Supplement G. DexFEM CONSORT checklists for Bayesian adaptive trial: ABSTRACT and PAPER

Page 1. **Abstract.** Adaptive designs CONSORT Extension (ACE) checklist of information to include when reporting a randomised trial that used an adaptive design in a journal or conference abstract

Page 2. **Paper.** Adaptive designs CONSORT Extension (ACE) checklist of information to include when reporting a randomised trial that used an adaptive design

Abstract. Adaptive designs CONSORT Extension (ACE) checklist of information to include when reporting a randomised trial that used an adaptive design in a journal or conference abstract

Item	Description	Reported on: **page**: line
Title	Identification of study as randomised	**1**: 1
Authors	Contact details for the corresponding author	**1**: 20- 25
Trial design [a]	Description of the trial design (for example, parallel, cluster, non-inferiority); include the word "adaptive" in the content or at least as a keyword	**2**: 8-10
Methods		
Participants	Eligibility criteria for participants and the settings where the data were collected	**2**: 10-12
Interventions	Interventions intended for each group	**2**: 13-15
Objective	Specific objective or hypothesis	**2**: 4-6
Outcome [b]	Clearly defined primary outcome for this report	**2**: 16-17
Randomisation	How participants were allocated to interventions	**2**: 8
Blinding (masking)	Whether or not participants, care givers, and those assessing the outcomes were blinded to group assignment	**2**: 15-16
Results		
Numbers randomised	Number of participants randomised to each group	**2**: 21-22
Recruitment	Trial status	**2**: 20
Adaptation decisions made [c]	Specify what trial adaptation decisions were made in light of the pre-planned decision-making criteria and observed accrued data	-
Numbers analysed	Number of participants analysed in each group	**2**: 21
Outcome	For the primary outcome, a result for each group and the estimated effect size and its precision	**2**: 22-24
Harms	Important adverse events or side effects	**2**: 24- **3**: 2
Conclusions	General interpretation of the results	**3**: 4 -5
Trial registration	Registration number and name of trial register	**2**: 18
Funding	Source of funding	**3**: 7

[a] Modified item that requires reference to both CONSORT extension for abstracts (Hopewell et al.2008) and ACE;
[b] Item wording remains unchanged in reference to CONSORT extension for abstracts (Hopewell et al.2008), but we expanded the ACE explanatory text to clarify additional considerations for certain adaptive designs;
[c] New item that should only be applied in reference to ACE;
All unchanged items require reference to the CONSORT extension for abstracts (Hopewell et al. 2008).

Citation:
Dimairo M, Pallmann P, Wason J, Todd S, Jaki T, Julious SA, Mander AP, Weir CJ, Koenig F, Walton MK, Nicholl JP, Coates E, Biggs K, Hamasaki T, Proschan MA, Scott JA, Ando Y, Hind D, Altman DG; ACE Consensus Group. The Adaptive designs CONSORT Extension (ACE) statement: a checklist with explanation and elaboration guideline for reporting randomised trials that use an adaptive design. BMJ. 2020 Jun 17;369:m115. PMID: 32554564; PMCID: PMC7298567.

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Paper. Adaptive designs CONSORT Extension (ACE) checklist of information to include when reporting a randomised trial that used an adaptive design

Section/ Topic	Item no	Checklist item	**Page:** line no
Title and abstract	1a	Identification as a randomised trial in the title	**1**: 2
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see ACE checklist for abstracts)	**3**:2 to **4**:5
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	**7**:2 to **9**:4
	2b	Specific objectives or hypotheses	**9**:1 to **9**:4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	**9**: 6-11, **10**: 21-**11**:8
	3b«ǂ	Type of adaptive design used, with details of the pre-planned trial adaptations and the statistical information informing the adaptations	**9**: 8 **10**:23 - **11**:8
	3c«3b ‡	Important changes to the design or methods after trial commencement (such as eligibility criteria) outside the scope of the pre-planned adaptive design features, with reasons	**10**: 5 -**10**:8
Participants	4a	Eligibility criteria for participants	**9**: 18 – 24, **Suppl. B.1** Box
	4b	Settings and locations where the data were collected	**10**: 3- 19
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	**11**: 22-**12**:19
Outcomes	6a ‡	Completely define pre-specified primary and secondary outcome measures, including how and when they were assessed. Any other outcome measures used to inform pre-planned adaptations should be described with the rationale	**13**: 2- 14
	6b ‡	Any unplanned changes to trial outcomes after the trial commenced, with reasons	n.a.
Sample size and operating characteristics	7a ‡	How sample size and operating characteristics were determined	**14**: 4-8, & DexFEM design paper **Suppl. H**
	7b ‡‡	Pre-planned interim decision-making criteria to guide the trial adaptation process; whether decision-making criteria were binding or non-binding; pre-planned and actual timing and frequency of interim data looks to inform trial adaptations	**11**:1 -14 **Suppl. D.2:** Table A *footnote 1*
Randomisation			
Sequence generation	8a	Method used to generate the random allocation sequence	**11**: 9-14
	8b ‡	Type of randomisation; details of any restriction (such as blocking and block size); any changes to the allocation rule after trial adaptation decisions; any pre-planned allocation rule or algorithm to update randomisation with timing and frequency of updates	**11**: 10-12, **Suppl. D.2** Table A *both* footnotes
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	**11**: 9-12
Implement-ation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	**11**: 9-12,16-20
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	**11**: 17-19
	11b	If relevant, description of the similarity of interventions	**11**: 15-16
	11c ǂ	Measures to safeguard the confidentiality of interim information and minimise potential operational bias during the trial	**11**: 18-20

