Development of a computer-based algorithm for supporting community pharmacists in providing personalised lifestyle interventions for men with prostate cancer

ORIGINAL PAPER

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ABSTRACT

Background: The number of people living with and beyond a cancer diagnosis has increased, however survivors may experience long-term side-effects from treatment that can impact on physical fitness and cardiovascular health. Lifestyle interventions enhance outcomes after cancer treatment but innovations and technology are needed to provide consistency and scalability. Interventions to support exercise and dietary modification in secondary care settings have been limited by the lack of personalisation, clinician time and resources. Community pharmacies are well positioned to provide lifestyle advice for people with cancer and long-term conditions. This study is the first to develop a tailored lifestyle intervention using a computer algorithm to enable community pharmacists to provide personalised advice for cancer patients.

Objective: To create a computer-based algorithm to support community pharmacists to deliver a tailored lifestyle intervention for men during and after treatment for prostate cancer.

Method: An observational study was conducted at two UK centres involving 83 men with prostate cancer who were 3-36 months’ post-diagnosis. Physical fitness, strength and cardiovascular health were assessed. Qualitative interviews were undertaken with 20 participants to understand their interpretation of the assessment and analysed using a framework analysis. These data were used to inform our computer-based algorithm and lifestyle prescriptions.

Results: Physical fitness varied across participants. Limb strength was categorised with upper body strength low for 40% of men compared to their age (40 out of 83) and lower limb strength (44 of 83) 53% of men were low in comparison to age normative values. The Siconolfi step test provided classification of cardiopulmonary fitness with 26.5% (22 of 83) men unable to complete level 1 with very low physical fitness and 41% (34 of 83) of men moderate completing stage 2 of the test. Cardiovascular risk was categorised as high (>20% QRISK2) in 41% of men contributed to by the number of men who had a high hip to waist ratio 72 of 83 men (86.7%) indicating abdominal fat.
Three emergent themes from the qualitative analysis highlighted different perceptions of the physical assessment experience. The algorithm provided a clear pathway for decision making, that it was safe and effective to enable community pharmacists to prescribe tailored lifestyle advice for men with prostate cancer.

Conclusion: We have developed a computer algorithm that uses simple, safe and validated assessments to provide tailored lifestyle advice which addresses specific areas of cardiovascular risk, strength and physical fitness in men with prostate cancer. It generates a real-time lifestyle prescription at the point of care and has been integrated into the software platform used by pharmacies in the UK. The algorithm was integrated into the software platform used by pharmacies within the UK.
INTRODUCTION

*Improving cancer survivors’ lifestyle to reduce future health risks*

In 2012, there were more than 32 million people living beyond 5 years of a cancer diagnosis globally [1] and in the UK half of all people diagnosed will now survive 10 years or more [2]. Cancer is increasingly being recognised as a chronic disease and survivors are at elevated risk of disease recurrence and cardio metabolic problems [3, 4]. Comorbid conditions such as obesity, hypertension, chronic heart disease and mental health problems, which are commonly reported in cancer survivors [5-7], are linked with poorer survival, reduced quality of life and higher healthcare costs [8]. Evidence for the positive impact of lifestyle interventions in relation to recovery from cancer and reducing comorbidity has been well documented in several systematic reviews and meta-analyses [9-11]. Real-time assessments of health and function are needed to support effective lifestyle interventions in follow up care and this is increasingly important as survivorship services are transferred to primary and community care settings [12, 13]. Technology supported physical activity and nutrition interventions are an opportunity to deliver health interventions to adults with cancer, however current programmes lack an evidence base for benefit [14].

The number of men with prostate cancer living longer is increasing because of improvements in diagnosis and the introduction of better treatments [15]. Prostate cancer is one of the most commonly diagnosed cancers in developed countries [1] and 1.1 million men are diagnosed per year globally. This accounts for 15% of all cancer diagnoses in men [16]. In the United Kingdom (UK), over 47,000 men are diagnosed with prostate cancer each year and 84% are now surviving 10 years or more [17]. Enhancing men’s health by addressing factors such as obesity and physical inactivity are vital, as excess body weight and poor lifestyle behaviours are associated with increased risk of prostate cancer recurrence, aggressiveness and comorbidity [18-20]. Furthermore, prostate cancer treatments such as androgen deprivation therapy (ADT), widely used as an adjunct for localised and high-risk disease, have been associated with adverse cardiovascular effects [21-26]. Specific lifestyle recommendations for men on ADT exist in the UK with the National Institute for Health and Care Excellence (NICE) advocating a 12-week exercise programme to reduce fatigue symptoms [27]. Cardio-oncology recommendations for people with cancer on hormone therapies advise pre-assessment of existing cardiovascular disease and lifestyle intervention to reduce risk of adverse-effects [28-30]. There is a growing requirement to include lifestyle interventions as part of the cancer pathway, with recent reports highlighting the value of prehabilitation and rehabilitation for recovery [31-33].

*Community pharmacy have a role in supporting cancer survivors*
Improved survivorship has shifted cancer care from secondary to primary and community care, providing links to existing health and well-being services. Lifestyle or physical activity on prescription schemes (PARs) for individuals with long-term conditions have been implemented in primary care settings for promoting health in a range of conditions [34-36]. However, people with cancer are included as eligible ‘at-risk’ populations only in Australia and New Zealand [37]. PARs aim to increase a patient’s physical activity levels via general practitioner or nurse referral to a specialist sport and exercise practitioner-led supervised exercise programme [38]. Such interventions have been shown to increase self-reported physical activity and improve health but have the recognised issues of poor adherence and high costs [39-41]. Increasingly, pharmacy teams are being encouraged to provide brief interventions to promote obesity management and increase physical activity in people with long-term conditions, as a supplement to such schemes [42].

