PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A community pharmacy lifestyle intervention to increase physical activity and improve cardiovascular health of men with prostate cancer: a phase II feasibility study
AUTHORS	Lemanska, Agnieszka; Poole, Karen; Griffin, Bruce; Manders, Ralph; Saxton, John M; Turner, Lauren; Wainwright, Joe; Faithfull, Sara

VERSION 1 - REVIEW

REVIEWER	Alexander R. Lucas Wake Forest University School of Medicine United States
REVIEW RETURNED	23-Jul-2018

GENERAL COMMENTS	Overall the paper provides evidence that community-based programs that are less structured than the typical university or academic medical center-based programs can result in positive outcomes for cancer survivors. Strengths of this manuscript are the novelty of the approach, utilizing a variety of settings and commercial business models employed by different pharmacies involved in the project, the involvement of patient advocates in the design of the intervention. Another strength is the web-based platform that forms the foundation for this project, given its already widespread use, which suggests scaling up of the project is feasible. The dropout rate of patients enrolled in the study is a potential limitation, given this was a non-randomized study; however, this is not completely unexpected with a low contact intervention. Overall this is a well-conducted study with clear goals and processes and I commend the authors for their work. I have only a limited number of queries and comments. Major Concerns: 1. None. Abstract 1. The abstract is clearly written and describes the major findings of the study. Conclusions are reasonable. Introduction 2. None Methods

	3. Intervention –an aspect of the intervention was the provision of resistance bands (page 5, line 50-51). While it is understood the primary outcomes for this study were related to feasibility, did the authors capture the typical use-patterns of the strength training component of the intervention? This clearly important for the functional strength of prostate cancer patients and not captured by objective metrics (i.e. accelerometers). There is an adapted version of the Godin questionnaire to capture strength training, though it is not clear whether this is what you used here (page 6, line38-39). Results 4. Adverse events are mentioned as part of the feasibility outcomes, but it is not clear what the rate of adverse events was. Were there reported falls, injuries from testing etc.? 5. Related to the point about capturing strength exercise mentioned above. On page 10, lines 53-55, it is stated that accelerometry is a strength of the study. That is not entirely accurate. Objective measures are important but should not be used alone. It is incorrect to state that they provide the ability to evaluate activity according to the FITT principle. Type of exercise is certainly not always possible to determine via accelerometry. This is important to consider with an older population of individuals, many of whom may get physical activity (of a moderate to vigorous intensity) via activities of daily living and a variety of leisure pursuits (e.g. gardening). The authors may consider mentioning how type of activity likely impacts on adherence as a point for discussion. Discussion 6. Given the wide standard deviation in MVPA and the fact that obese individuals (most of the sample) are less likely to see changes in MVPA, it seems reasonable to consider utilizing a stepped approach or adaptive design for the next iteration of the study. Do obese men require a more intensive dietary intervention up front, before being prescribed exercise or in conjunction with exercise? Given initial characteristics (MVPA) determined change it would be interesting to know how the sample of recruitment men differed from those who declined participation. Do the authors have any sense of this information? Potential interviews with a sample who declined participation? 7. Also related to a future iteration of your intervention, can behavioral counseling be integrated (or automated somewhat) _into the web-based platform to improve the long-term adherence to your protocol?

REVIEWER	Teresa Corbett University of Southampton UK
REVIEW RETURNED	24-Jul-2018

GENERAL COMMENTS	Dear authors, Thank you for giving me the opportunity to review your manuscript. It is a very well-written and interesting paper. I have made some comments below that I hope will help you to improve and clarify some points for the reader. Introduction

