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A randomised controlled feasibility trial of surgery versus no surgery as part of multi-modality treatment in stage III-N2 non-small cell lung cancer (The PIONEER Trial)

Melissa Perry[1], Ashleigh Ward[1], Sally Taylor[1,2], Emily Harris[1], Selina Tsim[3], Neal Navani[4], David Baldwin[5], Ian Woolhouse[6], John Edwards[7], Seamus Grundy[8], Jonathan Robson[9], Sarah Rhodes[2], Nathan Burnside[5], Fiona Blackhall[1,2], Corinne Faivre-Finn[1,2], Janelle Yorke[1,2†] & Matthew Evison[2,10†]

[1]The Christie NHS Foundation Trust; [2]University of Manchester; [3]Queen Elizabeth University Hospital Glasgow; [4]University College London Hospital; [5]Nottingham University Hospitals; [6]Queen Elizabeth Hospital Birmingham; [7]Sheffield Teaching Hospitals NHS Foundation Trust, Northern General Hospital; [8]Northern Care Alliance NHS Trust; [9]Leeds Teaching Hospitals NHS Trust; [10]Wythenshawe Hospital, Manchester University NHS Foundation Trust. †Joint senior authors

Background & Aims

- Optimal treatment for stage III-N2 non-small cell lung cancer (NSCLC) requires surgical or non-surgical multi-modality treatment.
- Studies have failed to demonstrate superiority of either approach.
- Evidence exploring patient/carer quality of life across the different treatment pathways is limited.
- Data describing the N2 population in the United Kingdom (UK), and the proportion of patients with resectable disease is also limited.

Aim: To determine the feasibility and acceptability of conducting this trial whilst addressing the above.

Methods:

Randomised controlled feasibility trial recruiting from eight UK sites.