Section/ Topic	Item no	Checklist item	Page: line no
Statistical methods	12a ‡	Statistical methods used to compare groups for primary and secondary outcomes, and any other outcomes used to make pre-planned adaptations	**13**:16 –**14**: 3 **Suppl. E**
	12b« ǂ	For the implemented adaptive design features, statistical methods used to estimate treatment effects for key endpoints and to make inferences	**13**: 17-22, **13**: 23-**14**: 3
	12c«2 b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	n.a.
Results			
Participant flow	13a ‡	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome and any other outcomes used to inform pre-planned adaptations, if applicable	**15**: Fig 2 *Trial primary outcome used for adaptations*
	13b	For each group, losses and exclusions after randomisation, together with reasons	**15**: Fig 2 **Suppl. D.1, D.3**
Recruitment and adaptations	14a ‡	Dates defining the periods of recruitment and follow-up, for each group	**16**: 2-4
	14b †	Why the trial ended or was stopped	*Timed out, but achieved one short of target n*
	14c ǂ	Specify what trial adaptation decisions were made in light of the pre-planned decision-making criteria and observed accrued data	**Suppl. D.2**: Table A *1st footnote*
Baseline data	15a«15 †	A table showing baseline demographic and clinical characteristics for each group	Table 1 pg **32-33** *but this is for 2 groups - placebo and all (6) active groups combined*
	15b ǂ	Summary of data to enable the assessment of similarity in the trial population between interim stages	**Suppl D.2**: Table A
Numbers analysed	16 †	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	**34:** Table 2, Row 1
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)	**16**: 18-19 **34:** Table 2 lower half **16**: 22-**17**:2 **17**: Figure 3 **17**: 8-18 **18**:1 Figure 4 **Suppl D.5**: Table **Suppl. D.6-D.8** Figures x 3
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	*Derived binary outcomes are reported as absolute effect sizes – see **13**:25-**14**:3*
	17c ǂ	Report interim results used to inform interim decision-making	**Suppl D.2**: Table B
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) [1]	**18**: 9- **19**:3 **Suppl. D.8**
Discussion			
Limitations	20 †	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	**19**: 15 - **20**: 17 **21**: 15 - **22**: 2
Generalisabil -ity	21 †	Generalisability (external validity, applicability) of the trial findings	**19**: 10-14 **22**: 21-**23**: 6

Section/ Topic	Item no	Checklist item	Page: line no
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	**22**: 8 - 20 **23**: 12 - **24**: 2 **24**: 11- 15 *RIC panel*
Other information			
Registration	23	Registration number and name of trial registry	**2**: 19 **9**: 13-16
Protocol	24a«24	Where the full trial protocol can be accessed	Study 3 in **Suppl. F** or in protocol accessed at dx.doi.org/10.17504/protocols.io.bpw3mpgn
SAP and other relevant trial documents	24b ǂ	Where the full statistical analysis plan and other relevant trial documents can be accessed	**Suppl. E** & *in DexFEM papers already published - links given in* ***Suppl. H***
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	**3**: 7 **14**: 10-12 **26**: 2-18

SAP, statistical analysis plan; ACE, Adaptive designs CONSORT Extension;
"X« Y" means original CONSORT 2010 item Y has been renumbered to X;
"X«" means item reordering resulted in new item X replacing the number of the CONSORT 2010 item X.
ǂ New items that should only be applied in reference to ACE;
‡ Modified items that require reference to both CONSORT 2010 and ACE;
‡‡ Replacement (modified) item that only requires reference to ACE;
† Item wording remains unchanged in reference to CONSORT 2010 but we expanded the ACE explanatory text to clarify additional considerations for certain adaptive designs. These unchanged items require reference to CONSORT 2010 except item 14b.

Citation:

Dimairo M, Pallmann P, Wason J, Todd S, Jaki T, Julious SA, Mander AP, Weir CJ, Koenig F, Walton MK, Nicholl JP, Coates E, Biggs K, Hamasaki T, Proschan MA, Scott JA, Ando Y, Hind D, Altman DG; ACE Consensus Group. The Adaptive designs CONSORT Extension (ACE) statement: a checklist with explanation and elaboration guideline for reporting randomised trials that use an adaptive design. BMJ. 2020 Jun 17;369:m115. PMID: 32554564; PMCID: PMC7298567.

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