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The iPROMOS Protocol: A Stepped-Wedge Study to Implement Routine Patient Reported Outcomes in a Medical Oncology Outpatient Setting

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Manuscripts

1 **The iPROMOS Protocol: A Stepped-Wedge Study to**
2 **Implement Routine Patient Reported Outcomes in a**
3 **Medical Oncology Outpatient Setting**

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For peer review only

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2
3 54 Abstract:

4
5 55 Introduction: Patient Reported Outcomes (PROMs) are data capture tools that collect
6
7 56 information directly from patients. Several large research studies provide evidence
8
9 57 that use of PROMs in routine care provides benefits to mortality and morbidity
10
11 58 outcomes in medical oncology patients. Despite this, implementation of PROMs in
12
13 59 daily clinical routine is slow and challenging.

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16
17 60 Methods and Analysis: This study will use a stepped-wedge design to assess the
18
19 61 implementation of a PROM intervention in highly frequented medical oncology
20
21 62 outpatient clinics. During a lead-in period of four weeks, control data will be
22
23 63 collected. The intervention will then be implemented for four weeks in Clinic 1
24
25 64 initially, then in Clinic 2 for another four weeks. 500 patient encounters will be
26
27 65 measured over the 12 weeks in total. The process of implementation will be informed
28
29 66 and evaluated using the Medical Research Council (MRC) Guidelines for
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31 67 Implementing Complex Interventions. The study will be guided by the iPARIHS
32
33 68 framework approach to implementation. The intervention and implementation
34
35 69 outcomes will be measured using qualitative and quantitative data.

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39 70 Ethics and Dissemination: Ethical approval has been obtained, approval number
40
41 71 HREC/16/QRBW/100.

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45 72 Trial Registration Number: Australian New Zealand Clinical Trials Registry
46
47 73 (ANZCTR): ACTRN12618000398202.

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50 74 Article Summary:

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3 76 Strengths and limitations of this study
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6 77 Limitations:
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10 78 • One non-blinded researcher will implement the intervention, collect and analyse the
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12 79 data.
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14 80 • Response bias and social desirability bias (of both health professionals and patients
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17 81 that choose to participate)
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19 82 • Bias by the Hawthorne Effect whereby clinics being observed during the pre-
20
21 83 implementation phase may start to change practice.
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25 84 Strengths
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- 28 85 • A stepped-wedge design ensures an incremental implementation into clinical
29
30 86 practice.
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32 87 • Prospective use of an implementation framework will make sure that enablers and
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35 88 barriers in the setting are collected and reported allowing the findings from this
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37 89 study to inform future integration of PROMs into routine clinical care.
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3 93 Introduction:
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6 94 *What are Patient Reported Outcome Measures (PROMs)?*
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10 95 The Federal Drug Administration (FDA) defines PROMs as “any report of the status
11
12 96 of a patient’s health condition that comes directly from the patient, without
13
14 97 interpretation of the patient’s response by a clinician or anyone else” [1]. Revicki et al
15
16 98 (2000) describe PROMs as validated self-reporting assessment tools that capture
17
18 99 the patient experience [2]. PROMs have been extensively evaluated for their
19
20
21 100 sensitivity, specificity, overall accuracy and predictive value. They are now regarded
22
23 101 to have excellent precision, similar to many other widely-used clinical assessment
24
25 102 tools including pathological tests or medical imaging reports [3]. PROMs can provide
26
27 103 an overview of a patient’s physical, emotional, functional or overall health status, or
28
29 104 can be used to assess specific treatment outcomes or symptoms [4].
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33 105 *PROMs in clinical practice*
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36 106 PROMs are commonly used as outcome measures in research. However more
37
38 107 recently there is evidence that their real-time application in clinical practice can
39
40 108 enhance clinical interactions and improve patient experience. Several studies have
41
42 109 shown improved quality of life (QOL) [3, 5] as well as improved communication and
43
44 110 care planning [6, 7] following their use during routine care delivery. Two recent
45
46 111 studies demonstrated improvements in patient mortality and morbidity when
47
48 112 technology-facilitated PROMs data collection was incorporated in oncology care [5,
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51 113 8, 9].
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3 114 Given these evidence-based benefits, translating these findings into practice by
4
5 115 integrating PROMs into routine clinical care is the next required step in the
6
7 116 implementation cycle.
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10 117 *The Complexities of Implementing PROMs into the Clinical Setting*
11

12
13 118 A number of systematic reviews [3, 10, 11] reported that multiple organisational,
14
15 119 technical and clinical factors need to be overcome before introducing PROMs. In
16
17 120 particular, a lack of engagement from health care professionals, concerns about the
18
19 121 workflow of generating and filing of PROM reports, and lack of clearly defined
20
21 122 approaches in how to respond to the PROM data that indicate a patient need (e.g.
22
23 123 elevated pain or depression) have been identified as barriers to successful
24
25 124 implementation. The International Society of Quality of Life (ISOQOL) advocates a
26
27 125 stepwise approach to implementing PROMs, and provides a User's Guide [12],
28
29 126 which was updated in 2018. Klinkhammer-Schalke (2014) identified that a stepwise
30
31 127 approach was most useful when integrating a PROM intervention into routine care,
32
33 128 as it allows cycles of iterative learning during the implementation [7].
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38 129 Incorporating PROMs into clinical practice should be considered a complex
39
40 130 intervention, with many elements impacting on the intervention, and vice versa [13]
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43 131 Given these complexities, it has been recommended to use an implementation
44
45 132 framework to increase the likelihood of success when aiming to integrate PROMs
46
47 133 into routine care [14]. Use of a framework approach can help to consider both the
48
49 134 processes and intended outcomes of implementation. The Promoting Action
50
51 135 Research in Health Services (i-PARIHS) framework appears well suited, as it
52
53 136 highlights elements for consideration within the context (e.g. the features of the
54
55 137 particular clinic in which PROMs are to be integrated), the stakeholders (e.g.
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2
3 138 patients, clinicians, administrative staff) impacted by the intervention, and the
4
5 139 evidence surrounding the intervention (e.g. how much do stakeholders value the new
6
7 140 PROM information presented to them) [15]. A unique feature of iPARIHS is that it
8
9 141 stresses the central importance of a facilitator, who works with the local stakeholders
10
11 142 to adapt the evidence-based intervention for the local context. Antune's (2014)
12
13 143 systematic review provided evidence for the important role of a facilitator of the
14
15 144 implementation process [3], with enhanced successful uptake if one was present
16
17 145 [16,17]. For example, Baskerville et al (2012) showed that medical practices were
18
19 146 2.76 more likely to adopt evidence-based guidelines when a facilitator was working
20
21 147 in the local context [16].
22
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24

25 148 Besides the implementation framework, the Medical Research Council (MRC)
26
27 149 Guidelines for Implementation of Complex Interventions can provide guidance on
28
29 150 how to best incorporate pre-specified process measure. The Guidelines "can be
30
31 151 used to assess fidelity and quality of implementation, clarify causal mechanisms and
32
33 152 identify contextual factors associated with variation in outcomes" [17]. The MRC
34
35 153 approach ensures active evaluation throughout the implementation, and highlights
36
37 154 how to mitigate the impact that the introduction of new workflows has on the context,
38
39 155 participants and the intervention.
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44 156 In summary, the aim of this implementation study is to investigate implementation of
45
46 157 symptom reporting PROMs system into the outpatient oncology setting. The
47
48 158 objective of the intervention will be to increase detection of symptoms by clinicians
49
50 159 using the PROMs data. The implementation objectives include the successful
51
52 160 engagement of clinicians to use PROMs in clinical practice, the successful use of
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3 161 technology to obtain PROMs data from patients and present reports to clinicians,
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5 162 and the identification of appropriate local strategies to respond to PROM information.
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8 163 Methods and Analysis:
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11 164 *Study design*
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14 165 This mixed-methods study will use a stepped wedge cluster design. PROMs will be
15
16 166 introduced sequentially into two independent clinics, and all intervention and
17
18 167 implementation outcomes will be prospectively evaluated. The stepped wedge
19
20 168 approach has been chosen as it is a pragmatic solution for the systematic
21
22 169 introduction of a complex intervention [18], and has been successfully used in a
23
24 170 number of studies related to service delivery improvements [19, 20]. Another
25
26 171 advantage of this study design is that it limits bias by randomly assigning the clinics
27
28 172 to the intervention in sequential order. There are key elements that require attention
29
30 173 with this study design including the consideration of timing of study time-points,
31
32 174 cluster equivalence within the setting and intervention uptake assessed by process
33
34 175 measures [21, 22].
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39 176 The first clinic will be observed during a current standard practice lead-in period for
40
41 177 four weeks, then introduced into the iPROMOS intervention, while the other clinic will
42
43 178 continue with current standard practice and await implementation of iPROMOS. Data
44
45 179 collection and intervention time-points are presented Table 1.
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48

49 180 Table 1: Cluster stepped-wedge study design for iPROMOS
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Timepoint	T1 (weeks 0-4)	T2 (weeks 4-8)	T3 (weeks 8-12)
Clinic 1	Control Data	Intervention	Intervention
Clinic 2	Control Data	Control Data	Intervention

181 This protocol was co-designed with clinicians, academics and patient
 182 representatives. The iPROMOS intervention was informed by pre-implementation
 183 data collected from health professionals and relevant local stakeholders (Table 2).
 184 Reporting will follow Standards for Reporting Implementation Studies (StaRI)[23].