	• There is not a lot of background information given about previous studies/theory that may have informed the design of the study- I think this would be useful to set the scene for the reader • The link to CVD is not clear- the authors could elaborate further on why this link is important/ relevant • What role do pharmacists currently play?- what skills do they have that mean that they are well placed to deliver this support? Is it likely to add much to their current role? Methods • How were the pharmacies recruited? • How did you assess MCPA in those who were excluded because they met the CMO guidelines for PA? Were these individuals recruited and excluded after baseline assessments? • On page 6- the paragraph on training could be re-worded to clarify who received the training- was it pharmacists only? Or did the other members of the team (technicians, non-pharmacist team members etc.) also receive training? • Was there an assessment to establish that training was successful and that necessary skills had been obtained? • Was there a fidelity assessment of whether the training was implemented in practice? Outcomes • Were cut-offs for feasibility/ acceptability defined a-priori (E.g. What was a feasible/acceptable rate of recruitment, consent, retention etc.?) • Who administered the outcome measures? Qualitative data • When did the focus groups take place? Pharmacy teams were asked about training- was this interview after training or at the end of the trial? Might this impact how they spoke about the training? • Why did you use focus groups rather than individual interviews? • How did you select the sample of study participants who were interviewed? Quantitative findings • Be careful not to overstate findings of efficacy tests- what do these findings tell us about the feasibility and acceptability of the intervention (apart from establishing sample size for future RCT)? • The sample size mentioned is based on differences rather than predictors- is the sample size adequate for regression analyses? PPI • Who were the volunteers- had they had treatment? How were they recruited? Discussion • Why was randomisation not assessed in this feasibility study? • The description of gender specific barriers is quite vague- why is it important to understand gender specific barriers? • Were there any differences in those receiving or not receiving treatment? Were different approaches used for those who had had treatment vrs those on watchful waiting/active surveillance? What implications might these differences have for intervention delivery? Does this approach possibly work better/ worse for a specific group? • What difference might altruistic participation have on your sample? • Were those who took part possibly healthier than those who did not? • In terms of limitations, the demographics indicate that the majority were white and more than two-thirds of the sample were not deprived. Further 87.9 % were married. Is this due to the area in which the study took place? Or is it an issue in how you

	recruited? How might you remedy this in a future trial- or is it important to do so? • In terms of number of participants recruited per pharmacy- was the number reflective of the size of the pharmacy… or were some pharmacy types better than others? What are the characteristics of those pharmacies that engaged more with the study/ took on more ppts? • What about the cost-effectiveness of an intervention like this? • In your discussion about ppt reaching guidelines, I would suggest that you read some of the work by Nanette Mutrie- She discusses realistic goal setting and incremental improvements as being superior approaches than simply asking sedentary participants to reach guideline expectations.

REVIEWER	Lauren Howard Duke University School of Medicine, USA
REVIEW RETURNED	28-Aug-2018

GENERAL COMMENTS	In this study, Agnieszka et al. present a phase II feasibility study to assess a lifestyle intervention in men with localized prostate cancer. There are a number of statistical issues that must be addressed. 1. It is preferable to report 25th and 75th percentiles over IQR to show the skew of the variables. 2. Why was a formal variable selection technique not used? Did the authors test for collinearity between variables in Table 2? 3. Was the linearity of continuous variables in Table 2 examined? For example, is it appropriate to treat CCI as continuous? 4. Figure 3 is confusing. What are some of the changes significant even though the confidence interval crosses 1? What is the null hypothesis here? Is it appropriate to be looking at mean changes when the change does not seem normally distributed for the measures reported in the Methods. 5. Figure 3 caption: “All significant changes are in a positive direction and are marked with a red marker.” Positive should be changed to favorable to avoid confusion.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1	
Overall the paper provides evidence that community-based programs that are less structured than the typical university or academic medical center-based programs can result in positive outcomes for cancer survivors. Strengths of this manuscript are the novelty of the approach, utilizing a variety of settings and commercial business models employed by different pharmacies involved in the project, the involvement of patient advocates in the design of the intervention. Another strength is the web-	

