Supplemental Material to

Metoclopramide to prevent pneumonia in patients with stroke and a nasogastric tube. Data from the PRECIOUS trial.

Wouter M Sluis,[1] Jeroen C de Jonge,[1] Hendrik Reinink,[1] Lisa J Woodhouse,[2] Willeke F Westendorp,[3] Philip M Bath,[2] Diederik van de Beek,[3] H Bart van der Worp,[1] for the PRECIOUS investigators

Table of contents

Supplementary Table 1. Primary and secondary outcomes of patients with or without a nasogastric tube inserted the first day after randomization.

Outcome*	**normal food**	**nasogastric tube**	**p-value**
	n= 1047	n= 329	
Pneumonia			
Diagnosed by treating physician	119 (11.4)	126 (38.3)	**p < 0.001**
Adjudicated by adjudication panel	28 (2.7)	51 (15.5)	**p < 0.001**
All infections			
Diagnosed by treating physician	213 (20.3)	151 (45.9)	**p < 0.001**
Adjudicated by adjudication panel	65 (6.2)	63 (19.1)	**p < 0 .001**
Urinary tract infections			
Diagnosed by treating physician	76 (7.3)	20 (6.10	p = 0.543
Adjudicated by adjudication panel	29 (2.8)	9 (2.7)	p = 1.000
Death	168 (16.0)	136 (41.3)	**p < 0.001**
Death or dependency	697 (66.6)	304 (92.4)	**p < 0.001**

mRS at 90 days (median: IQR)	3.0 (2.0 – 4.0)	4.0 (3.0-5.0)	**p < 0.001**

Abbreviations: mRS = modified Rankin Scale, IQR = interquartile range
* all numbers are n (%) unless stated otherwise

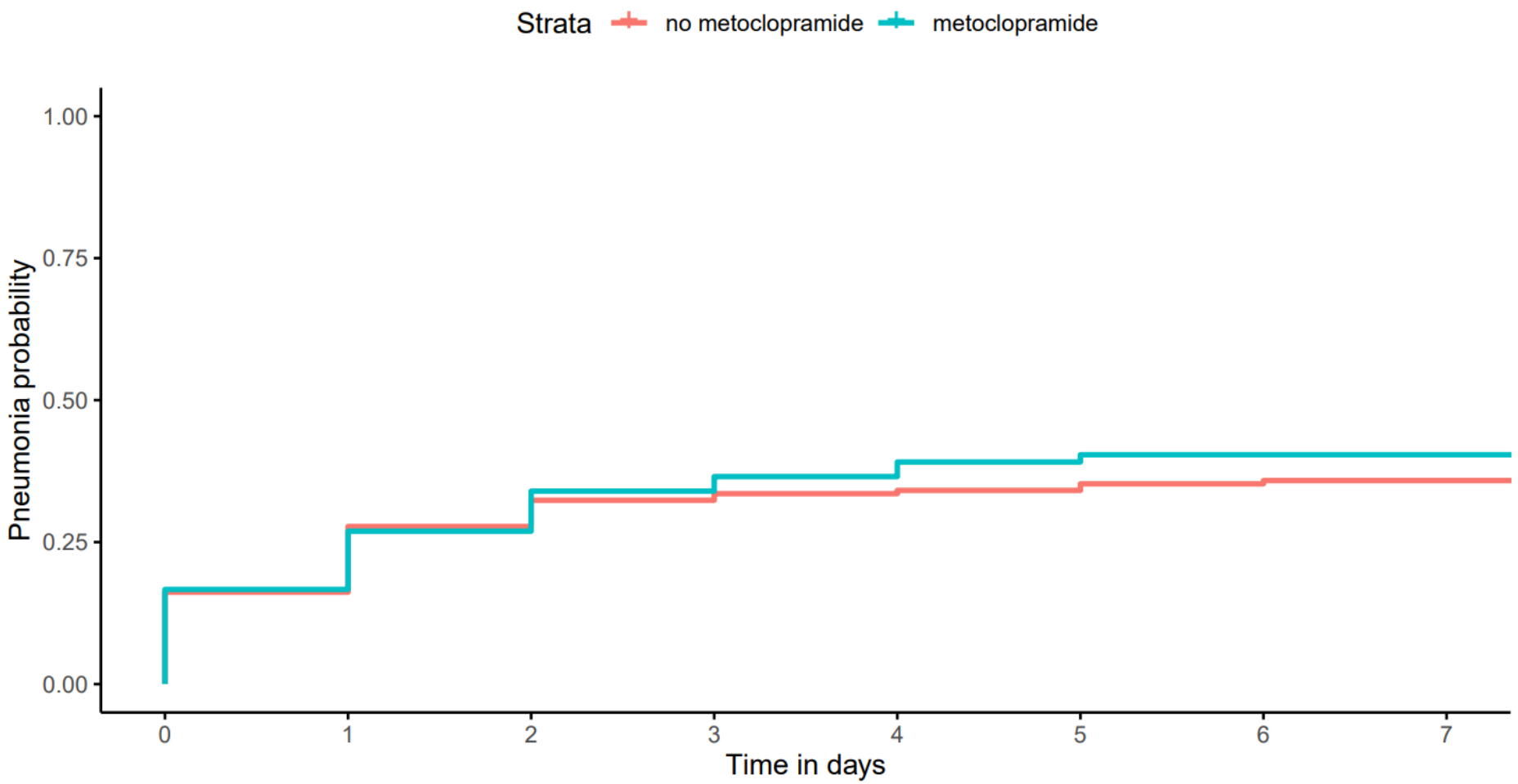
Supplementary Table 2. Outcome of cox-regression analysis for cumulative pneumonia incidence in patients with a nasogastric tube allocated to pneumonia or those who were not

