitment projection (reported *vs* not reported)	1.80	0.91 -3.56	0.093	1.16	0.55 - 2.43	0.699
Sponsor (industry *vs* investigator)	0.30	0.19 - 0.48	<0.001	0.30	0.18 - 0.51	<0.001

RCTs discontinued for reasons other than poor recruitment (N=125), RCTs with unclear completion status (N=70), cluster RCTs (N=2), and pilot RCTs (N=54).

Logistic regression was based on all complete cases (N=637, target sample size missing in 6 cases) with all listed characteristics as fixed effects and research ethics committees as random intercept.

OR, odds ratio; RCT, randomized controlled trial; CI, confidence interval.

† In increments of 100

6: Factors associated with discontinuation of RCTs due to poor recruitment in RCTs only recruiting patients. *All listed variables were included as fixed effects in the logistic regression model.*

Characteristics	**Univariable**			**Multivariable ***		
	OR	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Centre						
Basel	Reference	-	-	-	-	-
Freiburg	0.94	0.51 - 1.72	0.830	0.64	0.33 - 1.22	0.172
Lausanne	0.97	0.48 - 1.98	0.938	0.65	0.31 - 1.39	0.270
Lucerne	1.34	0.42 - 4.30	0.621	1.58	0.46 - 5.52	0.469
Zurich	1.01	0.32 - 3.16	0.991	0.60	0.18 - 2.04	0.417
Hamilton	1.26	0.66 - 2.40	0.486	0.80	0.39 - 1.67	0.558
Planned total sample size	0.94†	0.90 - 0.99	0.010	0.95†	0.91 – 1.00	0.029
Control (placebo/no-active intervention *vs* active intervention)	0.91	0.58 - 1.43	0.686	0.82	0.50 – 1.34	0.430
Single centre status (*vs* multi-centre)	2.38	1.33 – 4.26	0.003	0.66	0.32 – 1.37	0.265
Design (cross-over *vs* parallel)	2.34	1.00 – 5.46	0.049	1.84	0.69 – 4.88	0.224
Methodological/logistical support (reported *vs* not reported)	0.49	0.30 – 0.79	0.004	0.59	0.34 – 1.00	0.053
Recruitment projection (reported *vs* not reported)	1.87	0.94 – 3.72	0.076	1.03	0.48 – 2.25	0.950
Sponsor (industry *vs* investigator)	0.25	0.16 – 0.40	< 0.001	0.24	0.14 – 0.41	<0.001

RCTs discontinued for reasons other than poor recruitment (N=148), RCTs with unclear completion status (N=70), cluster RCT (N=9), and pilot RCTs (N=51) were excluded. Logistic regression was based on complete cases including 611 RCTs; in 5 RCTs information about target sample size was missing.

OR, odds ratio; RCT, randomized controlled trial; CI, confidence interval.

† In increments of 100

7: Factors associated with discontinuation of RCTs due to poor recruitment in RCTs only recruiting patients. *The sponsor variable from the primary analysis was replaced by 'fully industry funded versus all others.*'

Characteristics	Univariable			Multivariable		
	OR	95% CI	p-value	OR	95% CI	p-value
Planned total sample size	0.94†	0.90 - 0.99	0.011	0.96†	0.92 – 1.00	0.049
Control (placebo/no-active intervention *vs* active intervention)	0.89	0.56 - 1.41	0.628	0.84	0.52 - 1.36	0.476
Single centre status (*vs* multi-centre)	2.41	1.35 – 4.32	0.003	0.72	0.35 - 1.49	0.375
Design (cross-over *vs* parallel)	2.37	1.01 – 5.53	0.046	1.88	0.71 – 5.00	0.203
Methodological/logistical support (reported *vs* not reported)	0.50	0.31 - 0.81	0.005	0.62	0.36 - 1.05	0.077
Recruitment projection (reported *vs* not reported)	1.71	0.84 - 3.47	0.138	1.10	0.52 - 2.33	0.797
Funding (fully industry *vs* all others)	0.24	0.15 - 0.39	<0.001	0.25	0.15 - 0.42	<0.001

RCTs discontinued for reasons other than poor recruitment (N=148), RCTs with unclear completion status (N=70), cluster RCT (N=9), and pilot RCTs (N=51) were excluded. Logistic regression was based on complete cases including 611 RCTs; in 5 RCTs information about target sample size was missing. All listed characteristics were included as fixed effects and research ethics committees as random intercept.

OR, odds ratio; RCT, randomized controlled trial.

† In increments of 100

8: Factors associated with non-publication of RCTs. *Logistic regression was based on all cases (N = 1017).*

Characteristics	Univariable			Multivariable		
	OR	95% CI	p-value	OR	95% CI	p-value
Planned total sample size	0.92*	0.90 - 0.95	<0.001	0.95*	0.93 - 0.97	<0.001
Multi centre status (*vs* single centre)	0.33	0.25 - 0.44	<0.001	0.49	0.33 - 0.72	<0.001
Industry sponsor (*vs* investigator)	0.94	0.73 - 1.22	0.649	1.50	1.10 - 2.04	0.010
Discontinued RCT (*vs* completed RCT)	2.48	1.84 - 3.36	<0.001	2.81	2.03 – 3.88	<0.001
RCT with patients (*vs* healthy volunteers)	0.27	0.17 - 0.41	<0.001	0.43	0.26 - 0.73	0.002

Logistic regression was based on all cases (N=1017); missing values were imputed using multiple imputations. All listed characteristics were included in the model as fixed effects and research ethics committees as random intercept

CI, confidence interval; OR, odds ratio; RCT, randomized controlled trial.

* In increments of 100