based platform that forms the foundation for this project, given its already widespread use, which suggests scaling up of the project is feasible. The dropout rate of patients enrolled in the study is a potential limitation, given this was a non-randomized study; however, this is not completely unexpected with a low contact intervention. Overall this is a well-conducted study with clear goals and processes and I commend the authors for their work. I have only a limited number of queries and comments.	
Major Concerns: 1. None.	
Abstract	
1. The abstract is clearly written and describes the major findings of the study. Conclusions are reasonable.	
Introduction	
2. None	
Methods	
3. Intervention –an aspect of the intervention was the provision of resistance bands (page 5, line 50-51). While it is understood the primary outcomes for this study were related to feasibility, did the authors capture the typical use-patterns of the strength training component of the intervention? This clearly important for the functional strength of prostate cancer patients and not captured by objective metrics (i.e. accelerometers).	The standard version of Godin questionnaire was used to capture leisure time physical activity of participants at baseline and 3 months. The median difference in the Godin score of participants was added to Table A1 to document the change in LTPA as an important outcome.
There is an adapted version of the Godin questionnaire to capture strength training, though it is not clear whether this is what you used here (page 6, line38-39).	Paragraph was added to clarify and elaborate based on the comment: An original version of the validated GLTEQ[50] was used in this study. It is a tool used internationally in oncology research to evaluate exercise interventions or assess a relative change in total exercise behaviour.[80] However, item content of the GLTEQ may lead to underreporting of resistance training activities such as those using resistance bands. Adapted GLTEQ versions designed to capture the resistance training have been reported.[81 82]
Results	
4. Adverse events are mentioned as part of the feasibility outcomes, but it is not clear what the rate of adverse events was. Were there reported falls, injuries from testing etc.?	Paragraph added: Adverse events There were no falls or injuries reported as a direct result of any of the research procedures. Three participants were stopped from performing the Siconolfi step test for safety reasons because they reported dizziness during

	the pre-assessment with the physical activity readiness questionnaire (PAR-Q).[62] A further 15 participants were stopped from participating in the Siconolfi step test because their heart rate or blood pressure was above the recommended safety limits (85% of the age-predicted maximum heart rate, 160 mmHg systolic or 110 mmHg diastolic blood pressure). They were referred to their general practitioners (GPs) and no exercise advice was provided.
5. Related to the point about capturing strength exercise mentioned above. On page 10, lines 53-55, it is stated that accelerometry is a strength of the study. That is not entirely accurate. Objective measures are important but should not be used alone. It is incorrect to state that they provide the ability to evaluate activity according to the FITT principle. Type of exercise is certainly not always possible to determine via accelerometry. This is important to consider with an older population of individuals, many of whom may get physical activity (of a moderate to vigorous intensity) via activities of daily living and a variety of leisure pursuits (e.g. gardening). The authors may consider mentioning how type of activity likely impacts on adherence as a point for discussion.	The use of accelerometery for the proposed primary outcome measure is a strength. It provides an objective evaluation of physical activity, with detailed information such as frequency, intensity, time (duration) and type of physical activity (FITT principle).[72] Was changed to: The use of accelerometery for the proposed primary outcome measure is a strength because it provides an objective evaluation of physical activity. Information about frequency, intensity and duration (time) of exercise can be obtained. However, accelerometery provides limited information in particular about the type of physical activity. This is important to consider in light of the FITT principle.[79] With an older population, individuals often get exercise via activities of daily living or leisure (for example walking or gardening). Therefore, to explore the adherence to exercise interventions, the objective measures such as accelerometery should not be used alone. Here, leisure-time physical activity was assessed using the self-reported GLTEQ. Upper-limb and lower-limb strengths were also assessed to objectively capture the potential changes due to the prescribed resistance training. In addition, analysis of men's perceptions and adherence to the intervention were also conducted using qualitative interviews. This is to capture the utilisation of resistance exercise bands and adherence to the strength training element of the intervention. This is important for the functional strength of men but is not captured by accelerometery.
Discussion	
6. Given the wide standard deviation in MVPA and the fact that obese individuals (most of the	Men with higher MVPA levels at baseline, showed no improvement in MVPA over the