	aHR (95% CI)
Pneumonia	
Diagnosed by treating physician	1.17 (0.77-1.78) †
Adjudicated by infection panel	0.99 (0.54-1.82) †

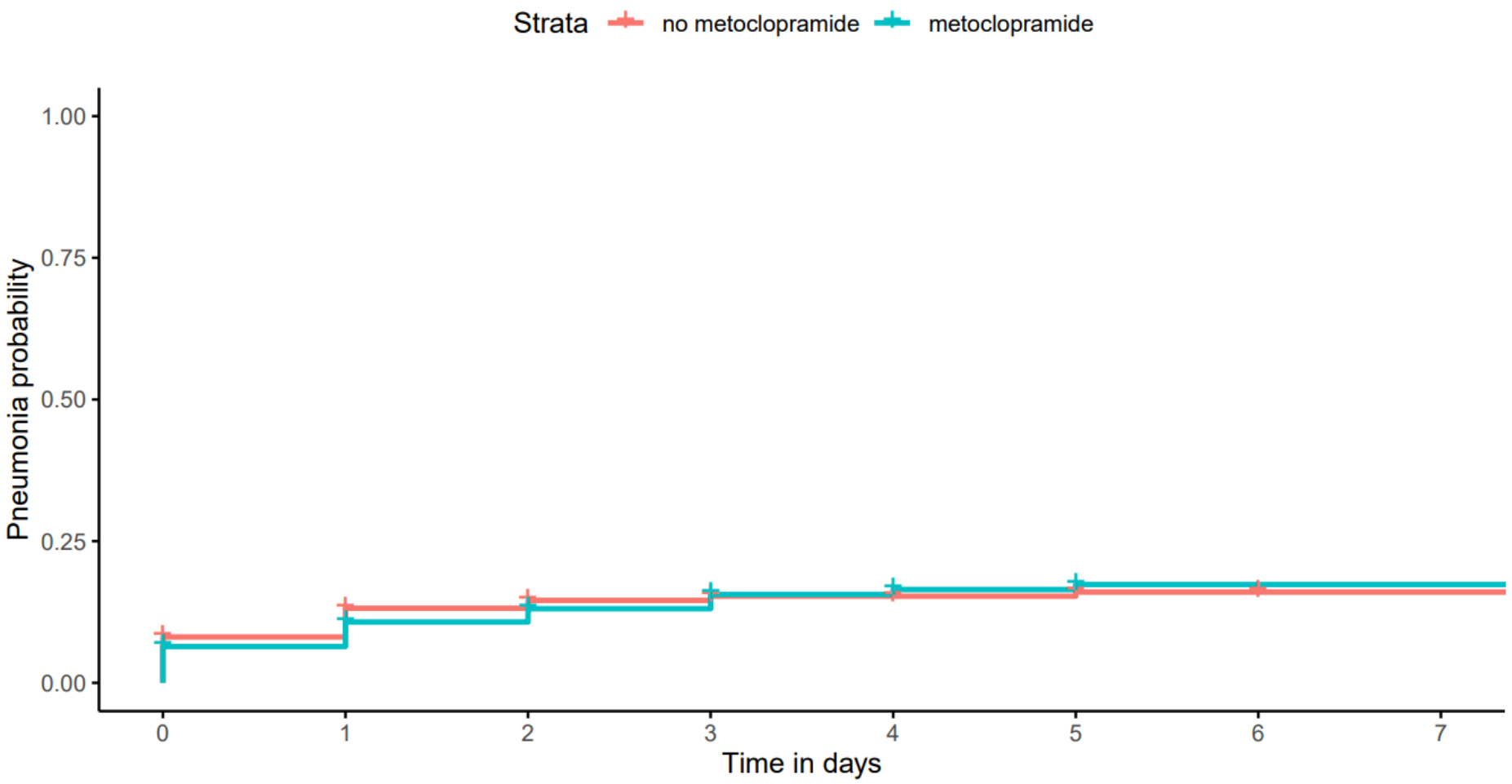
Abbreviations: HR = adjusted Hazard Ratio, CI = confidence interval