185 Table 2: Summary of pre-implementation information and how it informed
 186 implementation design

Aim	Data collected	Description of Findings	Implementation strategies
To engage health professionals and patients	Physical environment mapped Field notes Focus groups/interviews with multi-disciplinary team members and patient representatives of enablers and barriers Staff survey of knowledge, PROMs data format, enablers and barriers	The physical environment is busy but movement of patients, staff and medical records is established There are a number of established treatment pathways for patient care based on disease group, stage of disease and treatment regimen Previous interventions have been unsuccessful due to a lack of collaboration with staff and patients Knowledge about PROMs and current evidence is different across health discipline groups	Touch-screen computers will be positioned for easy access by patients as they enter the clinic area PROMs reports will be made available to staff prior to patient encounter PROMs data entry design, and equipment was sourced in collaboration with consumer representatives Information resources were developed in collaboration with staff and patient representatives, including posters, information sheets, staff brochures and inservice material

<p>To effectively incorporate technology</p>	<p>Field notes</p> <p>Map of Information Technology Systems that interact with patient care, including the physical environment</p>	<p>Many electronic medical records systems interact with patients and staff but not with each other. If PROMs data becomes a report it can be stored as such in the patient's medical record</p> <p>Paper-based reports can be more easily integrated into patient records</p> <p>Development of a system specific for each individual health service is expensive and time consuming. It is unclear whether this would be integrated into current IT systems, or become another log on for staff, which reduces their likelihood of engagement. No ready-made system could be identified for purchase.</p>	<p>A simple electronic data capture system (REDCap) will be used to collect PROMs data and generate reports. A simple set-up provides the flexibility needed for integration and implementation whilst ensuring the fidelity of the intervention.</p> <p>Developing/funding a more sophisticated platform for collecting PROMs from patients can be informed by the successful implementation process.</p>
<p>To manage and respond to PROMs data</p>	<p>Focus groups/interviews and field notes to map referral and communication pathways</p> <p>iPARIHS Context assessments of clinical areas [15]</p>	<p>Reports can inform referrals, in the format of documentation in the medical record, verbal communication or by email. The best approach needs to be identified with the relevant clinical team/area.</p> <p>Symptom assessment by clinicians uses CTCAE⁴ v4.0 as standard practice</p> <p>Allied health and specialist nurse roles are in place for management of specific</p>	<p>Alerts criteria will be generated directly to the appropriate specialist nurse and allied health team member to integrate into their practice.</p> <p>PROMs reports will be used to inform assessment and clinical decision making</p>

⁴ CTCAE is the Common Terminology Criteria for Adverse Events, developed by the US Department of Health and Human Services which offers provides universal assessment and grading of symptoms of disease and treatment

		symptoms	
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187 *Patient and Public Statement:*

188 Consumer representatives within the health services, and on a research advisory
189 group were approached to discuss the project. They confirmed a need for patient
190 self-reporting of symptoms that are integrated into routine care. Their reports would
191 need to be available to staff so that their concerns could be actioned. During the
192 development of the protocol, consumer representatives were involved in the
193 development of patient resources and collection of pre-implementation data. They
194 also assessed the burden of the intervention on patients

195 Results will be disseminated on information boards in the health service, and
196 reported back to Consumer Representative forums.

197 *Key features of the intervention:*

198 Based on the published evidence [5] and data from local clinicians as summarised in
199 Table 2, the PRO-CTCAE was selected as the PROM to be implemented, as it was
200 developed to extend an assessment by clinicians using the CTCAE [24], and has
201 been demonstrated to provide significant benefits for patient care and outcomes [9].
202 This PROM allows patients to report how much they experience each symptom, and
203 the impact on their daily activities, on a five-point Likert scale (ranging from 'none' to
204 'very much'). The core set of questions includes anorexia, constipation, dyspnoea,
205 diarrhoea, fatigue, nausea, pain, sensory neuropathy, vomiting, cough, low mood
206 and anxiety. Basch's (2016) study used a weekly completion schedule on an app
207 with alerts sent to clinicians in real-time [5]. However, use of apps for patient
208 reporting was not compatible with the health service's patient confidentiality policy.

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3 209 The intervention was adapted to include PROM reporting only during scheduled
4
5 210 attendances for outpatient clinic appointments. Thus, reporting to clinicians will occur
6
7 211 in line with existing clinic visits, which may be weekly or less frequently depending on
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9 212 cancer diagnosis, stage and treatment regimen. PROMs reports will be made
10
11 213 available for health professionals to view and respond to. This could include referring
12
13 214 the patient to allied health or supportive care, counselling, or additional
14
15 215 pharmacological support (e.g. adjusting pain medications). PROMS will be added in
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17 216 paper format to the patient chart, and in keeping with local practice, will be scanned
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20 217 into the electronic medical record at a later date.
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23 218 In summary, the iPROMOS intervention consists of, a) patients self-reporting
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25 219 symptoms (PRO-CTCAE PROM) using a touchscreen computer with data captured
26
27 220 on a custom-built REDCap database; b) reports of this information are generated in
28
29 221 real time; c) these reports are available to all healthcare team members and filed in
30
31 222 the patients' medical record; and, d) a copy of the report is also provided to the
32
33 223 patient. Usual care is clinician assessment of symptoms without the additional use of
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35 224 a PROM.
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39 225 In the co-design process, using the broader research evidence, investigated to
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41 226 support clinician's recommendations, a reported symptom of grade 2 or higher for
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43 227 nausea, vomiting or anorexia, and grade 3 for all other symptoms is considered
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45 228 significant [5]. If there is an increase in symptoms greater than 2 points from the
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47 229 previous visit, this will also trigger a referral by established pathways to the relevant
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50 230 allied health professional.
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53 231 *Setting of the implementation:*
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3 232 This project will be conducted in a tertiary teaching/quaternary referral hospital-
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5 233 located in South-East Queensland, Australia. The health service for this centre is
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7 234 the largest in Australia, with the oncology outpatients' department running up to 14
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9 235 clinics in one day. Each of these clinics are oncologist specific, providing service for
10
11 236 treatment, surveillance and follow-up for the patients in their care.
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15 237 Contextual pre-implementation information has revealed key factors for successful
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17 238 integration of the intervention (Table 2). Most importantly, the intervention needs to
18
19 239 engage all members of the multi-disciplinary team and the staff who will have access
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21 240 to the PROM information to address symptoms, disease management and
22
23 241 treatment. To make this likely, the facilitator will aim to integrate the PROM collection
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25 242 and reporting as much as possible into the existing workflow processes already in
26
27 243 place at the clinic. Evidence shows that workflows differ greatly between hospitals
28
29 244 and even within clinics in a hospital, and that staff are reluctant to change anything
30
31 245 that interrupts established practice, given the very complex environment they are
32
33 246 managing [25]. They are only willing to take on a new intervention when the benefits
34
35 247 and processes for patient care are tangible and clear. For successful
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37 248 implementation, it has been identified that it is necessary to integrate with existing
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39 249 patient care pathways and technological infrastructure, rather than impose another
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41 250 layer, which would likely be met with resistance [25].
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46 251 *Participants:*
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49 252 This study will collect data from two main groups of participants: a) patients; and b)
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51 253 the clinicians caring for them.
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3 254 a) *Patients* who attend the randomised medical oncology outpatients' clinics for
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5 255 treatment, medical review, active surveillance, or routine follow-up, with
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7 256 sufficient English to read the questionnaires. Patients with significant
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9 257 cognitive impairment, visual difficulties, or from a non-English speaking
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11 258 background who might have difficulty completing the forms will be excluded
12
13 259 from the study.

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17 260 *Patient Screening and Recruitment:* Patients attending selected clinics will be
18
19 261 invited to the use touchscreen computer to complete PROM information. The
20
21 262 first page of the PROM collection form provides a Patient Information Sheet
22
23 263 and Consent form. Potential participants will need to read the information and
24
25 264 accept to enter PROM reporting platform. If they do not wish to, they can
26
27 265 choose to decline. Patient information will also be visible on a poster
28
29 266 displayed in the clinical waiting area.

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33 267 b) *Staff* who care for these patients' including nursing and medical staff,
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35 268 pharmacists, dietitians, welfare workers, social workers, psychologists,
36
37 269 speech therapists, physiotherapists and other allied health workers are
38
39 270 eligible.

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43 271 *Staff participation:* an opt-out approach to consent staff has been approved by
44
45 272 the ethics committee. Multidisciplinary staff will be contacted using various
46
47 273 communication channels, directly by the facilitator-researcher to collect pre-
48
49 274 implementation information, as well as through distribution of information
50
51 275 brochures and poster developed in collaboration with the clinical teams.

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55 276 *Methods of evaluation:*

277 *Process Measures used for implementation evaluation:*

278 Table 3: Process Measures of Implementation Evaluation

279

Process measuring tool	Method of collection	Approach to analysis
Context: <ol style="list-style-type: none"> 1. Description of factors impacting and impacted 2. Description of barriers and enablers 	Facilitator field notes and site journal	Qualitative: content analysis for a structured analysis
Feasibility: <ol style="list-style-type: none"> 1. Number of patients that approached the touchscreen computer without prompting 2. Time taken to complete PROM by patients 3. Time required to assist patients complete PROM 4. Number of return completions by patients 5. Time taken to respond to report by staff 	Counts Data from data-capture program Self-report by staff Field notes	Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis
Fidelity: <ol style="list-style-type: none"> 1. Number of missing encounters by patients 2. Number of missing case report forms 3. Reasons for missing data 	Counts Case report form data Field notes	Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis
Reach: <ol style="list-style-type: none"> 1. Number of staff that answered "yes" to whether they knew about the implementation 2. Number of staff that stated that required 	Counts Case report form data Field notes	Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis

<p>education about PROMs</p> <p>3. Number of staff that independently used PROMs report</p> <p>4. Staff groups that responded to PROMs data</p>		
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281 In accordance with the MRC Guidelines for Complex Interventions the iterative
 282 implementation will be evaluated using both quantitative and qualitative process
 283 measures as described in Table 3.

284 Following the iPARIHS framework, data will be collected by the facilitator who works
 285 closely within the context. In this protocol, the facilitator will collect and use process
 286 measures, with protocol-specified data collected at pre-specified time-points (Table
 287 4).

288 Plan Do Study Act Cycles (PDSA) will be performed every 21 days as an interim
 289 data analysis to evaluate progress, and to report these findings to clinicians so that
 290 collaborative strategies can be established that maximise implementation. The
 291 purpose of each PDSA cycle is to summarise and reflect on the implementation
 292 process and improve it for the next cycle [15].

293

294 *Outcomes of the implementation:*

295 Table 4: Outcomes of the implementation

Outcome Measure	Method of Data Collection	Approach to analysis
% patients completing PROM form	Nominator of PROMs in electronic data capture; denominator of booking schedule of patients that	Quantitative: Descriptive Statistical Analysis; longitudinal analyses of % change.

	attended clinic; facilitator field notes of reasons for any missing data	Qualitative: Content analysis
% staff acknowledging PROM data	Case report forms; facilitator field notes	Quantitative: Descriptive Statistical Analysis; longitudinal analyses of % change. Qualitative: Content analysis
% PROMs in medical record	Communication in the medical record; completed PROMs in electronic data capture; referral data	Quantitative: Descriptive Statistical Analysis Qualitative: Content analysis
Acceptability of PROM reporting for staff and patients	Staff survey Focus groups, interviews and field notes	Quantitative: Descriptive Statistical Analysis Qualitative: Content Analysis to identify themes and interpret

296

297 The primary outcome of interest is successful implementation, and has been
 298 operationalised as “PROM reports are made available to clinicians in 85% of
 299 encounters, 70% of clinicians will respond to PROM data, and of those 50% of
 300 responses will be noted in the patients’ medical record”. This was selected as other
 301 studies reported that clinicians and patients are satisfied at such level of service
 302 when use is identified as feasible and acceptable [26, 27].

303 Secondary outcomes will measure patient and staff acceptance. Staff surveys will be
 304 distributed at the end of the PROMs data collection to capture change from baseline
 305 in staff knowledge, and identified facilitators and barriers.