sample) are less likely to see changes in MVPA, it seems reasonable to consider utilizing a stepped approach or adaptive design for the next iteration of the study. Do obese men require a more intensive dietary intervention up front, before being prescribed exercise or in conjunction with exercise?	course of the study. In addition, obesity was identified as a barrier to increasing MVPA. Although these men were not achieving recommended MVPA levels, they were potentially able to increase physical activity (in lower levels) and still gain health benefits. Was changed to Men with higher MVPA levels at baseline, showed no improvement in MVPA over the course of the study. In addition, obesity was identified as a barrier to increasing MVPA. Although these men were not achieving recommended MVPA levels, they were potentially able to increase physical activity for example via the leisure-time exercise (such as walking or grading). This still provides health benefits but may not be captured by accelerometery and therefore underreported in the MVPA outcome. Age-specific accelerometer cut-offs have been devised by Rejeski et al. 2016[77] and should be used to increase the sensitivity of physical activity intensity classifications, personalised advice and to improve the potential for capturing clinically meaningful improvements. In this respect, the extent to which current CMO physical activity guidelines are appropriate for older prostate cancer patients is unknown. They may be unrealistic in terms of what older or obese cancer survivors can achieve. We therefore suggest, that lifestyle advice should be tailored to age, weight and individual capabilities, including the setting of realistic goals,[78] with the ultimate aim of achieving (or exceeding) CMO recommendations. Overweight and obese men were a significant proportion (78%) of the sample and they were less likely to improve their MVPA. They may potentially benefit from a tailored or stepped approach to weight loss during or prior the exercise intervention.
Given initial characteristics (MVPA) determined change it would be interesting to know how the sample of recruitment men differed from those who declined participation. Do the authors have any sense of this information? Potential interviews with a sample who declined participation?	Although it would certainly enrich the evidence behind this study. No interviews were conducted with men who declined participation. It was due to the nature of the recruitment strategy. After receiving an invitation letter, participants who wanted to / were interested to participate

	contacted the research team and were then screened for eligibility. We have information on age and index of multiple deprivation IMD. There was no statistically significant difference between the population invited, those who did not respond, and those who responded. This information will be reported elsewhere.
7. Also related to a future iteration of your intervention, can behavioral counseling be integrated (or automated somewhat) _into the web-based platform to improve the long-term adherence to your protocol?	Sentence added: In addition, the results show that the significant increase in MVPA at three months was not sustained over six months. Therefore, to maintain adherence and long-term benefits of the intervention, it would be beneficial to consider how maintenance can be enhanced through behaviour change techniques for future evaluations of this intervention.
Reviewer: 2	
Thank you for giving me the opportunity to review your manuscript. It is a very well-written and interesting paper. I have made some comments below that I hope will help you to improve and clarify some points for the reader.	
Introduction	
There is not a lot of background information given about previous studies/theory that may have informed the design of the study- I think this would be useful to set the scene for the reader	Section amended: This aim of this phase II study is to assess the feasibility and acceptability of a community pharmacy lifestyle intervention to improve physical activity and cardiovascular health of men with prostate cancer. This is an innovative research and to our knowledge, the first study to develop and test a lifestyle intervention in a community pharmacy setting for men living with and beyond prostate cancer diagnosis. In prostate cancer, lifestyle interventions have been shown to reduce side-effects of ADT[10 11 34] and to decrease risk of cardiovascular comorbidity.[35 36] In a feasibility study, Bourke et al. (2011) showed short-term improvements in exercise and dietary behaviour due to a supervised exercise programme combined with a dietary advice.[37] A primary care walking programme with older adults showed improvement in step counts which resulted in health benefits [38] A novel delivery approach via community pharmacies is presented here. The study is