† adjusted for age, sex, stroke severity, pre-stroke mRS, chronic obstructive pulmonary disease and allocation to ceftriaxone

Supplementary Figure 1. Kaplan-Meier curve showing cumulative pneumonia incidence (as diagnosed by the treating physician) for patients with a nasogastric tube randomized to treatment with metoclopramide or no metoclopramide.



Supplementary Figure 2. Kaplan-Meier curve showing cumulative pneumonia incidence (as diagnosed by the adjudication panel) for patients with a nasogastric tube randomized to treatment with metoclopramide or no metoclopramide.



Supplementary Table 3. Primary and secondary outcomes in patients with a nasogastric tube within 24 hours after randomization

Outcome*	**no metoclopramide**	**metoclopramide**	**aOR**
	n= 131	n= 114	
Pneumonia			
Diagnosed by treating physician	42 (32.1)	39 (34.2)	1.24 (0.67 – 2.28)†
Adjudicated by infection panel	18 (13.7)	17 (14.9)	1.27 (0.59 – 2.74)†
All infections			
Diagnosed by treating physician	54 (41.2)	46 (40.4)	1.09 (0.61 – 1.95)†
Adjudicated by infection panel	24 (18.3)	20 (17.5)	1.03 (0.51 – 2.07)†
Urinary tract infections			
Diagnosed by treating physician	9 (6.9)	4 (3.5)	0.63 (0.16 – 2.42)†
Adjudicated by infection panel	6 (4.6)	1 (0.9)	0.22 (0.02 – 2.10)†
Death	56 (42.7)	65 (57.0)	1.00 (0.57– 1.75) ‡
Death or dependency	119 (90.8)	109 (95.6)	2.56 (0.79 – 8.33) ‡
mRS (median (IQR))	4.0 (3.0 - 5.0)	4.0 (4.0 – 5.0)	1.19 (0.74 – 1.91) ‡

Abbreviations: aOR = adjusted odds ratio, mRS = modified Rankin scale, IQR = interquartile range,
* all numbers are n (%) unless stated otherwise

† adjusted for age, sex, stroke severity, pre-stroke mRS, chronic obstructive pulmonary disease and allocation to ceftriaxone