306 *Outcomes of the intervention:*

307 Table 5: Outcome Measures of the Intervention

Outcome Measure	Methods of collection	Approach to analysis
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Symptoms assessment by clinicians	Medical record entries, case report forms	Comparison of proportion of patients with symptom assessment between intervention and control group using chi-square test
Response to symptom information	Medical record entries, case report forms	Proportion of patients referred for supportive care interventions compared between intervention and control groups using chi-square test
Change in symptom reporting and responding from pre-intervention to during intervention	Medical record entries, case report forms, PROM electronic data capture	Proportion of patients before to during intervention period using chi-square analysis and process control analysis
Presentations to the emergency department	Medical record entries	Proportion of patients before to during intervention period using chi-square analysis and process control analysis
Hospital admissions	Medical record entries	Proportion of patients before to during intervention period using chi-square analysis and process control analysis

308

309 The primary outcome measure of the intervention will be counts of health
 310 professional notes in the patients' chart about a symptom being of concern (for
 311 example pain). As well as this, the response to such symptoms will be recorded (e.g.
 312 referral to pain specialist).

313 Secondary outcomes will be an improvement in patient quality of life, presenting as a
 314 clinically significant reduction in measured symptoms. More detailed explanation of
 315 outcome measures is provided in Table 5.

316 *Sample size:*

1
2
3 317 To obtain an estimate of a minimal number of observations that should be included
4
5 318 in each cluster in this study, Berry et al's (2014) results were used [28]. These
6
7 319 researchers identified that a PROMs intervention increased symptom detection by
8
9 320 10%. Using these findings, and 80% power, given a baseline detection level of 0.75,
10
11 321 500 participant encounters would be needed to show improvement by 10% or more.

12
13
14
15 322 *Methods of Analysis:*

16
17
18 323 *Quantitative analyses:* Quantitative measures have been designed for the process
19
20 324 measures of implementation evaluation, the outcome measures of the
21
22 325 implementation and the outcome measures of the intervention. Descriptive statistics
23
24 326 including counts, frequencies and proportions will be used to summarize data
25
26 327 collected. Other statistical analyses to be used will include chi-square analysis for
27
28 328 comparing proportions, linear mixed models for longitudinal analyses, and statistical
29
30 329 control process analysis to identify trends over time.

31
32
33 330 Data from both clusters will be analysed using inverse variance weighting so that the
34
35 331 difference can be estimated for all patient encounters. This analysis can be used to
36
37 332 adjust for cancer types, or clustering by clinicians [29]. This analysis will provide a
38
39 333 measure of the intra-cluster effect, which can then be used for power calculations in
40
41 334 future larger studies [30].

42
43
44
45 335 *Qualitative data:*

46
47
48 336 The facilitator site journal will be used to record observations, and will be content
49
50 337 analysed to identify key themes, as a part of each PDSA cycle every 21 days.

51
52
53 338 The analysis of the facilitator site field notes will be used to triangulate other
54
55 339 research findings highlighting aspects in need of further investigation. The function

1
2
3 340 of field notes is to identify processes in a given situation and describe how
4
5 341 participants contribute to, and impact, these [31]. Extracted data will be interpreted in
6
7 342 keeping with Miles and Huberman's approach (2014) using field notes to inform the
8
9 343 content analysis to "decide what things mean, noting regularities, patterns,
10
11 344 explanation, possible configurations, causal flows and propositions"[32] .
12
13

14 345 *Data monitoring*

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16
17
18 346 Data monitoring will ascertain high data quality, ensure rigour and mitigate biases.
19
20

21 347 Data monitoring will be done through three processes:
22
23

- 24 348 1. Quantitative data will be double entered for a random sample of 10% records,
25
26 349 and all records will be double entered should the error rate be greater than
27
28 350 5%.
29
30
- 31 351 2. Monthly meetings with expert facilitators who are not involved with the project
32
33 352 to reflect on the implementation and evaluation of the project.
34
- 35 353 3. Supervision and oversight by the study team not directly involved in the
36
37 354 process of implementation.
38
39

40 355 *Safety Reporting*

41
42
43
44 356 The main purpose of the secondary outcome measures of the intervention is to
45
46 357 measure the safety of using this implementation approach. A potential safety issue
47
48 358 is that when patients complete the PROMs they expect that staff will act on that
49
50 359 information. If the implementation is not successful, staff may not do this in a timely
51
52 360 fashion or at all, and patients who report symptoms may not receive suitable
53
54 361 treatment. Any such issues where a PROMs report was not acted on will be noted
55
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3 362 and described using the data collection tools for the project. The facilitator will raise
4
5 363 any issues where patient safety is at risk.
6

7
8 364 *Ethical Considerations*
9

10 365 This project has received ethical approval from the Royal Brisbane and Women's
11
12 366 Hospital Human Research Ethics Committee number HREC/16/QRBW/100.
13
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15
16 367 *Discussion:*
17

18
19 368 This study proposes that successful implementation of PROMs requires
20
21 369 sophisticated attention to the local clinical setting and existing clinical workflows, and
22
23 370 can overcome barriers previously experienced in other settings by following a pre-
24
25 371 specified implementation approach with an experienced facilitator. It is important to
26
27 372 investigate implementation strategies as clinical trials have demonstrated significant
28
29 373 benefits for patients, but also reported the difficulties of using PROMs in complex
30
31 374 health systems outside the highly structured context of a clinical trial. Systematic
32
33 375 reviews recommend a structured implementation approach that takes into account
34
35 376 the many elements present in the health system into which PROMs are introduced.
36
37 377 The use of the iPARIHS framework with the MRC Guidelines for Implementation of
38
39 378 Complex Interventions, built upon the work of ISOQOL, offers an implementation
40
41 379 strategy that addresses the issues identified in the research to date. This study offers
42
43 380 an opportunity to scientifically measure implementation, potentially rapidly implement
44
45 381 PROMs into clinical practice and to inform future research and clinical practice.
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50 382 Trial Status: Opened on 25 March 2018 and will continue until 12 months after the
51
52 383 last PROMs reporting encounter.
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56 384 *References:*
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43 476 supervisory team participated in the implementation science based approach of
44
45 477 protocol development.
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19 488 Contributorship statement:
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23
24 490 the drafting of this publication, particularly with expertise in implementation science
25
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27
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29
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31
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12
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17
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19 510 Competing interests statement:
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22 511 There are none to declare
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BMJ Open

The iPROMOS Protocol: A Stepped-Wedge Study to Implement Routine Patient Reported Outcomes in a Medical Oncology Outpatient Setting

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Primary Subject Heading:	Oncology
Secondary Subject Heading:	Health services research, Oncology, Patient-centred medicine, Evidence based practice
Keywords:	PROMs, implementation, complex intervention, PRO-CTCAE, iPARIHS

SCHOLARONE™
Manuscripts

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4 1 **The iPROMOS Protocol: A Stepped-Wedge Study to**
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7 2 **Implement Routine Patient Reported Outcomes in a**
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3 54 Abstract:
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5 55 Introduction: Patient Reported Outcomes (PROMs) are data capture tools that collect
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7
8 56 information directly from patients. Several large research studies provide evidence
9
10 57 that use of PROMs in routine care provides benefits to mortality and morbidity
11
12 58 outcomes in medical oncology patients. Despite this, implementation of PROMs in
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14
15 59 daily clinical routine is slow and challenging.
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17
18 60 Methods and Analysis: This study will use a stepped-wedge design to assess the
19
20 61 implementation of a PROM intervention in highly frequented medical oncology
21
22 62 outpatient clinics. During a lead-in period of four weeks, control data will be
23
24 63 collected. The intervention will then be implemented for four weeks in Clinic 1
25
26 64 initially, then in Clinic 2 for another four weeks. 500 patient encounters will be
27
28 65 measured over the 12 weeks in total. The process of implementation will be informed
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30 66 and evaluated using the Medical Research Council (MRC) Guidelines for
31
32 67 Implementing Complex Interventions. The study will be guided by the iPARIHS
33
34 68 framework approach to implementation. The intervention and implementation
35
36 69 outcomes will be measured using qualitative and quantitative data.
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42 70 Ethics and Dissemination: Ethical approval has been obtained, approval number
43
44 71 HREC/16/QRBW/100 by the Royal Brisbane and Women's Hospital Human
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46 72 Research Ethics Committee. Results will be disseminated in peer reviewed journals
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48 73 and at scientific meetings.
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52 74 Trial Registration Number: Australian New Zealand Clinical Trials Registry
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54 75 (ANZCTR): ACTRN12618000398202.
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77 Article Summary:

78 Strengths and limitations of this study

79 Limitations:

- 80 • One non-blinded researcher will implement the intervention, collect and
81 analyse the data.
- 82 • Response bias and social desirability bias (of both health professionals and
83 patients that choose to participate)
- 84 • Bias by the Hawthorne Effect whereby clinics being observed during the pre-
85 implementation phase may start to change practice.

86 Strengths

- 87 • A stepped-wedge design ensures an incremental implementation into clinical
88 practice.
- 89 • Prospective use of an implementation framework will make sure that enablers
90 and barriers in the setting are collected and reported allowing the findings
91 from this study to inform future integration of PROMs into routine clinical care.

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3 95 Introduction:
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6 96 *What are Patient Reported Outcome Measures (PROMs)?*
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10 97 The Federal Drug Administration (FDA) defines PROMs as “any report of the status
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12 98 of a patient’s health condition that comes directly from the patient, without
13
14 99 interpretation of the patient’s response by a clinician or anyone else” [1]. Revicki et al
15
16
17 100 (2000) describe PROMs as validated self-reporting assessment tools that capture
18
19 101 the patient experience [2]. PROMs have been extensively evaluated for their
20
21 102 sensitivity, specificity, overall accuracy and predictive value. They are now regarded
22
23 103 to have excellent precision, similar to many other widely-used clinical assessment
24
25 104 tools including pathological tests or medical imaging reports [3]. PROMs can provide
26
27 105 an overview of a patient’s physical, emotional, functional or overall health status, or
28
29 106 can be used to assess specific treatment outcomes or symptoms [4].
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34 107 *PROMs in clinical practice*
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38 108 PROMs are commonly used as outcome measures in research. However more
39
40 109 recently there is evidence that their real-time application in clinical practice can
41
42 110 enhance clinical interactions and improve patient experience. Several studies have
43
44 111 shown that using PROMs in routine care leads to improved quality of life (QOL) [3, 5]
45
46 112 as well as improved communication, decision-making, care planning and patient
47
48 113 satisfaction [6-8]. Two recent studies demonstrated improvements in patient mortality
49
50 114 and morbidity when technology-facilitated PROMs data collection was incorporated
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53 115 in oncology care [5, 9, 10].
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3 116 Given these evidence-based benefits, translating these findings into practice by
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5 117 integrating PROMs into routine clinical care is the next required step in the
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8 118 implementation cycle.
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11 119 *The Complexities of Implementing PROMs into the Clinical Setting*