	aligned with the vision of the Royal Pharmaceutical Society of Great Britain (2017), which is for the pharmacy workforce to develop more patient-centred roles and to expand primary care services into cancer follow-ups.[39] This is also advocated by the NHS and NICE.[16 40 41] The development and evaluation of this intervention were guided by the MRC complex intervention framework.[42] The evaluation of the feasibility and acceptability included an assessment of the delivery model (via community pharmacy), participant recruitment, consent and retention rates, and acceptability of the outcome measures. This study also provided preliminary evidence of the intervention efficacy, and enabled an assessment of the effect size change in the primary outcome to inform a future randomised controlled trial.
The link to CVD is not clear- the authors could elaborate further on why this link is important/ relevant	A sentence has been added as follows: Exercise has been shown to reduce hormone therapy-related fatigue[12] and improve cardiovascular health.[13] This is of particular importance given the potential increased risk of cardiovascular disease associated with androgen deprivation therapy (ADT) used to treat prostate cancer.[14 15]
What role do pharmacists currently play?- what skills do they have that mean that they are well placed to deliver this support? Is it likely to add much to their current role?	The following text was added: Community pharmacies are well placed to deliver this care due to easy access and availability of professional expertise. This includes consultation skills and the clinical knowledge regarding management of long-term conditions and side-effects of medications including ADT. They currently deliver services such as Medication Use Reviews (MURs), NHS Health Checks, diet and exercise advice, alcohol and smoking cessation.[30] The role of community pharmacies is rapidly evolving in response to the healthcare demands of an ageing population, with multiple long-term conditions including cancer.[31] Examples of health promotion and lifestyle interventions include the Healthy Living Pharmacy framework[32] and NHS services such as flu vaccination.[33]
Methods	
How were the pharmacies recruited?	The following sentences were added:

	The community pharmacy lifestyle intervention was delivered by nine community pharmacies between June 2016 and April 2017. The nine community pharmacies were recruited based on location (proximity to the cancer centre and spread across the locality) and commercial business model. They were drawn from three different commercial business models, including independent community pharmacy, mid-size nationwide community pharmacy limited company (> 500 pharmacies), and large nationwide pharmacy limited company (> 1500 pharmacies). Pharmacy teams were identified and consented to participation in the study. This included participation in the mandatory training.
How did you assess MCPA in those who were excluded because they met the CMO guidelines for PA? Were these individuals recruited and excluded after baseline assessments?	The MVPA was assessed based on self-report, using CMO definitions of the type and duration of physical activity. For example, patients who reported that they trained and run marathons or who vigorously cycle long distances, were informed about the minimal benefits oft his low level intervention and were excluded. The paragraph has been clarified as follows: Eligibility criteria included at least one of three cardiovascular risk factors: overweight or obese (BMI ≥ 25), and/or on active androgen deprivation therapy (ADT), and/or diagnosed hypertension. Men who were already physically active were excluded because the focus of this intervention was on those with high needs. The definition by the UK's Chief Medical Officer (CMO) of a minimum 150 minutes of moderate physical activity or a minimum of 75 minutes of vigorous physical activity per week in 10 or more minute bouts[43] was used. Men, who on an initial screening, reported physical activity that exceeded CMO guidelines (for example football, cycling or running for more than three hours a week) were excluded.
On page 6- the paragraph on training could be re-worded to clarify who received the training- was it pharmacists only? Or did the other members of the team (technicians, non-pharmacist team members etc.) also receive training?	Done Training in how to deliver all aspects of the intervention was provided to pharmacy teams before the study. This consisted of existing modules from the Centre for Pharmacy Postgraduate Education (CPPE) on consultation skills and cardiovascular health, and a one-day skills-based, competency training delivered by the research team. A team approach was