‡ adjusted for age, stroke severity, pre-stroke mRS and history of diabetes

PRECIOUS investigators

Bart van der Worp, Jeroen de Jonge, Wouter Sluis, Rik Reinink, Berber Zweedijk, University Medical Center Utrecht, Utrecht, the Netherlands. Diederik van de Beek, Willeke Westendorp, Amsterdam UMC, Amsterdam, the Netherlands; Henk Kerkhoff, Elles Zock, Corry Deuling, Albert Schweitzer Ziekenhuis, the Netherlands; Sebastiaan de Bruijn, Yvonne Drabbe-Coops, Amy Nijst, Haga ziekenhuis, the Hague, the Netherlands; Marieke Wermer, Ghislaine Holswilder, LUMC, Leiden, the Netherlands; Korne Jellema, Peggy Sorensen, Haaglanden Medical Center, the Hague, the Netherlands; Vincent Kwa, Sarah Godefrooij, OLVG, Amsterdam, the Netherlands; Ben Jansen, Esther Santegoets, St Elisabeth Ziekenhuis, Tilburg, the Netherlands; Tobien Schreuder, Tiny Sporken, Zuyderland Medical Center, Heerlen, the Netherlands; Sanne Zinkstok, Kitty Harrison, Tergooi Medical Center, Hilversum, the Netherlands; Walid Moudrous, Chantal van der Spoel, Arienne Verwijs-Bode, Maasstad ziekenhuis, Rotterdam, the Netherlands; Malcolm Macleod, Allan MacRaild, Royal Infirmary of Edinburgh, Edinburgh, UK; Ruth Davies, Jessica Teasdale, Arrowe Park Hospital, Wirral, UK; Anand Nair, Venetia Johnson, Calderdale Royal Hospital, Calderdale, UK; Dipankar Dutta, Matthew Robinson, Jill Greig, Gloucestershire Royal Hospital, Gloucester, UK; Rohan Pathansali, Deborah Ward, Jon Glass, Jonnie Aeron-Thomas, Myriam Aissa, Fong Kum Chan, Staci Conway, Beatrix Sari, Maria Tibaja, King's College Hospital, London, UK; Martin Cooper, Inez Wynter, Sherwood Forest Hospital, Sutton in Ashfield, UK; Kailash Krishnan, Camille Hutchinson, Ben Jackson, Nottingham University Hospitals, Nottingham, UK; Khalid Rashed. Sarah Board, Yeovil District Hospital, Yeovil, UK; Louise Shaw, Suzanne Lucas, Joanne Avis, Telma Costa, Lauren Pearce, Royal United Hospital, Bath, UK; Alastair Wilson, Johann Selvarajah, Angela Welch, Shirley Mitchell, Queen Elisabeth University Hospital, Glasgow, UK; Jessica Redgrave, Emma Richards, Jo Howe, Royal Hallamshire Hospital, Sheffield, UK; Mary Joan Macleod, Janice Irvine, Vicky Taylor, Aberdeen Royal Infirmary, Aberdeen, UK; Philip Clatworthy, Kerry Smith, North Bristol NHS Trust, Bristol, UK; Vasileois Papavasileiou, Emelda Veraque, Dean Waugh, Leeds Teaching Hospitals NHS Trust, Leeds, UK; Vera Cvoro, Mandy Couser, Amanda McGrego, Victoria Hospital, Kirkcaldy, UK; Brian Clarke, Ghatala Rita, Cai Hua Sim, Sarah Stratton, St. George Hospital, London, UK; Omid Halse , Peter Wilding, Sheila Mashate, Vaishali Dave, Imperial College, London, UK; Usman Ghani, Faith Omoregie, Yates Kimberley, University Hospital Coventry and Warwickshire, Coventry, UK; Janika Korv, Tartu University Hospital, Tarty, Estonia; Katrin Antsov, Parnu Hospital, Parnu, Estonia; Katrin Gross-Paju, West Talinn Hospital, Tallinn, Estonia; Inga Kalju, Maarja Kaarlop, East Tallinn Hospital, Tallinn, Estonia; Gotz Thomalla, Hannes Appelbohm, Christoph Brosinski, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; Gerhard Hamann, Michaela Vogel, Bezirkskrankenhaus Günzburg, Günzburg, Germany; Michael Rosenkranz, Stefan Boskamp, Albertinen-Krankenhaus Hamburg, Hamburg, Germany; Christoph Gumbinger, Peter Ringleb, Elisabeth Beyrle, Universitätsklinikum Heidelberg, Heidelberg, Germany; Georg Royl, Susanne Ribau, Universitätsklinikum Schleswig-Holstein, Lübeck, Germany; Sven Poli, Julia Zeller, Sonja Ruschitzka, Universitätsklinikum Tübingen, Tübingen, Germany; Susanne Müller, Andrea Schirmer, Universitätsklinikum Ulm, Ulm, Germany; George Ntaios, Efstathia Karagkiozi, Larissa University Hospital, Larissa, Greece; Sophie Vassilopoulou, Aeginition Hospital, Athens, Greece; Haralampos Milionis, Angelos Liontos, Ioannina University Hospital, Ioannina, Greece;