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13
14 120 A number of systematic reviews [3, 11, 12] reported that multiple organisational,
15
16 121 technical and clinical factors need to be overcome before introducing PROMs. In
17
18 122 particular, a lack of engagement from health care professionals, concerns about the
19
20 123 workflow of generating and filing of PROM reports, and lack of clearly defined
21
22 124 approaches in how to respond to the PROM data that indicate a patient need (e.g.
23
24 125 elevated pain or depression) have been identified as barriers to successful
25
26 126 implementation. The International Society of Quality of Life (ISOQOL) advocates a
27
28 127 stepwise approach to implementing PROMs, and provides a User's Guide [13],
29
30 128 which was updated in 2018. Klinkhammer-Schalke (2014) identified that a stepwise
31
32 129 approach was most useful when integrating a PROM intervention into routine care,
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34 130 as it allows cycles of iterative learning during the implementation [7].
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41 131 Incorporating PROMs into clinical practice should be considered a complex
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43 132 intervention, with many elements impacting on the intervention, and vice versa [14]
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45 133 Given these complexities, it has been recommended to use an implementation
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47 134 framework to increase the likelihood of success when aiming to integrate PROMs
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49 135 into routine care [15]. Use of a framework approach can help to consider both the
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51 136 processes and intended outcomes of implementation. The Promoting Action
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53 137 Research in Health Services (i-PARIHS) framework appears well suited, as it
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55 138 highlights elements for consideration within the context (e.g. the features of the
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57 139 particular clinic in which PROMs are to be integrated), the stakeholders (e.g.
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3 140 patients, clinicians, administrative staff) impacted by the intervention, and the
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5 141 evidence surrounding the intervention (e.g. how much do stakeholders value the new
6
7 142 PROM information presented to them) [16]. A unique feature of iPARIHS is that it
8
9 143 stresses the central importance of a facilitator, who works with the local stakeholders
10
11 144 to adapt the evidence-based intervention for the local context. Antune's (2014)
12
13 145 systematic review provided evidence for the important role of a facilitator of the
14
15 146 implementation process [3], with enhanced successful uptake if one was present
16
17 147 [17,18]. For example, Baskerville et al (2012) showed that medical practices were
18
19 148 2.76 more likely to adopt evidence-based guidelines when a facilitator was working
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21 149 in the local context [17].
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27 150 Besides the implementation framework, the Medical Research Council (MRC)
28
29 151 Guidelines for Implementation of Complex Interventions can provide guidance on
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31 152 how to best incorporate pre-specified process measure. The Guidelines "can be
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33 153 used to assess fidelity and quality of implementation, clarify causal mechanisms and
34
35 154 identify contextual factors associated with variation in outcomes" [18]. The MRC
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37 155 approach ensures active evaluation throughout the implementation, and highlights
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39 156 how to mitigate the impact that the introduction of new workflows has on the context,
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41 157 participants and the intervention.
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47 158 In summary, the aim of this implementation study is to investigate implementation of
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49 159 symptom reporting PROMs system into the outpatient oncology setting. The
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51 160 objective of the intervention will be to increase detection of symptoms by clinicians
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53 161 using the PROMs data. The implementation objectives include the successful
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55 162 engagement of clinicians to use PROMs in clinical practice, the successful use of
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3 163 technology to obtain PROMs data from patients and present reports to clinicians,
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5 164 and the identification of appropriate local strategies to respond to PROM information.
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9 165 Methods and Analysis:

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12 166 *Study design*
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16 167 This mixed-methods study will use a stepped wedge cluster design. PROMs will be
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18 168 introduced sequentially into two independent clinics, and all intervention and
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20 169 implementation outcomes will be prospectively evaluated. The stepped wedge
21
22 170 approach has been chosen as it is a pragmatic solution for the systematic
23
24 171 introduction of a complex intervention [19], and has been successfully used in a
25
26 172 number of studies related to service delivery improvements [20, 21]. Another
27
28 173 advantage of this study design is that it limits bias by randomly assigning the clinics
29
30 174 to the intervention in sequential order. There are key elements that require attention
31
32 175 with this study design including the consideration of timing of study time-points,
33
34 176 cluster equivalence within the setting and intervention uptake assessed by process
35
36 177 measures [22, 23].
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42 178 The first clinic will be observed during a current standard practice lead-in period for
43
44 179 four weeks, then introduced into the iPROMOS intervention, while the other clinic will
45
46 180 continue with current standard practice and await implementation of iPROMOS. Data
47
48 181 collection and intervention time-points are presented Table 1.
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52
53 182 Table 1: Cluster stepped-wedge study design for iPROMOS
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Timepoint	T1 (weeks 0-4)	T2 (weeks 4-8)	T3 (weeks 8-12)
Clinic 1	Control Data	Intervention	Intervention
Clinic 2	Control Data	Control Data	Intervention

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3 183 This protocol was co-designed with clinicians, academics and patient
4
5 184 representatives. The iPROMOS intervention was informed by pre-implementation
6
7 185 data collected from health professionals and relevant local stakeholders (Table 2).
8
9
10 186 Reporting will follow Standards for Reporting Implementation Studies (StaRI)[24].
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13
14 187 Table 2: Summary of pre-implementation information and how it informed
15
16 188 implementation design
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Aim	Data collected	Description of Findings	Implementation strategies
To engage health professionals and patients	Physical environment mapped Field notes Focus groups/interviews with multi-disciplinary team members and patient representatives of enablers and barriers Staff survey of knowledge ⁴ , PROMs data format, enablers and barriers	The physical environment is busy but movement of patients, staff and medical records is established There are many established treatment pathways for patient care based on disease group, stage of disease and treatment regimen Previous interventions have been unsuccessful due to a lack of collaboration with staff and patients Knowledge about PROMs and current evidence is different across health discipline groups	Touch-screen computers will be positioned for easy access by patients as they enter the clinic area PROMs reports will be made available to staff prior to patient encounter PROMs data entry design, and equipment was sourced in collaboration with consumer representatives Information resources were developed in collaboration with staff and patient representatives, including posters, information sheets, staff brochures and inservice material

⁴ The staff survey was modelled on Rouette's (2015) assessing knowledge and perceptions about PROs, including barriers and facilitators [26]

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<p>To effectively incorporate technology</p>	<p>Field notes</p> <p>Map of Information Technology Systems that interact with patient care, including the physical environment</p>	<p>Many electronic medical records systems interact with patients and staff but not with each other. If PROMs data becomes a report it can be stored as such in the patient's medical record</p> <p>Paper-based reports can be more easily integrated into patient records</p> <p>Development of a system specific for each individual health service is expensive and time consuming. It is unclear whether this would be integrated into current IT systems, or become another log on for staff, which reduces their likelihood of engagement. No ready-made system could be identified for purchase.</p>	<p>A simple electronic data capture system (REDCap) will be used to collect PROMs data and generate reports. A simple set-up provides the flexibility needed for integration and implementation whilst ensuring the fidelity of the intervention.</p> <p>Developing/funding a more sophisticated platform for collecting PROMs from patients can be informed by the successful implementation process.</p>
<p>To manage and respond to PROMs data</p>	<p>Focus groups/interviews and field notes to map referral and communication pathways</p> <p>iPARIHS Context assessments of clinical areas [15]</p>	<p>Reports can inform referrals, in the format of documentation in the medical record, verbal communication or by email. The best approach needs to be identified with the relevant clinical team/area.</p> <p>Symptom assessment by clinicians uses CTCAE⁵ v4.0 as standard practice</p> <p>Allied health and specialist nurse roles are in place for</p>	<p>Alerts criteria will be generated directly to the appropriate specialist nurse and allied health team member to integrate into their practice.</p> <p>PROMs reports will be used to inform assessment and clinical decision making</p>

⁵ CTCAE is the Common Terminology Criteria for Adverse Events, developed by the US Department of Health and Human Services which offers provides universal assessment and grading of symptoms of disease and treatment

		management of specific symptoms	
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189 *Patient and Public Statement:*

190 Consumer representatives within the health services, and on a research advisory
 191 group were approached to discuss the project. They confirmed a need for patient
 192 self-reporting of symptoms that are integrated into routine care. Their reports would
 193 need to be available to staff so that their concerns could be actioned. During the
 194 development of the protocol, consumer representatives were involved in the
 195 development of patient resources and collection of pre-implementation data. They
 196 also assessed the burden of the intervention on patients

197 Results will be disseminated on information boards in the health service, and
 198 reported back to Consumer Representative forums.

199 *Key features of the intervention:*

200 Based on the published evidence [5] and data from local clinicians as summarised in
 201 Table 2, the PRO-CTCAE⁶ was selected as the PROM to be implemented, as it was
 202 developed to extend an assessment by clinicians using the CTCAE [25], and has
 203 been demonstrated to provide significant benefits for patient care and outcomes [10].
 204 This PROM allows patients to report how much they experience each symptom, and
 205 the impact on their daily activities, on a five-point Likert scale (ranging from 'none' to

⁶ PRO-CTCAE is a validated (119 of 124 items met at least 1 construct validity criterion) symptom-reporting PROM that has been demonstrated to be reliable (test-retest reliability was 0.7 or greater for 36 of 49 prespecified items) and responsive (item changes corresponded to the QLQ-C30 scale) [27]. There are a number of studies that have demonstrated that the PRO-CTCAE is acceptable to patients from differing cancer populations internationally [28,29]

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3 206 'very much'). The core set of questions includes anorexia, constipation, dyspnoea,
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5 207 diarrhoea, fatigue, nausea, pain, sensory neuropathy, vomiting, cough, low mood
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8 208 and anxiety. Basch's (2016) study used a weekly completion schedule on an app
9
10 209 with alerts sent to clinicians in real-time [5]. However, use of apps for patient
11
12 210 reporting was not compatible with the health service's patient confidentiality policy.
13
14 211 The intervention was adapted to include PROM reporting only during scheduled
15
16 212 attendances for outpatient clinic appointments. Thus, reporting to clinicians will occur
17
18 213 in line with existing clinic visits, which may be weekly or less frequently depending on
19
20 214 cancer diagnosis, stage and treatment regimen. PROMs reports will be made
21
22 215 available for health professionals to view and respond to. This could include referring
23
24 216 the patient to allied health or supportive care, counselling, or additional
25
26 217 pharmacological support (e.g. adjusting pain medications). PROMS will be added in
27
28 218 paper format to the patient chart, and in keeping with local practice, will be scanned
29
30 219 into the electronic medical record at a later date.

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36 220 In summary, the iPROMOS intervention consists of, a) patients self-reporting
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38 221 symptoms (PRO-CTCAE PROM) using a touchscreen computer with data captured
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40 222 on a custom-built REDCap database; b) reports of this information are generated in
41
42 223 real time; c) these reports are available to all healthcare team members and filed in
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44 224 the patients' medical record; and, d) a copy of the report is also provided to the
45
46 225 patient. Usual care is clinician assessment of symptoms without the additional use of
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48 226 a PROM.

