PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Active Surveillance of Chemotherapy-Related Symptom Burden in Ambulatory Cancer Patients via the Implementation of Electronic Patient Reported Outcomes and Sensor-enabled Vital Signs Capture – Protocol for a Decentralized Feasibility Pilot Study
AUTHORS	Offodile, Anaeze; DiBrito, Sandra; Finder, Janice; Shete, Sanjay; Jain, Sanchita; Delgado, Domenica; Miller, Christopher; Davidson, Elenita; Overman, MJ; Peterson, Susan

VERSION 1 – REVIEW

REVIEWER	Bradford, Natalie Queensland University of Technology, Cancer and Palliative Care Outcomes Centre
REVIEW RETURNED	08-Nov-2021

GENERAL COMMENTS	The objectives of the protocol are appropriate for a pilot, study to identify the feasibility of recruitment, acceptability and implementation of the intervention, as well and enable a sample size calculation to be determined for a future trial. The measures described are appropriate for the aims. The study protocol is clear and easy to read and includes a description of patient and public involvement for the study, as well as ethical considerations. I have only a few minor comments/suggestions 1. There is a disconnect between the title, abstract and body of the document in that abstract describes collecting symptom information, but not the use of sensor enabled, or biometric digital monitoring devices. Please include the addition of these details to the abstract also. 2. Page 8 line 10- sentence: 'Furthermore, the American Society of Oncology (ASCO) has strongly advocated for the increased integration of information technology into patient care.' Are you meaning personalised information technology? As general information technology already underpins much patient care 3. There are several typos that require attention: a. Abstract Page 1 Line 22- The sentence not quite complete, missing a descriptive noun – I suggest – "single-arm feasibility pilot study of technology-enhanced outpatient chemotherapy symptom management intervention or system b. Introduction page 7, line 24: … in these clinical settings have been associated with reduced

REVIEWER	Richards, Hollie University of Bristol, Population Health Sciences
REVIEW RETURNED	10-Nov-2021

GENERAL COMMENTS	This protocol outlines an interesting and important feasibility study which will contribute to enhancing the field of electronic monitoring for cancer patients using patient reported outcomes and biometrics. I have made some minor comments and queries, outlined below: 1. The authors state that to the best of their knowledge there are no similar clinical trials using biometrics and symptom burden measures. Could I draw the authors attention to the following publication which, although it doesn't use biometric measures, may be useful: Absolom et al 2021 Phase 3 Randomized Controlled Trial of eRAPID: eHealth Intervention During Chemotherapy. Journal of Clinical Oncology https://pubmed.ncbi.nlm.nih.gov/33417506/ 2. Patient population: The authors state they will recruit at least three patients from ethnic minorities. I'm unfamiliar with ethnic demographics of the area - is 12% a representative sample? 3. Exclusion criteria: Are the authors able to provide a definition of 'physical disability' as an exclusion criteria? This population is likely to be impaired by their condition and it would be useful to have a clearer outline of what level of impairment would exclude a patient from inclusion. 4. The authors state that the 'thresholds' for scores that will generate email alerts or outputs will be adapted from the CTCAE. Could the authors provide more detail about how these thresholds will be established and if their validation is part of the feasibility study? For example, will clinical outcomes be used to test and triangulate the threshold scores and the appropriateness of the output they generate? 5. The Vivify platform will be provided to all participants and is an integral part of the RPM system. The authors declare no conflict of interest and no specific funding source supporting this project - are the authors able to clarify and expand on this point (e.g. is the Vivify platform already available to patients as part of standard clinical practice at this Centre?)

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Natalie Bradford, Queensland University of Technology Comments to the Author:
The objectives of the protocol are appropriate for a pilot, study to identify the feasibility of recruitment, acceptability and implementation of the intervention, as well and enable a sample size calculation to be determined for a future trial. The measures described are appropriate for the aims.
The study protocol is clear and easy to read and includes a description of patient and public involvement for the study, as well as ethical considerations.
Authors' Response: We thank Dr. Bradford for taking the time to review our protocol and appreciate her compliments of our design.
I have only a few minor comments/suggestions

1. There is a disconnect between the title, abstract and body of the document in that abstract describes collecting symptom information, but not the use of sensor enabled, or biometric digital monitoring devices. Please include the addition of these details to the abstract also.
Authors' Response: We appreciate Dr. Bradford drawing our attention to the incongruity of the title, abstract and body of the text. We have now harmonized these elements by:
1) Amending the title to "Active Surveillance of Chemotherapy-Related Symptom Burden in Ambulatory Cancer Patients via the Implementation of Electronic Patient Reported Outcomes and Sensor-enabled Vital Signs Capture – Protocol for a Decentralized Feasibility Pilot Study"
2) Reflecting in the abstract that Bluetooth-enabled biometric monitoring devices will be used to capture vital sign information and that these devices are able to integrate with the HIPAA-compliant table interface.
2. Page 8 line 10- sentence: 'Furthermore, the American Society of Oncology (ASCO) has strongly advocated for the increased integration of information technology into patient care.' Are you meaning personalized information technology? As general information technology already underpins much patient care

Authors' Response: We agree with Dr. Bradford that IT is already heavily integrated, and as she correctly assumed, we were insinuating personalized IT for both the inpatient and outpatient settings. We have specified these details in the introduction section to make our reference less vague.
3. There are several typos that require attention:
a. Abstract Page 1 Line 22- The sentence not quite complete, missing a descriptive noun – I suggest – "single-arm feasibility pilot study of technology-enhanced outpatient chemotherapy <u>symptom management intervention or system</u></i
Authors' Response: We have updated this sentence.
b. Introduction page 7, line 24: … in these clinical settings have been associated <u>with</u> reduced
Authors' Response: We have updated this sentence.