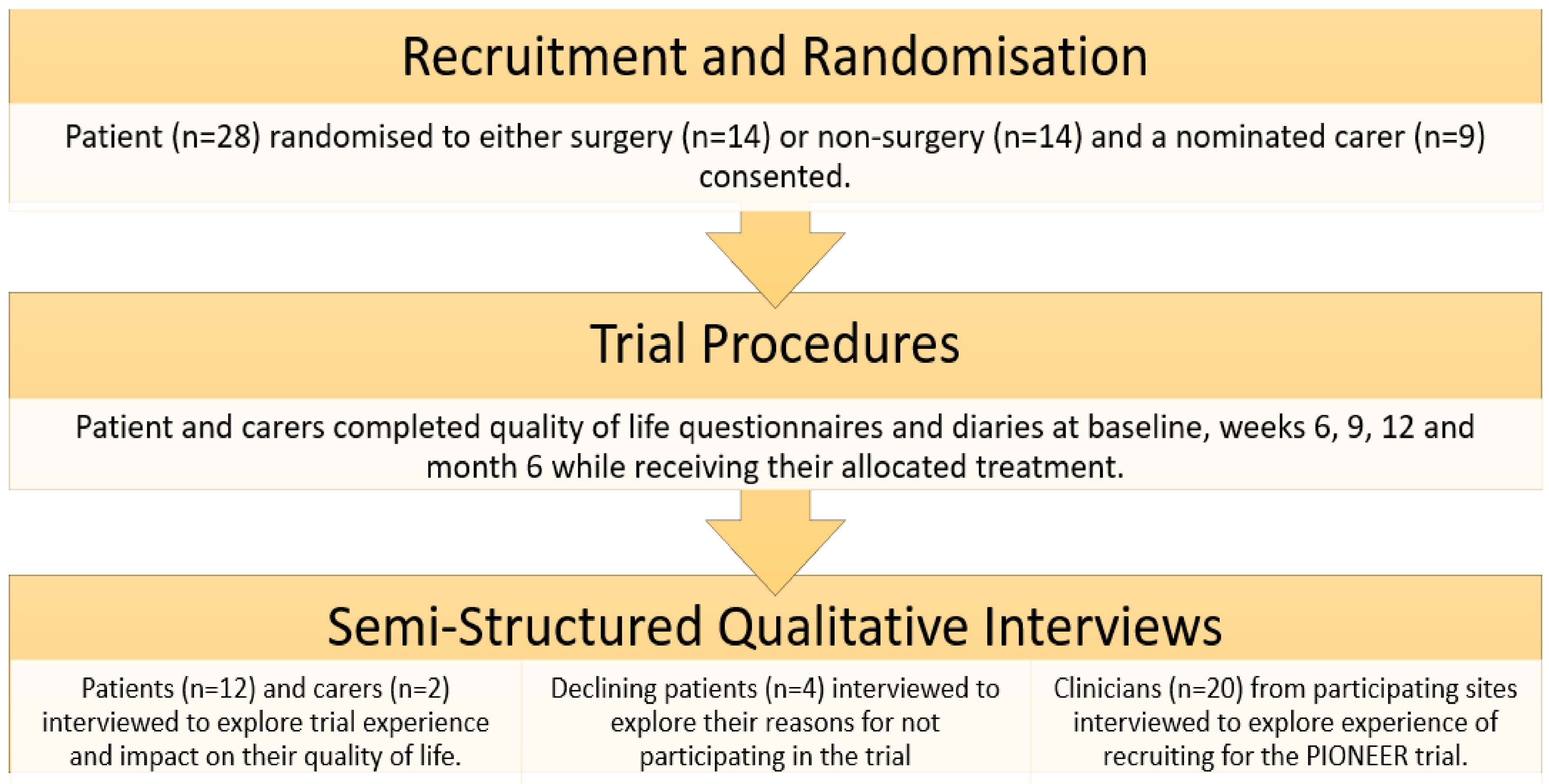

Figure 1: Flow diagram showing trial methodology

Results

- 276 patients with stage III-N2 NSCLC were assessed for eligibility; **224 (81%) were ineligible.**
- Of the 52 eligible patients, seven declined a research consultation (e.g., not approached due to strong treatment preference and therefore did not want to discuss the study), 17 patients formally declined.
- Of the 45 patients approached, **28 (62%) patients and nine of their carers consented.**
- COVID-19 delayed site opening and impacted recruitment.
- **No patients swapped or withdrew from their treatments;** 13 (46%) patients completed 6-month questionnaires.
- **Feasibility metrics (amber rating) were met but with significant challenges.**

Table 1: Pre-defined feasibility success metrics and how they were met

Pre-defined metrics	Proceed with minor changes	Proceed with significant modifications	Do not proceed	Results
Recruitment	50 or more patients recruited	25 – 49 patients recruited	24 or fewer patients recruited	28 participants randomised
Treatment fidelity	At least 80% of randomised participants receive allocated treatment	At least 70% of randomised participants receive allocated treatment	Less than 69% of randomised participants receive allocated treatment	No participants chose to change treatment arms or withdraw from their allocated treatment 20 (71%) of participants received allocated treatment. Eight participants deviated from planned treatment, but deviations were in line with protocol and standard practice.
Rate of assessment attrition at 3 and 6 months	Less than 30% at 3 and 6 months	Less than 60% at 3 and 6 months	61% or more at 3 and 6 months	14 (50%) did not provide useable QLQC-30 Global Health Status outcome at 3 months 16 (57%) did not provide useable QLQC-30 Global Health Status outcome at 6 months