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53 227 In the co-design process, using the broader research evidence, investigated to
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55 228 support clinician's recommendations, a reported symptom of grade 2 or higher for
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57 229 nausea, vomiting or anorexia, and grade 3 for all other symptoms is considered
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3 230 significant [5]. If there is an increase in symptoms greater than 2 points from the
4
5 231 previous visit, this will also trigger a referral by established pathways to the relevant
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7 232 allied health professional.
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11 233 *Setting of the implementation:*
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14 234 This project will be conducted in a tertiary teaching/quaternary referral hospital-
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16 235 located in South-East Queensland, Australia. The health service for this centre is
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18 236 the largest in Australia, with the oncology outpatients' department running up to 14
19
20 237 clinics in one day. Each of these clinics are oncologist specific, providing service for
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22 238 treatment, surveillance and follow-up for the patients in their care.
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27 239 Contextual pre-implementation information has revealed key factors for successful
28
29 240 integration of the intervention (Table 2). Most importantly, the intervention needs to
30
31 241 engage all members of the multi-disciplinary team and the staff who will have access
32
33 242 to the PROM information to address symptoms, disease management and
34
35 243 treatment. To make this likely, the facilitator will aim to integrate the PROM collection
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37 244 and reporting as much as possible into the existing workflow processes already in
38
39 245 place at the clinic. Evidence shows that workflows differ greatly between hospitals
40
41 246 and even within clinics in a hospital, and that staff are reluctant to change anything
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43 247 that interrupts established practice, given the very complex environment they are
44
45 248 managing [26]. They are only willing to take on a new intervention when the benefits
46
47 249 and processes for patient care are tangible and clear. For successful
48
49 250 implementation, it has been identified that it is necessary to integrate with existing
50
51 251 patient care pathways and technological infrastructure, rather than impose another
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53 252 layer, which would likely be met with resistance [26].
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3 253 *Participants:*
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7 254 This study will collect data from two main groups of participants: a) patients; and b)
8
9 255 the clinicians caring for them.
10

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12 256 a) *Patients* who attend the randomised medical oncology outpatients' clinics for
13
14 257 treatment, medical review, active surveillance, or routine follow-up, with
15
16 258 sufficient English to read the questionnaires. Patients with significant
17
18 259 cognitive impairment, visual difficulties, or from a non-English speaking
19
20 260 background who might have difficulty completing the forms will be excluded
21
22 261 from the study.
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27 262 *Patient Screening and Recruitment:* Patients attending selected clinics will be
28
29 263 invited to the use touchscreen computer to complete PROM information. The
30
31 264 first page of the PROM collection form provides a Patient Information Sheet
32
33 265 and Consent form. Potential participants will need to read the information and
34
35 266 accept to enter PROM reporting platform. If they do not wish to, they can
36
37 267 choose to decline. Patient information will also be visible on a poster
38
39 268 displayed in the clinical waiting area.
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44 269 b) *Staff* who care for these patients' including nursing and medical staff,
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46 270 pharmacists, dietitians, welfare workers, social workers, psychologists,
47
48 271 speech therapists, physiotherapists and other allied health workers are
49
50 272 eligible.
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55 273 *Staff participation:* an opt-out approach to consent staff has been approved by
56
57 274 the ethics committee. Multidisciplinary staff will be contacted using various
58
59 275 communication channels, directly by the facilitator-researcher to collect pre-
60

276 implementation information, as well as through distribution of information

277 brochures and poster developed in collaboration with the clinical teams.

278 *Methods of evaluation:*

279 *Process Measures used for implementation evaluation:*

280 Table 3: Process Measures of Implementation Evaluation

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Process measuring tool	Method of collection	Approach to analysis
Context: <ol style="list-style-type: none"> 1. Description of factors impacting and impacted 2. Description of barriers and enablers 	Facilitator field notes and site journal	Qualitative: content analysis for a structured analysis
Feasibility: <ol style="list-style-type: none"> 1. Number of patients that approached the touchscreen computer without prompting 2. Time taken to complete PROM by patients 3. Time required to assist patients complete PROM 4. Number of return completions by patients 5. Time taken to respond to report by staff 	Counts Data from data-capture program Self-report by staff Field notes	Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis
Fidelity: <ol style="list-style-type: none"> 1. Number of missing encounters by patients 2. Number of missing case report forms 3. Reasons for missing data 	Counts Case report form data Field notes	Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis

<p>Reach:</p> <ol style="list-style-type: none"> 1. Number of staff that answered “yes” to whether they knew about the implementation 2. Number of staff that stated that required education about PROMs 3. Number of staff that independently used PROMs report 4. Staff groups that responded to PROMs data 	<p>Counts</p> <p>Case report form data</p> <p>Field notes</p>	<p>Quantitative: descriptive statistics</p> <p>Qualitative: content analysis for a structured analysis</p>
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283 In accordance with the MRC Guidelines for Complex Interventions the iterative
 284 implementation will be evaluated using both quantitative and qualitative process
 285 measures as described in Table 3.

286 Following the iPARIHS framework, data will be collected by the facilitator who works
 287 closely within the context. In this protocol, the facilitator will collect and use process
 288 measures, with protocol-specified data collected at pre-specified time-points (Table
 289 4).

290 Plan Do Study Act Cycles (PDSA) will be performed every 21 days as an interim
 291 data analysis to evaluate progress, and to report these findings to clinicians so that
 292 collaborative strategies can be established that maximise implementation. The
 293 purpose of each PDSA cycle is to summarise and reflect on the implementation
 294 process and improve it for the next cycle [16].

295

296 *Outcomes of the implementation:*

297 Table 4: Outcomes of the implementation

Outcome Measure	Method of Data Collection	Approach to analysis
% patients completing PROM form	Nominator of PROMs in electronic data capture; denominator of booking schedule of patients that attended clinic; facilitator field notes of reasons for any missing data	Quantitative: Descriptive Statistical Analysis; longitudinal analyses of % change. Qualitative: Content analysis
% staff acknowledging PROM data	Case report forms; facilitator field notes	Quantitative: Descriptive Statistical Analysis; longitudinal analyses of % change. Qualitative: Content analysis
% PROMs in medical record	Communication in the medical record; completed PROMs in electronic data capture; referral data	Quantitative: Descriptive Statistical Analysis Qualitative: Content analysis
Acceptability of PROM reporting for staff and patients	Staff survey Focus groups, interviews and field notes	Quantitative: Descriptive Statistical Analysis Qualitative: Content Analysis to identify themes and interpret

298

299 The primary outcome of interest is successful implementation, and has been
 300 operationalised as “PROM reports are made available to clinicians in 85% of
 301 encounters, 70% of clinicians will respond to PROM data, and of those 50% of
 302 responses will be noted in the patients’ medical record”. This was selected as other
 303 studies reported that clinicians and patients are satisfied at such level of service
 304 when use is identified as feasible and acceptable [27, 28].

305 Secondary outcomes will measure patient and staff acceptance. Staff surveys will be
 306 distributed at the end of the PROMs data collection to capture change from baseline
 307 in staff knowledge, and identified facilitators and barriers.

308 *Outcomes of the intervention:*

309 Table 5: Outcome Measures of the Intervention

Outcome Measure	Methods of collection	Approach to analysis
Symptoms assessment by clinicians	Medical record entries, case report forms	Comparison of proportion of patients with symptom assessment between intervention and control group using chi-square test
Response to symptom information	Medical record entries, case report forms	Proportion of patients referred for supportive care interventions compared between intervention and control groups using chi-square test
Change in symptom reporting and responding from pre-intervention to during intervention	Medical record entries, case report forms, PROM electronic data capture	Proportion of patients before to during intervention period using chi-square analysis and process control analysis
Presentations to the emergency department	Medical record entries	Proportion of patients before to during intervention period using chi-square analysis and process control analysis
Hospital admissions	Medical record entries	Proportion of patients before to during intervention period using chi-square analysis and process control analysis

310

311 The primary outcome measure of the intervention will be counts of health
 312 professional notes in the patients' chart about a symptom being of concern (for
 313 example pain). As well as this, the response to such symptoms will be recorded (e.g.
 314 referral to pain specialist).

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3 315 Secondary outcomes will be an improvement in patient quality of life, presenting as a
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5 316 clinically significant reduction in measured symptoms. More detailed explanation of
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7 317 outcome measures is provided in Table 5.
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11 318 *Sample size:*
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14 319 Berry et al (2014) conducted an RCT which compared symptom reports between
15
16 320 clinics using an electronic reporting tool. They assessed both processes and
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18 321 outcomes of care, comparing the impact of PROM reports between the control and
19
20 322 intervention clinics. It was used to guide the sample size calculations because this
21
22 323 study measured the identification of symptoms in usual care versus a symptom-
23
24 324 PROMs intervention. To obtain an estimate of a minimal number of observations that
25
26 325 should be included in each cluster in this study, Berry et al's (2014) results were
27
28 326 used [29]. These researchers identified that a PROMs intervention increased
29
30 327 symptom detection by 10%. Using these findings, and 80% power, given a baseline
31
32 328 detection level of 0.75, 500 participant encounters would be needed to show
33
34 329 improvement by 10% or more.
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40 330 *Methods of Analysis:*
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44 331 *Quantitative analyses:* Quantitative measures have been designed for the process
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46 332 measures of implementation evaluation, the outcome measures of the
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48 333 implementation and the outcome measures of the intervention. Descriptive statistics
49
50 334 including counts, frequencies and proportions will be used to summarize data
51
52 335 collected. Other statistical analyses to be used will include chi-square analysis for
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54 336 comparing proportions, linear mixed models for longitudinal analyses, and statistical
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56 337 control process analysis to identify trends over time.
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3 338 Data from both clusters will be analysed using inverse variance weighting so that the
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5 339 difference can be estimated for all patient encounters. This analysis can be used to
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7 340 adjust for cancer types, or clustering by clinicians [30]. This analysis will provide a
8
9 341 measure of the intra-cluster effect, which can then be used for power calculations in
10
11 342 future larger studies [[31].
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16 343 *Qualitative data:*
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19 344 The facilitator site journal will be used to record observations, and will be content
20
21 345 analysed to identify key themes, as a part of each PDSA cycle every 21 days.
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25 346 The analysis of the facilitator site field notes will be used to triangulate other
26
27 347 research findings highlighting aspects in need of further investigation. The function
28
29 348 of field notes is to identify processes in a given situation and describe how
30
31 349 participants contribute to, and impact, these [32]. Extracted data will be interpreted in
32
33 350 keeping with Miles and Huberman's approach (2014) using field notes who propose
34
35 351 an analysis of systematic coding, word by word, presenting the data visually to
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37 352 identify patterns [33] .
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42 353 *Data monitoring*
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45 354 Data monitoring will ascertain high data quality, ensure rigour and mitigate biases.
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49 355 Data monitoring will be done through three processes:
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53 356 1. Quantitative data will be double entered for a random sample of 10% records,
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55 357 and all records will be double entered should the error rate be greater than
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57 358 5%.
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3 359 2. Monthly meetings with expert facilitators who are not involved with the project
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5 360 to reflect on the implementation and evaluation of the project.