	adopted for the training and delivery of the intervention. Non-pharmacist members of the team delivered the assessment, and pharmacists provided the lifestyle consultation and advice. Therefore, each pharmacy nominated at least one pharmacist and at least one pharmacy technician or dispensing assistant (National Vocational Qualification level 2 or 3) to undertake the training. It was evaluated using a training evaluation form that was administered immediately after the training.
Was there an assessment to establish that training was successful and that necessary skills had been obtained?	Sentence was added: The CPPE Declaration of Competence Framework[46] was used to assess the success of the training and that the necessary skills to deliver the intervention have been obtained.
Was there a fidelity assessment of whether the training was implemented in practice?	Sentence added: To assess fidelity, pharmacies were visited on a monthly basis. This visit was also used to calibrate the blood testing equipment. In addition, the data entered by pharmacy teams was monitored on a regular basis.
Outcomes	
Were cut-offs for feasibility/ acceptability defined a-priori (E.g. What was a feasible/acceptable rate of recruitment, consent, retention etc.?)	This is a very good point and we did not define feasibility end points a priori. We reviewed the feasibility and acceptability outcomes on ongoing basis based on feedback from the steering group and reference values form other published studies. This is a global initiative so we also compared our timelines and recruitment rates against other interventions.
Who administered the outcome measures?	Done. Information added as follows: These outcomes were measured at both pharmacy visits. They were administered via postal questionnaires at baseline, three months (only MEDAS and PAM) and at six months. See pg 6 of the manuscript (secondary outcome measures Section) for more detail.
Qualitative data	
When did the focus groups take place? Pharmacy teams were asked about training- was this interview after training or at the end of the trial? Might this impact how they spoke about the training?	The training was evaluated both immediately after the training and also during qualitative focus groups. Sentences added:

	It (training) was evaluated using a training evaluation form that was administered immediately after the training.
Why did you use focus groups rather than individual interviews?	A group approach to interviewing was adopted because we wanted to enable interaction between members of pharmacy teams. The paragraph was amended as follows: Two focus groups were held with the participating pharmacy teams at the end of the project to collect information on the feasibility and acceptability of intervention components and to obtain feedback on their preparatory training. This gave them an opportunity to discuss experiences as a group of healthcare professionals across pharmacy teams.
How did you select the sample of study participants who were interviewed?	Paragraph added: Semi-structured interviews with a consecutive sample of study participants were also conducted to collect the information on their overall perception and engagement with different intervention components. Six months after enrolment, 44 of the 116 participants were consecutively approached to take part in an interview. Of these, five men declined without providing a reason and three declined due to the timing of the interviews. 36 men gave written consent and 33 men were interviewed (in three cases, it was not possible to find a mutually convenient time). The focus groups and interviews were audio-recorded, transcribed and analysed thematically.
Quantitative findings	
Be careful not to overstate findings of efficacy tests- what do these findings tell us about the feasibility and acceptability of the intervention (apart from establishing sample size for future RCT)?	This statement was an error and it was deleted: The effect size change in this outcome was used to evaluate the efficacy of the intervention and to estimate sample size. (for a future RCT to evaluate the efficacy of the intervention).
The sample size mentioned is based on differences rather than predictors- is the sample size adequate for regression analyses?	The sample size for this feasibility study was 113 men (including an estimated 25% attrition) to detect a 22% difference in moderate to vigorous physical activity (MVPA) with 90% power, and two-tailed significance level of 5%. The regression analysis in this manuscript model dichotomised Increase in MVPA (Yes / No) using a set of independent variables

	identified from the literature as potential factors that may affect it. While it is a valid point that sample size was not designed to undertake the prediction modelling. However, it is also important to note that the purpose of the regression analysis is not prediction but exploratory analysis of the effect (link between potential contributors / barriers to change). We hope that the reviewer agrees that there is value in this regression model and that it contributes an important information in this manuscript.
PPI	
Who were the volunteers- had they had treatment? How were they recruited?	Sentence amended: Two volunteers, who are prostate cancer survivors, were involved in the co-design of the intervention resources, training of the community pharmacy teams, and supported project management and governance.
Discussion	
Why was randomisation not assessed in this feasibility study?	A sentence added This feasibility study did not test randomisation of participants. This was guided by a requirement from the funder that the intervention was provided to all participants. This is a limitation and will require further user involvement and consultations to explore feasibility and acceptability prior to a future RCT.
The description of gender specific barriers is quite vague- why is it important to understand gender specific barriers?	This paragraph was deleted due to word limit.
Were there any differences in those receiving or not receiving treatment? Were different approaches used for those who had had treatment vrs those on watchful waiting/active surveillance? What implications might these differences have for intervention delivery? Does this approach possibly work better/ worse for a specific group?	All our participant completed a treatment as an eligibility criterion. We did not have any participant on AS or WW. It was because we were looking at ameliorating effects of treatment and risk factors associated with the treatment. This lifestyle intervention would still be beneficial for AS/ WW patients (due to high rates of obesity and higher than general population cardiometabolic risks) but it is true that the intervention and information provision and would need to be adapted to the needs of this group pf patients.
What difference might altruistic participation have on your sample?	Paragraph amended: In addition, studies show that individuals participate in clinical research for altruistic reasons.[65] Men who participated were not only keen to improve their health and fitness but also