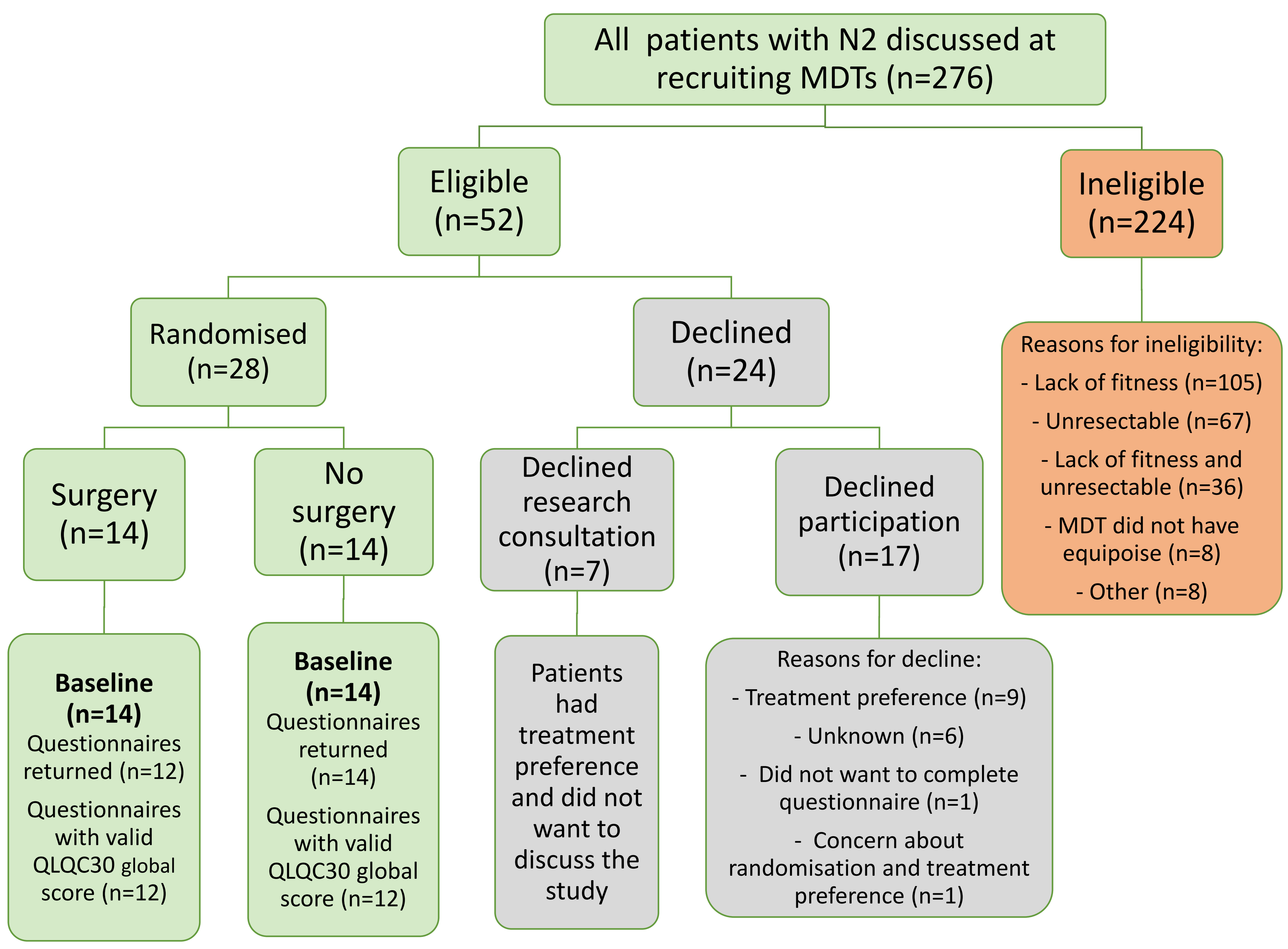

Figure 2: Consort diagram showing flow of patients through the recruitment phase

Table 2: Examples of themes from qualitative interviews

Participant group	Overarching theme	Sub-theme	Quote
Consented patient	Pre-trial experience	Motivation to participate	"You know, if there's anything I could do to help then I would do. So that's why I got introduced to the PIONEER study really."
	Impact on patient and carer QOL	Impact on patients QOL	"So that's the impact, my social life has been curtailed but it's been if you like tweaked and finer tuned so that I can carry out the important things, if it's a family meeting or whatever"
Consented carer	Impact on carer	Psychological impact	"Yeah it's obviously quite a worrying time, there's lots and lots of information that needs to be processed, there's lots of decisions that need to be made that could be life altering so yeah psychologically I think it's a tough period for anybody to go through"
	Role of carer	Attitudes to caring	"I wouldn't say it was a burden because you know I'd do anything for friend or family or somebody I was caring for so I wouldn't say it was a burden"
Multidisciplinary team (MDT) member	Role of clinician	Clinician bias	"If they are of a good performance status then any difficulty in recruitment is generally clinician based, not wanting to recommend the trials"
	Patient factors	Patient preference	"I think if they were a bit older they kind of wanted the radiotherapy route rather than surgery, if they were a bit younger they wanted the surgery route"
Declined patient	Decision making process	Reason for decline	"But because of the two treatment paths and I had a kind of clear way forward that would suit me better, that was the only reason I turned it down. And I was a bit sad to do that"

Conclusion: Despite challenges such as site opening delays and fewer eligible patients than anticipated; we successfully recruited 28 patients and collected a wealth of data on patients with N2 disease. Requirements for a fully powered trial (with modifications) were met. An international trial is likely to be needed to meet required sample size. Eligibility criteria should be modified in any future trials to increase the pool of eligible patients and maximise chances of recruitment.

Funding: *This poster presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Reference Number PB-PG-1217-20039).*

***Acknowledgements**: All patients, carers and clinicians who participated in the study*

Date of preparation: *13/03/2024*

ClinicalTrials.gov ID: NCT04540757