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8 361 3. Supervision and oversight by the study team not directly involved in the
9
10 362 process of implementation.

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13 363 *Ethical Considerations:*

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16 364 This project has received ethical approval from the Royal Brisbane and Women's
17
18 365 Hospital Human Research Ethics Committee number HREC/16/QRBW/100.

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22 366 *Safety considerations*

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25 367 The main purpose of the secondary outcome measures of the intervention is to
26
27 368 measure the safety of using this implementation approach. A potential safety issue
28
29 369 is that when patients complete the PROMs they expect that staff will act on that
30
31 370 information. If the implementation is not successful, staff may not do this in a timely
32
33 371 fashion or at all, and patients who report symptoms may not receive suitable
34
35 372 treatment. Any such issues where a PROMs report was not acted on will be noted
36
37 373 and described using the data collection tools for the project. The facilitator will raise
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39 374 any issues where patient safety is at risk.

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45 375 *Data deposition and curation:*

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48 376 All de-identified data will be stored on a REDCap database, on a secure university
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50 377 server. Patient information will be stored on their medical record, and hospital-based
51
52 378 servers that are password protected. Data will be stored for 5 years. A formal data
53
54 379 management plan has been developed and approved by the Queensland University
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56 380 of Technology Research Unit.

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3 381 *Dissemination of results*
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6 382 Results will be disseminated in peer-reviewed publications, and presented at
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9 383 national and international scientific meetings.
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16 385 *Discussion:*
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19 386 This study proposes that successful implementation of PROMs requires
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21 387 sophisticated attention to the local clinical setting and existing clinical workflows, and
22
23 388 can overcome barriers previously experienced in other settings by following a pre-
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25 389 specified implementation approach with an experienced facilitator. It is important to
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27 390 investigate implementation strategies as clinical trials have demonstrated significant
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29 391 benefits for patients, but also reported the difficulties of using PROMs in complex
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31 392 health systems outside the highly structured context of a clinical trial. Systematic
32
33 393 reviews recommend a structured implementation approach that considers the many
34
35 394 elements present in the health system into which PROMs are introduced. The use of
36
37 395 the iPARIHS framework with the MRC Guidelines for Implementation of Complex
38
39 396 Interventions, built upon the work of ISOQOL, offers an implementation strategy that
40
41 397 addresses the issues identified in the research to date. This study offers an
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43 398 opportunity to scientifically measure implementation, potentially rapidly implement
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45 399 PROMs into clinical practice and to inform future research and clinical practice.
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52 400 Trial Status: Opened on 25 March 2018 and will continue until 12 months after the
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54 401 last PROMs reporting encounter.
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58 402 References:
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23 412 *facilitators and barriers*. Palliat Med, 2014. 28(2): p. 158-75.
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56 450 *framework for the successful implementation of knowledge into practice.*
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59 499 protocol development.
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35
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37
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39
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41
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33 532 There are none to declare
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BMJ Open

The iPROMOS Protocol: A Stepped-Wedge Study to Implement Routine Patient Reported Outcomes in a Medical Oncology Outpatient Setting

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Manuscripts

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2
3 54 Abstract:
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5 55 Introduction: Patient Reported Outcomes (PROMs) are data capture tools that collect
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8 56 information directly from patients. Several large research studies provide evidence
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10 57 that use of PROMs in routine care provides benefits to mortality and morbidity
11
12 58 outcomes in medical oncology patients. Despite this, implementation of PROMs in
13
14 59 daily clinical routine is slow and challenging.

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18 60 Methods and Analysis: This study will use a stepped-wedge design to assess the
19
20 61 implementation of a PROM intervention in highly frequented medical oncology
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22 62 outpatient clinics. During a lead-in period of four weeks, control data will be
23
24 63 collected. The intervention will then be implemented for four weeks in Clinic 1
25
26 64 initially, then in Clinic 2 for another four weeks. 500 patient encounters will be
27
28 65 measured over the 12 weeks in total. The process of implementation will be informed
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30 66 and evaluated using the Medical Research Council (MRC) Guidelines for
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32 67 Implementing Complex Interventions. The study will be guided by the iPARIHS
33
34 68 framework approach to implementation. The intervention and implementation
35
36 69 outcomes will be measured using qualitative and quantitative data.

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42 70 Ethics and Dissemination: Ethical approval has been obtained, approval number
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44 71 HREC/16/QRBW/100 by the Royal Brisbane and Women's Hospital Human
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46 72 Research Ethics Committee. Results will be disseminated in peer reviewed journals
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48 73 and at scientific meetings.

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52 74 Trial Registration Number: Australian New Zealand Clinical Trials Registry
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54 75 (ANZCTR): ACTRN12618000398202.
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77 Article Summary:

78 Strengths and limitations of this study

79 Limitations:

- 80 • One non-blinded researcher will implement the intervention, collect and
81 analyse the data.
- 82 • Response bias and social desirability bias (of both health professionals and
83 patients that choose to participate)
- 84 • Bias by the Hawthorne Effect whereby clinics being observed during the pre-
85 implementation phase may start to change practice.

86 Strengths

- 87 • A stepped-wedge design ensures an incremental implementation into clinical
88 practice.
- 89 • Prospective use of an implementation framework will make sure that enablers
90 and barriers in the setting are collected and reported allowing the findings
91 from this study to inform future integration of PROMs into routine clinical care.

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3 95 Introduction:
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6 96 *What are Patient Reported Outcome Measures (PROMs)?*
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10 97 The Federal Drug Administration (FDA) defines PROMs as “any report of the status
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12 98 of a patient’s health condition that comes directly from the patient, without
13
14 99 interpretation of the patient’s response by a clinician or anyone else” [1]. Revicki et al
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17 100 (2000) describe PROMs as validated self-reporting assessment tools that capture
18
19 101 the patient experience [2]. PROMs have been extensively evaluated for their
20
21 102 sensitivity, specificity, overall accuracy and predictive value. They are now regarded
22
23 103 to have excellent precision, similar to many other widely-used clinical assessment
24
25 104 tools including pathological tests or medical imaging reports [3]. PROMs can provide
26
27 105 an overview of a patient’s physical, emotional, functional or overall health status, or
28
29 106 can be used to assess specific treatment outcomes or symptoms [4].
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34 107 *PROMs in clinical practice*
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38 108 PROMs are commonly used as outcome measures in research. However more
39
40 109 recently there is evidence that their real-time application in clinical practice can
41
42 110 enhance clinical interactions and improve patient experience. Several studies have
43
44 111 shown that using PROMs in routine care leads to improved quality of life (QOL) [3, 5]
45
46 112 as well as improved communication, decision-making, care planning and patient
47
48 113 satisfaction [6-8]. Two recent studies demonstrated improvements in patient mortality
49
50 114 and morbidity when technology-facilitated PROMs data collection was incorporated
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53 115 in oncology care [5, 9, 10].
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3 116 Given these evidence-based benefits, translating these findings into practice by
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5 117 integrating PROMs into routine clinical care is the next required step in the
6
7 118 implementation cycle.
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10 11 119 *The Complexities of Implementing PROMs into the Clinical Setting* 12

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14 120 A number of systematic reviews [3, 11, 12] reported that multiple organisational,
15
16 121 technical and clinical factors need to be overcome before introducing PROMs. In
17
18 122 particular, a lack of engagement from health care professionals, concerns about the
19
20 123 workflow of generating and filing of PROM reports, and lack of clearly defined
21
22 124 approaches in how to respond to the PROM data that indicate a patient need (e.g.
23
24 125 elevated pain or depression) have been identified as barriers to successful
25
26 126 implementation. The International Society of Quality of Life (ISOQOL) advocates a
27
28 127 stepwise approach to implementing PROMs, and provides a User's Guide [13],
29
30 128 which was updated in 2018. Klinkhammer-Schalke (2014) identified that a stepwise
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32 129 approach was most useful when integrating a PROM intervention into routine care,
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34 130 as it allows cycles of iterative learning during the implementation [7].
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41 131 Incorporating PROMs into clinical practice should be considered a complex
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43 132 intervention, with many elements impacting on the intervention, and vice versa [14]
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45 133 Given these complexities, it has been recommended to use an implementation
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47 134 framework to increase the likelihood of success when aiming to integrate PROMs
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49 135 into routine care [15]. Use of a framework approach can help to consider both the
50
51 136 processes and intended outcomes of implementation. The Promoting Action
52
53 137 Research in Health Services (i-PARIHS) framework appears well suited, as it
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55 138 highlights elements for consideration within the context (e.g. the features of the
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57 139 particular clinic in which PROMs are to be integrated), the stakeholders (e.g.
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3 140 patients, clinicians, administrative staff) impacted by the intervention, and the
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5 141 evidence surrounding the intervention (e.g. how much do stakeholders value the new
6
7 142 PROM information presented to them) [16]. A unique feature of iPARIHS is that it
8
9 143 stresses the central importance of a facilitator, who works with the local stakeholders
10
11 144 to adapt the evidence-based intervention for the local context. Antune's (2014)
12
13 145 systematic review provided evidence for the important role of a facilitator of the
14
15 146 implementation process [3], with enhanced successful uptake if one was present
16
17 147 [17,18]. For example, Baskerville et al (2012) showed that medical practices were
18
19 148 2.76 more likely to adopt evidence-based guidelines when a facilitator was working
20
21 149 in the local context [17].
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27 150 Besides the implementation framework, the Medical Research Council (MRC)
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29 151 Guidelines for Implementation of Complex Interventions can provide guidance on
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31 152 how to best incorporate pre-specified process measure. The Guidelines "can be
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33 153 used to assess fidelity and quality of implementation, clarify causal mechanisms and
34
35 154 identify contextual factors associated with variation in outcomes" [18]. The MRC
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37 155 approach ensures active evaluation throughout the implementation, and highlights
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39 156 how to mitigate the impact that the introduction of new workflows has on the context,
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41 157 participants and the intervention.
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47 158 In summary, the aim of this implementation study is to investigate implementation of
48
49 159 symptom reporting PROMs system into the outpatient oncology setting. The
50
51 160 objective of the intervention will be to increase detection of symptoms by clinicians
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53 161 using the PROMs data. The implementation objectives include the successful
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55 162 engagement of clinicians to use PROMs in clinical practice, the successful use of
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3 163 technology to obtain PROMs data from patients and present reports to clinicians,
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5 164 and the identification of appropriate local strategies to respond to PROM information.
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9 165 Methods and Analysis:

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12 166 *Study design*
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16 167 This mixed-methods study will use a stepped wedge cluster design. PROMs will be
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18 168 introduced sequentially into two independent clinics, and all intervention and
19
20 169 implementation outcomes will be prospectively evaluated. The stepped wedge
21
22 170 approach has been chosen as it is a pragmatic solution for the systematic
23
24 171 introduction of a complex intervention [19], and has been successfully used in a
25
26 172 number of studies related to service delivery improvements [20, 21]. Another
27
28 173 advantage of this study design is that it limits bias by randomly assigning the clinics
29
30 174 to the intervention in sequential order. There are key elements that require attention
31
32 175 with this study design including the consideration of timing of study time-points,
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34 176 cluster equivalence within the setting and intervention uptake assessed by process
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36 177 measures [22, 23].
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42 178 The first clinic will be observed during a current standard practice lead-in period for
43
44 179 four weeks, then introduced into the iPROMOS intervention, while the other clinic will
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46 180 continue with current standard practice and await implementation of iPROMOS. Data
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48 181 collection and intervention time-points are presented Table 1.
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52
53 182 Table 1: Cluster stepped-wedge study design for iPROMOS
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Timepoint	T1 (weeks 0-4)	T2 (weeks 4-8)	T3 (weeks 8-12)
Clinic 1	Control Data	Intervention	Intervention
Clinic 2	Control Data	Control Data	Intervention

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3 183 This protocol was co-designed with clinicians, academics and patient
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5 184 representatives. The iPROMOS intervention was informed by pre-implementation
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7 185 data collected from health professionals and relevant local stakeholders (Table 2).
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9 186 Reporting will follow Standards for Reporting Implementation Studies (StaRI)[24].
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13 187 Table 2: Summary of pre-implementation information and how it informed
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15 188 implementation design
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Aim	Data collected	Description of Findings	Implementation strategies
To engage health professionals and patients	Physical environment mapped Field notes Focus groups/interviews with multi-disciplinary team members and patient representatives of enablers and barriers Staff survey of knowledge modelled on Rouette's (2015) assessing knowledge about PROMs including facilitators and barriers [25], PROMs data format, enablers and barriers. Questions are scored on a Likert scale with questions such as "My understanding	The physical environment is busy but movement of patients, staff and medical records is established There are many established treatment pathways for patient care based on disease group, stage of disease and treatment regimen Previous interventions have been unsuccessful due to a lack of collaboration with staff and patients Knowledge about PROMs and current evidence is different across health discipline groups	Touch-screen computers will be positioned for easy access by patients as they enter the clinic area PROMs reports will be made available to staff prior to patient encounter PROMs data entry design, and equipment was sourced in collaboration with consumer representatives Information resources were developed in collaboration with staff and patient representatives, including posters, information sheets, staff brochures and inservice material

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<p>of PROs is...(very poor, poor, fair, good, very good)", "My lack of understanding of PROs is a barrier to using them in clinical practice (almost never, rarely, sometimes, often, almost always)"</p>		
<p>To effectively incorporate technology</p> <p>Field notes</p> <p>Map of Information Technology Systems that interact with patient care, including the physical environment</p>	<p>Many electronic medical records systems interact with patients and staff but not with each other. If PROMs data becomes a report it can be stored as such in the patient's medical record</p> <p>Paper-based reports can be more easily integrated into patient records</p> <p>Development of a system specific for each individual health service is expensive and time consuming. It is unclear whether this would be integrated into current IT systems, or become another log on for staff, which reduces their likelihood of engagement. No ready-made system could be identified for purchase.</p>	<p>A simple electronic data capture system (REDCap) will be used to collect PROMs data and generate reports. A simple set-up provides the flexibility needed for integration and implementation whilst ensuring the fidelity of the intervention.</p> <p>Developing/funding a more sophisticated platform for collecting PROMs from patients can be informed by the successful implementation process.</p>
<p>To manage and respond to PROMs data</p> <p>Focus groups/interviews and field notes to map referral and</p>	<p>Reports can inform referrals, in the format of documentation in the medical record, verbal communication or by email.</p>	<p>Alerts criteria will be generated directly to the appropriate specialist nurse and allied health</p>

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<p>communication pathways</p> <p>iPARIHS Context assessments of clinical areas [15]</p>	<p>The best approach needs to be identified with the relevant clinical team/area.</p> <p>Symptom assessment by clinicians uses CTCAE v4.0 as standard practice. CTCAE is the Common Terminology Criteria for Adverse Events, developed by the US Department of Health and Human Services which offers universal assessment and grading of symptoms of disease and treatment</p> <p>Allied health and specialist nurse roles are in place for management of specific symptoms</p>	<p>team member to integrate into their practice.</p> <p>PROMs reports will be used to inform assessment and clinical decision making</p>
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189 *Patient and Public Involvement:*

190 The process of consumer engagement through protocol development informed the
 191 research question and study protocol. Consumer representatives within the health
 192 services, and on a research advisory group were approached to discuss the project.
 193 They confirmed a need for patient self-reporting of symptoms that are integrated into
 194 routine care. Their reports would need to be available to staff so that their concerns
 195 could be actioned. During the development of the protocol, consumer
 196 representatives were involved in the development of patient resources and collection
 197 of pre-implementation data. They also assessed the anticipated burden of the
 198 intervention on patients, and this will continue to be evaluated with consumer input
 199 through the study. This will be done through PDSA cycle evaluation from qualitative
 200 data collected and ongoing consumer representative input.

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3 201 Results will be disseminated on information boards in the health service, and
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5 202 reported back to Consumer Representative forums.
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9 203 *Key features of the intervention:*
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12 204 Based on the published evidence [5] and data from local clinicians as summarised in
13
14 205 Table 2, the PRO-CTCAE was selected as the PROM to be implemented, as it was
15
16 206 developed to extend an assessment by clinicians using the CTCAE [26], and has
17
18 207 been demonstrated to provide significant benefits for patient care and outcomes [10].
19
20 208 PRO-CTCAE is a validated (119 of 124 items met at least 1 construct validity
21
22 209 criterion) symptom-reporting PROM that has been demonstrated to be reliable (test-
23
24 210 retest was 0.7 or greater for 39 of 49 pre-specified terms) and responsive (item
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26 211 changes corresponded to the QLQ C-30 scale) [27]. There are a number of studies
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28 212 that have demonstrated that the PRO-CTCAE is acceptable to patients from differing
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30 213 cancer populations internationally [28,29]. This PROM allows patients to report how
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32 214 much they experience each symptom, and the impact on their daily activities, on a
33
34 215 five-point Likert scale (ranging from 'none' to 'very much'). The core set of questions
35
36 216 includes anorexia, constipation, dyspnoea, diarrhoea, fatigue, nausea, pain, sensory
37
38 217 neuropathy, vomiting, cough, low mood and anxiety. Basch's (2016) study used a
39
40 218 weekly completion schedule on an app with alerts sent to clinicians in real-time [5].
41
42 219 However, use of apps for patient reporting was not compatible with the health
43
44 220 service's patient confidentiality policy. The intervention was adapted to include
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46 221 PROM reporting only during scheduled attendances for outpatient clinic
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48 222 appointments. Thus, reporting to clinicians will occur in line with existing clinic visits,
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50 223 which may be weekly or less frequently depending on cancer diagnosis, stage and
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52 224 treatment regimen. PROMs reports will be made available for health professionals to
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3 225 view and respond to. This could include referring the patient to allied health or
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5 226 supportive care, counselling, or additional pharmacological support (e.g. adjusting
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7 227 pain medications). PROMS will be added in paper format to the patient chart, and in
8
9 228 keeping with local practice, will be scanned into the electronic medical record at a
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11 229 later date.
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16 230 In summary, the iPROMOS intervention consists of, a) patients self-reporting
17
18 231 symptoms (PRO-CTCAE PROM) using a touchscreen computer with data captured
19
20 232 on a custom-built REDCap database; b) reports of this information are generated in
21
22 233 real time; c) these reports are available to all healthcare team members and filed in
23
24 234 the patients' medical record; and, d) a copy of the report is also provided to the
25
26 235 patient. Usual care is clinician assessment of symptoms without the additional use of
27
28 236 a PROM.
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33 237 In the co-design process, using the broader research evidence, investigated to
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35 238 support clinician's recommendations, a reported symptom of grade 2 or higher for
36
37 239 nausea, vomiting or anorexia, and grade 3 for all other symptoms is considered
38
39 240 significant [5]. If there is an increase in symptoms greater than 2 points from the
40
41 241 previous visit, this will also trigger a referral by established pathways to the relevant
42
43 242 allied health professional.
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48 243 *Setting of the implementation:*
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51 244 This project will be conducted in a tertiary teaching/quaternary referral hospital-
52
53 245 located in South-East Queensland, Australia. The health service for this centre is
54
55 246 the largest in Australia, with the oncology outpatients' department running up to 14
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3 247 clinics in one day. Each of these clinics are oncologist specific, providing service for
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5 248 treatment, surveillance and follow-up for the patients in their care.
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9 249 Contextual pre-implementation information has revealed key factors for successful
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11 250 integration of the intervention (Table 2). Most importantly, the intervention needs to
12
13 251 engage all members of the multi-disciplinary team and the staff who will have access
14
15 252 to the PROM information to address symptoms, disease management and
16
17 253 treatment. To make this likely, the facilitator will aim to integrate the PROM collection
18
19 254 and reporting as much as possible into the existing workflow processes already in
20
21 255 place at the clinic. Evidence shows that workflows differ greatly between hospitals
22
23 256 and even within clinics in a hospital, and that staff are reluctant to change anything
24
25 257 that interrupts established practice, given the very complex environment they are
26
27 258 managing [30]. They are only willing to take on a new intervention when the benefits
28
29 259 and processes for patient care are tangible and clear. For successful
30
31 260 implementation, it has been identified that it is necessary to integrate with existing
32
33 261 patient care pathways and technological infrastructure, rather than impose another
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35 262 layer, which would likely be met with resistance [30].
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42 263 *Participants:*
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46 264 This study will collect data from two main groups of participants: a) patients; and b)
47
48 265 the clinicians caring for them.
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51 266 a) *Patients* who attend the randomised medical oncology outpatients' clinics for
52
53 267 treatment, medical review, active surveillance, or routine follow-up, with
54
55 268 sufficient English to read the questionnaires. Patients with significant
56
57 269 cognitive impairment, visual difficulties, or from a non-English speaking
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3 270 background who might have difficulty completing the forms will be excluded
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5 271 from the study.
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9 272 *Patient Screening and Recruitment:* Patients attending selected clinics will be
10
11 273 invited to the use touchscreen computer to complete PROM information. The
12
13 274 first page of the PROM collection form provides a Patient Information Sheet
14
15 275 and Consent form. Potential participants will need to read the information and
16
17 276 accept to enter PROM reporting platform. If they do not wish to, they can
18
19 277 choose to decline. Patient information will also be visible on a poster
20
21 278 displayed in the clinical waiting area.
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26 279 b) *Staff* who care for these patients' including nursing and medical staff,
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28 280 pharmacists, dietitians, welfare workers, social workers, psychologists,
29
30 281 speech therapists, physiotherapists and other allied health workers are
31
32 282 eligible.
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36 283 *Staff participation:* an opt-out approach to consent staff has been approved by
37
38 284 the ethics committee. Multidisciplinary staff will be contacted using various
39
40 285 communication channels, directly by the facilitator-researcher to collect pre-
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42 286 implementation information, as well as through distribution of information
43
44 287 brochures and poster developed in collaboration with the clinical teams.
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49 288 *Methods of evaluation:*
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52 289 *Process Measures used for implementation evaluation:*
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54 290 Table 3: Process Measures of Implementation Evaluation
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Process measuring tool	Method of collection	Approach to analysis