Reviewer: 2
Mrs. Hollie Richards, University of Bristol Comments to the Author:
This protocol outlines an interesting and important feasibility study which will contribute to enhancing the field of electronic monitoring for cancer patients using patient reported outcomes and biometrics. I have made some minor comments and queries, outlined below:
Authors' Response: We thank Mrs. Richards for taking the time to review our manuscript and for facilitating improvement by providing thoughtful questions.
1. The authors state that to the best of their knowledge there are no similar clinical trials using biometrics and symptom burden measures. Could I draw the authors attention to the following publication which, although it doesn't use biometric measures, may be useful:
Absolom et al 2021 Phase 3 Randomized Controlled Trial of eRAPID: eHealth Intervention During Chemotherapy. Journal of Clinical
Oncology https://urldefense.com/v3/__https://pubmed.ncbi.nlm.nih.gov/33417506/__;!!PfbeBCCAmug!1IRmJ4A0cXekjzUi9hXGbgR4WrvYkjggWczlFKQ-cglHaAE2eFoTyztyf_k01gwDsZPz$
Authors' Response: We appreciate Mrs. Richards for bringing our attention to this fantastic randomized controlled trial. Their study population, methods, and goals are in line with ours and their findings will certainly be useful to take into account when we evaluate our results, adding biometric measurements and caregiver input to the outcomes of interest.
2. Patient population: The authors state they will recruit at least three patients from ethnic minorities. I'm unfamiliar with ethnic demographics of the area - is 12% a representative sample?
Authors' Response: Thank you for this comment. Given the nature of the present feasibility pilot study, we did not conduct a formal sample size calculation. Our sample size of 25 was informed by the stepped rules of thumb (Whitehead et al. *Stat Methods Med Res*. 2016;25(3):1057–

10). Our goal is to recruit a pilot patient population that is meaningfully diverse with respect to gender, age, and ethnic background. We are not restricting our recruitment to only 3 minority patients; this number reflects the minimal viable number for our small pilot study.
3. Exclusion criteria: Are the authors able to provide a definition of 'physical disability' as an exclusion criteria? This population is likely to be impaired by their condition and it would be useful to have a clearer outline of what level of impairment would exclude a patient from inclusion.
Authors' Response: Our definition of physical disability is with respect to the level of impairment of a patient's ability to use the biometric devices and tablet interface. Examples include but not limited to severe visual, hearing or cognitive impairment which prevent a patient from reading or using the tablets and biometric devices, and inability to stand that would prevent them from using the weight scale. The manuscript has been amended accordingly.

4. The authors state that the 'thresholds' for scores that will generate email alerts or outputs will be adapted from the CTCAE. Could the authors provide more detail about how these thresholds will be established and if their validation is part of the feasibility study? For example, will clinical outcomes be used to test and triangulate the threshold scores and the appropriateness of the output they generate?
Authors' Response: We have now provided the threshold values for PRO-CTCAE scores and biometric values in the amended manuscript (Table 1 below). There are 2 categories of alerts, i.e. red and yellow, which refer to response time. Red alerts denote a call-center communication to the patient within 2 hours and yellow alerts will entail a same-day communication. For alerts generated in response to PRO-CTCAE values, an absolute grade > 3 or worsened by 2 points is a red alert while a grade of 2 is a yellow alert.

Biometric variable	Medium trigger	High trigger
BP Systolic (hypertension)	155- 179	>=180
Systolic (hypotension)	90-99	<=89
Diastolic (hypertension)	101-109	>110
Diastolic (hypotension)	None	None
Oxy sat	<94%	<90%
HR		
Bradycardia	None	<55
Tachycardia	None	>110
Finger stick	<70, >120	<55, > 150
Temp	>100.5,	>102
Weight	None	Loss of 10 lbs

5. The Vivify platform will be provided to all participants and is an integral part of the RPM system. The authors declare no conflict of interest and no specific funding source supporting this project - are the authors able to clarify and expand on this point (e.g. is the Vivify platform already available to patients as part of standard clinical practice at this Centre?)
Authors' Response: Thank for this clarifying question. This project is supported by internal institutional funds at MD Anderson Cancer Care as part of a strategic commitment to expanding our virtual care offerings. Utilization of the Vivify platform is currently limited to the pilot and eventual randomized controlled trial patient populations. It is currently not part of standard clinical practice until evidence of clinical efficacy has been established.

VERSION 2 – REVIEW

REVIEWER	Richards, Hollie University of Bristol, Population Health Sciences
REVIEW RETURNED	22-Feb-2022

GENERAL COMMENTS	Many thanks for responses to the comments, the additions improve the manuscript.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Mrs. Hollie Richards, University of Bristol
Comments to the Author:
Many thanks for your responses to the comments, the additions improve the manuscript.

Response: We appreciate the thoughtful feedback from Mrs. Richards and agree that the overall quality of the manuscript is improved.

Reviewer: 2
Competing interests of Reviewer: No competing interests

Response: We appreciate reviewer #2's feedback which was illustrative of his/hers expertise.