Athanasios Protogerou, Stamatia Samara, Laiko Hospital, Athens, Greece; Efsthathios Manios, Efthalia Mitsikosta, Alexandra Hospital, Athens, Greece; Laszlo Csiba, Krisztina Buzás-Petrócz, Csilla Vér, University of Debrecen, Debrecen, Hungary; Dániel Bereczki, Andrea Kovacs, Semmelweis University, Budapest, Hungary; Gábor Jakab, Uzsoki Hospital, Budapest, Hungary; Ferenc Nagy, Lõrinczy Ritta, Puskásné Emmer Mária, Jávorszky Ödön Hospital, Vác, Hungary; András Folyovich, Nadim Al-Muhanna, Szent János Hospital, Budapest, Hungary; László Szapáry, Eszter Jozifek, University of Pecs, Pecs, Hungary; Alfonso Ciccone, Giorgio Silvestrelli, Paola Danesi, Marco Russo, ASST di Mantova, Mantova, Italy; Nicola Gilberti, Spedali Civili, Brescia, Italy; Enrico Righetti, Ospedale Castiglione del Lago, Castiglione del Lago, Italy; Stefano Ricci, Maria Elena Mattace, Silvia Cenciarelli, Ospedale di Città di Castello, Città di Castello, Italy; Stefano Ricci, Ospedale Gubbio – Gualdo Tadino, Branca, Italy; Pietro Bassi, Ospedale San Giuseppe, Milano, Italy; Simona Marcheselli, IRCCS Istituto Clinico Humanitas, Rozzano, Italy; Alessia Giossi, ASST Cremona, Cremona, Italy; Paolo Candelaresi, Giovanna Servillo, Ospedale Antonio Cardarelli, Napoli, Italy; Eivind Berge, Anne Hege Aamodt, Oslo University Hospital, Oslo, Norway; Anne Gro Holtan, Notodden Sykehus, Notodden, Norway; Sameer Maini, Alesund Hospital, Alesund, Norway; Iwona Kurkowska, Michal Karlinski, Institute of Psychiatry and Neurology, Warsaw, Poland; Waldemar Fryze, Malgorzata Krzyzanowska, University of Gdansk, Gdansk, Poland; Waldemar Brola, Hospital Sw. Lukasza, Konskie, Poland; Piotr Sobolewski, Szpital Specjalistyczny Ducha Swietego, Sandomierz, Poland; Marta Bilik, Samodzielny Publiczny Specjalistyczny Szpital Zachodni im. św. Jana Pawła II, Grodzisk Mazowiecki, Poland.

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	n.a.
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n.a.
Sample size	7a	How sample size was determined	n.a.
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n.a.

Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	Protocol
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Protocol
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Protocol
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Protocol
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	7
	11b	If relevant, description of the similarity of interventions	n.a.
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	7-8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	n.a.
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	9 + figure 1
	13b	For each group, losses and exclusions after randomisation, together with reasons	9 + figure 1
Recruitment	14a	Dates defining the periods of recruitment and follow-up	9
	14b	Why the trial ended or was stopped	N.a.
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 1

Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	9
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	9+10
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	9
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	n.a.
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n.a.
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	11+12
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	12
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	11+12
Other information			
Registration	23	Registration number and name of trial registry	6
Protocol	24	Where the full trial protocol can be accessed, if available	Published, see reference 12
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	14+15

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.