	to contribute towards improving support for men after treatment. The main reasons for non-participation were: too busy, unwell or already physically active. Understanding of facilitators and barriers to participation will be used in the planning of successful recruitment strategy for a future trial.
Were those who took part possibly healthier than those who did not?	This maybe opposite in our study due to the recruitment criteria: Eligibility criteria included at least one of three cardiovascular risk factors: overweight or obese (BMI ≥ 25), and/or on active androgen deprivation therapy (ADT), and/or diagnosed hypertension. Men who were already physically active were excluded. We mention this bias in our discussion: The reported here number of 7% men achieving CMO guidelines is lower than the 12% reported for cancer patients in Galvao et al. 2015[71] and lower than the 38% reported for older adults in UK population.[72] This may be due to the recruitment bias resulting from targeting men with low physical activity levels and pre-existing cardiovascular risk factors, including obesity.
In terms of limitations, the demographics indicate that the majority were white and more than two-thirds of the sample were not deprived. Further 87.9 % were married. Is this due to the area in which the study took place? Or is it an issue in how you recruited? How might you remedy this in a future trial- or is it important to do so?	We believe that the lack of ethnic variability is due to the area. It is an area of low ethnic diversity. There is also potentially an element of black minorities not engaging in lifestyle interventions. To remedy this in a future trial, the recruitment needs to focus around a locality with a population with a higher rate of British ethnic minorities and we are discussing this with oncology CNS in some of the London area that have high population of black British. The section in the manuscript has been added to the limitations Section: The lack of ethnic variability is a limitation. The majority of our sample are white men so we did not explore ethnic differences in feasibility and acceptability. To remedy this in a future trial, the recruitment needs to take place in areas with higher rates of ethnic minorities.
In terms of number of participants recruited per pharmacy- was the number reflective of the size of the pharmacy… or were some pharmacy types better than others? What are the characteristics of those pharmacies that	A sentence was added: The number of consultations per pharmacy varied between 4 and 30 for the first assessment and 4 to 32 for the second

engaged more with the study/ took on more ppts?	assessment. This was primarily driven by the choice of participants and usually determined by the ease of access or proximity of a pharmacy. Due to staff changes and workload primarily related to the flu season, some participants moved to another pharmacy to complete their follow-up. Pharmacists could pick-up those appointments and the web-based system enabled this transfer.
What about the cost-effectiveness of an intervention like this?	The full evaluation of effectiveness and cost-effectiveness was not undertaken due to the scope of this feasibility study. We plan to publish a subsequent paper where we will report service evaluation data that were captured by participant-completed questionnaires at six months. We are currently working on an RCT to evaluate the effectiveness and cost effectiveness of the intervention. A sentence was amended: This study is an essential step towards an RCT to evaluate the effectiveness and cost-effectiveness of this community pharmacy lifestyle intervention for men with prostate cancer.
In your discussion about ppt reaching guidelines, I would suggest that you read some of the work by Nanette Mutrie- She discusses realistic goal setting and incremental improvements as being superior approaches than simply asking sedentary participants to reach guideline expectations.	Done and references added. Thank you!
Reviewer: 3	
In this study, Agnieszka et al. present a phase II feasibility study to assess a lifestyle intervention in men with localized prostate cancer. There are a number of statistical issues that must be addressed.	
1. It is preferable to report 25th and 75th percentiles over IQR to show the skew of the variables.	Median (IQR) has been replaced by Median (Q1, Q3) in Table 1 of baseline patient demographics
2. Why was a formal variable selection technique not used? Did the authors test for collinearity between variables in Table 2?	We have now applied a formal and systematic variable selection procedure. A backwards elimination procedure. We have also tested for collinearity with in the model and the Spearman r's were less than 0.7 in the full model and are < 0.4 in the final model.