<p>Context:</p> <ol style="list-style-type: none"> 1. Description of factors impacting and impacted 2. Description of barriers and enablers 	<p>Facilitator field notes and site journal</p>	<p>Qualitative: content analysis for a structured analysis</p>
<p>Feasibility:</p> <ol style="list-style-type: none"> 1. Number of patients that approached the touchscreen computer without prompting 2. Time taken to complete PROM by patients 3. Time required to assist patients complete PROM 4. Number of return completions by patients 5. Time taken to respond to report by staff 	<p>Counts Data from data-capture program Self-report by staff Field notes</p>	<p>Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis</p>
<p>Fidelity:</p> <ol style="list-style-type: none"> 1. Number of missing encounters by patients 2. Number of missing case report forms 3. Reasons for missing data 	<p>Counts Case report form data Field notes</p>	<p>Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis</p>
<p>Reach:</p> <ol style="list-style-type: none"> 1. Number of staff that answered “yes” to whether they knew about the implementation 2. Number of staff that stated that required education about PROMs 3. Number of staff that independently used PROMs report 	<p>Counts Case report form data Field notes</p>	<p>Quantitative: descriptive statistics Qualitative: content analysis for a structured analysis</p>

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4. Staff groups that responded to PROMs data

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293 In accordance with the MRC Guidelines for Complex Interventions the iterative
294 implementation will be evaluated using both quantitative and qualitative process
295 measures as described in Table 3.

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296 Following the iPARIHS framework, data will be collected by the facilitator who works
297 closely within the context. In this protocol, the facilitator will collect and use process
298 measures, with protocol-specified data collected at pre-specified time-points (Table
299 4).

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300 Plan Do Study Act Cycles (PDSA) will be performed every 21 days as an interim
301 data analysis to evaluate progress, and to report these findings to clinicians so that
302 collaborative strategies can be established that maximise implementation. The
303 purpose of each PDSA cycle is to summarise and reflect on the implementation
304 process and improve it for the next cycle [16].

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306 *Outcomes of the implementation:*

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307 Table 4: Outcomes of the implementation

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Outcome Measure	Method of Data Collection	Approach to analysis
% patients completing PROM form	Nominator of PROMs in electronic data capture; denominator of booking schedule of patients that	Quantitative: Descriptive Statistical Analysis; longitudinal analyses of % change. Qualitative: Content analysis

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	attended clinic; facilitator field notes of reasons for any missing data	
% staff acknowledging PROM data	Case report forms; facilitator field notes	Quantitative: Descriptive Statistical Analysis; longitudinal analyses of % change. Qualitative: Content analysis
% PROMs in medical record	Communication in the medical record; completed PROMs in electronic data capture; referral data	Quantitative: Descriptive Statistical Analysis Qualitative: Content analysis
Acceptability of PROM reporting for staff and patients	Staff survey Focus groups, interviews and field notes	Quantitative: Descriptive Statistical Analysis Qualitative: Content Analysis to identify themes and interpret

308

309 The primary outcome of interest is successful implementation, and has been
 310 operationalised as “PROM reports are made available to clinicians in 85% of
 311 encounters, 70% of clinicians will respond to PROM data, and of those 50% of
 312 responses will be noted in the patients’ medical record”. This was selected as other
 313 studies reported that clinicians and patients are satisfied at such level of service
 314 when use is identified as feasible and acceptable [31, 32].

315 Secondary outcomes will measure patient and staff acceptance. Staff surveys will be
 316 distributed at the end of the PROMs data collection to capture change from baseline
 317 in staff knowledge, and identified facilitators and barriers.

318 *Outcomes of the intervention:*

319 Table 5: Outcome Measures of the Intervention

Outcome Measure	Methods of collection	Approach to analysis
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Symptoms assessment by clinicians	Medical record entries, case report forms	Comparison of proportion of patients with symptom assessment between intervention and control group using chi-square test
Response to symptom information	Medical record entries, case report forms	Proportion of patients referred for supportive care interventions compared between intervention and control groups using chi-square test
Change in symptom reporting and responding from pre-intervention to during intervention	Medical record entries, case report forms, PROM electronic data capture	Proportion of patients before to during intervention period using chi-square analysis and process control analysis
Presentations to the emergency department	Medical record entries	Proportion of patients before to during intervention period using chi-square analysis and process control analysis
Hospital admissions	Medical record entries	Proportion of patients before to during intervention period using chi-square analysis and process control analysis

320

321 The primary outcome measure of the intervention will be counts of health
 322 professional notes in the patients' chart about a symptom being of concern (for
 323 example pain). As well as this, the response to such symptoms will be recorded (e.g.
 324 referral to pain specialist).

325 Secondary outcomes will be an improvement in patient quality of life, presenting as a
 326 clinically significant reduction in measured symptoms. More detailed explanation of
 327 outcome measures is provided in Table 5.

328 *Sample size:*

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3 329 Berry et al (2014) conducted an RCT which compared symptom reports between
4
5 330 clinics using an electronic reporting tool. They assessed both processes and
6
7 331 outcomes of care, comparing the impact of PROM reports between the control and
8
9 332 intervention clinics. It was used to guide the sample size calculations because this
10
11 333 study measured the identification of symptoms in usual care versus a symptom-
12
13 334 PROMs intervention. To obtain an estimate of a minimal number of observations that
14
15 335 should be included in each cluster in this study, Berry et al's (2014) results were
16
17 336 used [33]. These researchers identified that a PROMs intervention increased
18
19 337 symptom detection by 10%. Using these findings, and 80% power, given a baseline
20
21 338 detection level of 0.75, 500 participant encounters would be needed to show
22
23 339 improvement by 10% or more.
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30 340 Methods of Analysis:

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33 341 *Quantitative analyses:* Quantitative measures have been designed for the process
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35 342 measures of implementation evaluation, the outcome measures of the
36
37 343 implementation and the outcome measures of the intervention. Descriptive statistics
38
39 344 including counts, frequencies and proportions will be used to summarize data
40
41 345 collected. Other statistical analyses to be used will include chi-square analysis for
42
43 346 comparing proportions, linear mixed models for longitudinal analyses, and statistical
44
45 347 control process analysis to identify trends over time.
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49 348 Data from both clusters will be analysed using inverse variance weighting so that the
50
51 349 difference can be estimated for all patient encounters. This analysis can be used to
52
53 350 adjust for cancer types, or clustering by clinicians [34]. This analysis will provide a
54
55 351 measure of the intra-cluster effect, which can then be used for power calculations in
56
57 352 future larger studies [35].
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3 353 *Qualitative data:*
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7 354 The facilitator site journal will be used to record observations, and will be content
8
9 355 analysed to identify key themes, as a part of each PDSA cycle every 21 days.
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12 356 The analysis of the facilitator site field notes will be used to triangulate other
13
14 357 research findings highlighting aspects in need of further investigation. The function
15
16 358 of field notes is to identify processes in a given situation and describe how
17
18 359 participants contribute to, and impact, these [36]. Extracted data will be interpreted in
19
20 360 keeping with Miles and Huberman's approach (2014) using field notes who propose
21
22 361 an analysis of systematic coding, word by word, presenting the data visually to
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24 362 identify patterns [37] .
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29 363 *Data monitoring*
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33 364 Data monitoring will ascertain high data quality, ensure rigour and mitigate biases.
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36 365 Data monitoring will be done through three processes:
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40 366 1. Quantitative data will be double entered for a random sample of 10% records,
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42 367 and all records will be double entered should the error rate be greater than
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44 368 5%.
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46
47 369 2. Monthly meetings with expert facilitators who are not involved with the project
48
49 370 to reflect on the implementation and evaluation of the project.
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51 371 3. Supervision and oversight by the study team not directly involved in the
52
53 372 process of implementation.
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57 373 *Ethical and dissemination:*
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3 374 This project has received ethical approval from the Royal Brisbane and Women's
4
5 375 Hospital Human Research Ethics Committee number HREC/16/QRBW/100.
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9 376 *Safety considerations*

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11
12 377 The main purpose of the secondary outcome measures of the intervention is to
13
14 378 measure the safety of using this implementation approach. A potential safety issue
15
16 379 is that when patients complete the PROMs they expect that staff will act on that
17
18 380 information. If the implementation is not successful, staff may not do this in a timely
19
20 381 fashion or at all, and patients who report symptoms may not receive suitable
21
22 382 treatment. Any such issues where a PROMs report was not acted on will be noted
23
24 383 and described using the data collection tools for the project. The facilitator will raise
25
26 384 any issues where patient safety is at risk.
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32 385 *Data deposition and curation:*

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35 386 All de-identified data will be stored on a REDCap database, on a secure university
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37 387 server. Patient information will be stored on their medical record, and hospital-based
38
39 388 servers that are password protected. Data will be stored for 5 years. A formal data
40
41 389 management plan has been developed and approved by the Queensland University
42
43 390 of Technology Research Unit.
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48 391 *Dissemination of results*

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51 392 Results will be disseminated in peer-reviewed publications, and presented at
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53 393 national and international scientific meetings.
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3 395 *Discussion:*
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6 396 This study proposes that successful implementation of PROMs requires
7
8 397 sophisticated attention to the local clinical setting and existing clinical workflows, and
9
10 398 can overcome barriers previously experienced in other settings by following a pre-
11
12 399 specified implementation approach with an experienced facilitator. It is important to
13
14 400 investigate implementation strategies as clinical trials have demonstrated significant
15
16 401 benefits for patients, but also reported the difficulties of using PROMs in complex
17
18 402 health systems outside the highly structured context of a clinical trial. Systematic
19
20 403 reviews recommend a structured implementation approach that considers the many
21
22 404 elements present in the health system into which PROMs are introduced. The use of
23
24 405 the iPARIHS framework with the MRC Guidelines for Implementation of Complex
25
26 406 Interventions, built upon the work of ISOQOL, offers an implementation strategy that
27
28 407 addresses the issues identified in the research to date. This study offers an
29
30 408 opportunity to scientifically measure implementation, potentially rapidly implement
31
32 409 PROMs into clinical practice and to inform future research and clinical practice.
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40 410 Trial Status: Opened on 25 March 2018 and will continue until 12 months after the
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42 411 last PROMs reporting encounter.
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45 412 *References:*
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28
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59 533 Contributorship statement:

1
2
3 534 NR and MJ drafted the protocol for this publication. AM contributed significantly to
4
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6
7
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56 554 Competing interests statement:

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59 555 There are none to declare
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For peer review only