	Table 2 has been amended accordingly to reflect the change in the final model after the backwards elimination. A sentence was added in the methods section: Collinearity between independent variables was tested using Spearman r.
3. Was the linearity of continuous variables in Table 2 examined? For example, is it appropriate to treat CCI as continuous?	We tested for linearity of continuous variables and log odds in each univariate model. To correct for this assumption, CCI and IMD scores have been categorised in the regression models. Table 2 has been amended. Only age and Time in MVPA remain as continuous variables in Table 2 as the linearity assumption was fulfilled. The test in Methods has been amended: Multi-level logistic regression was used to examine the relationship between potential factors influencing change in MVPA over three months. A binary (yes/no) variable of increase in MVPA was used as a dependant variable. Pharmacy effect was included as a random variable. Univariate models were fitted with the following independent variables: baseline time in MVPA, age, BMI status, cancer treatment, ADT, marital status, IMD decile, and CCI score. The final multivariate model was created using a backward elimination procedure and statistical significance of $P < 0.1$ as cut-off. Collinearity between independent variables was tested using Spearman r. $P < 0.05$ was considered statistically significant. Caption of Table 2 was amended as follows: Table 2. Results of multilevel logistic regressing using binary (yes/no) variable of increase in MVPA as a dependant variable. Pharmacy (clustering effect) was included as a random effect. Factors that can potentially contribute to the change in MVPA over time were explored using univariate regression. The following independent variables were included: baseline time in MVPA (continuous), age (continuous), BMI status (categorical; normal, overweight, obese), cancer treatment (categorical; radiotherapy, surgery), ADT (categorical; yes, no), marital status (categorical; single, partner),

	employment status (categorical, unemployed / retired, working), IMD decile (categorical; 1-3, 4-6, 7-8, 9-10), and CCI score (categorical; mild, moderate, severe). A backward elimination procedure and statistical significance of $P < 0.1$ was used to derive a final multivariate model. $P < 0.05$ was considered statistically significant. Abbreviations: ADT, androgen deprivation therapy; BMI, body mass index; CCI, Charlson comorbidity index; IMD, index of multiple deprivation; MVPA, moderate to vigorous physical activity.
4. Figure 3 is confusing. What are some of the changes significant even though the confidence interval crosses 1? What is the null hypothesis here?	There was an error in Figure 3 in the way the standardised mean differences were calculated. This has now been corrected and Figure 3 replaced. The P-values to assess the significance of change over time were correctly calculated and remain unchanged.
Is it appropriate to be looking at mean changes when the change does not seem normally distributed for the measures reported in the Methods.	The normality of variables as well as of the change over time has been tested and lower body strength has been removed from Figure 3 as it showed skewed distribution.
5. Figure 3 caption: “All significant changes are in a positive direction and are marked with a red marker.” Positive should be changed to favorable to avoid confusion.	The caption and the legend of Figure 3 has been changed.

VERSION 2 – REVIEW

REVIEWER	Alexander Lucas Virginia Commonwealth University, School of Medicine USA
REVIEW RETURNED	25-Jan-2019

GENERAL COMMENTS	The authors have addressed my previous concerns satisfactorily and the changes in response to other reviewers have improved the manuscript in general. Thank you again for the opportunity to review your work.