Community pharmacies are well-positioned to provide general lifestyle advice for people with cancer due to their experience with health checks, smoking cessation and obesity management [43-45]. High street pharmacists are accessible and understand behavioural change techniques [43]. Pharmacists can enquire about physical activity at medicine reviews, refer their clients to local services and integrate brief advice about physical activity into routine consultations [46]. However, for such advice to be most effective it needs to be responsive to the person’s own lifestyle needs, co-morbidities and existing level of physical fitness. Community pharmacists have limited training in physical activity assessment, knowledge of exercise advice or cancer treatment adverse effects but with more training and support tools, could effectively deliver lifestyle interventions for cancer survivors [47, 48]. Pharmacists also need skills in motivating men to maintain and adhere to healthy lifestyle changes [49]. The challenge is to ensure that lifestyle interventions are personalised, appealing and accessible [50]. This requires innovations in assessment and technology tools that can be used within existing computer technology used by pharmacy teams.

*Developing algorithm-led computer interventions for pharmacy*

Remote support for lifestyle interventions is a growing area of patient care, which is driven by the rising use of internet, smartphones and mobile technology [51, 52]. Digital health behaviour change interventions (DCBIs) have mainly focused on direct communication with patients using text messages, email and web-based applications [53]. These have been shown to be successful in empowering people with long-term conditions [54] and cancer survivors [55] and can be used to promote lifestyle change and increase physical activity [56]. Digital technology holds promise to encourage behaviour change but needs methodologies and tailored approaches to promote user engagement [14, 53]. Computer-based tailoring is a method of assessing individuals and selecting
communication content using data driven decision rules that produce feedback automatically from a database of content elements [57]. The use of use of computer-based tailoring for supporting lifestyle interventions in a community pharmacy setting is unique and is based on the recommended guidance for developing digital interventions to promote behaviour change in health and healthcare [53]. In this study, we assessed: (i) objective measurements of cardio metabolic health, strength and physical fitness of men with prostate cancer that could be undertaken within a pharmacy, (ii) how to communicate risk and promote lifestyle behaviour change, and (iii) developed a computer algorithm to provide a safe and personalised lifestyle prescription at the point of care.

METHOD

Study Design

This study employed a multi-stage, mixed methods approach to intervention development, underpinned by the Medical Research Council’s (MRC) framework [58] and was the modelling phase of a larger study. An algorithm was developed which informed the creation of the computerised lifestyle prescription. This phase provided the opportunity to collect detailed information on the physical fitness, strength and cardio metabolic health of men after a prostate cancer diagnosis, using an observational, longitudinal study design. Data was collected from May 2014-2015 from two localities within the UK. These data informed the parameters required to develop a personalised lifestyle prescription that could be delivered in a community pharmacy setting.

Participants, setting and recruitment

We recruited 83 men with prostate cancer up to 36 months’ post-diagnosis and stable as defined by PSA values (Surgical patients: <0.4ng/ml. Radiotherapy patients: <0.4ng/ml, if nadir (0.2ng/ml or less), Androgen Deprivation Therapy (ADT) patients with a Prostate Specific Antigen (PSA): 10ng/ml or less). Entry criteria also included being at least 3 months’ post radiotherapy or at least 6 months’ post brachytherapy or surgical treatment and with one or more of the following risk factors: BMI over or under the ‘normal’ range (underweight <18.5 Kg/m² or overweight ≥25Kg/m²), on ADT, diagnosed or treated for high blood pressure (140/90mmHg or higher). Men with confirmed cardiovascular disease, pulmonary disease, myocardial infarction, on current use of active treatment (excluding ADT) were excluded. Identification, eligibility and screening are outlined in Figure 1.
Figure 1 CONSORT diagram of recruitment, eligibility and participation in the study

Assessed for eligibility
(Surrey 139, Newcastle unknown)

Consented to pass on contact details to University of Surrey
(n=90) (Surrey 69, Newcastle 21)

Consented (n=84)
(Surrey 63, Newcastle 21)

Excluded (n=4)
Reasons: due to disease progression (n=1), other health problems (n=2), Relocated (n=1)
Declined (n=2)

Withdrawn (n=1)
Reason: bad back

Attended Visit 1 (n=83)
(Surrey 62, Newcastle 21)

Excluded (n=5)
At high risk and advised not to complete all physical assessments

Completed all Visit 1 Assessments (n=78)
(Surrey 58, Newcastle 20)

Withdrawn (n=6)
Reasons: Lost to follow up (n=1), Ill health (n=5),
Declined (n=8)
Attended Visit 2 (n=64)
(Surrey 47, Newcastle 17)

Semi-structured telephone interviews (n=20)
(Surrey 10, Newcastle 10)
Data Collection
Data were collected at two time points three months apart, data from the first-time point was used for developing the computer based algorithm. Cardiovascular health, physical fitness and strength were assessed by the following tests:

Cardiovascular health and metabolic risk
Blood pressure, blood tests for (non-fasted) glucose, cholesterol and lipid were used to inform QRisk2 (cardiovascular risk prediction score). Height, body weight, waist and hip circumference were measured, and body mass index (BMI) calculated, by standard procedures.

Physical fitness
The Siconolfi step test [59, 60] is a validated submaximal test which is predictive of cardiopulmonary fitness. A prior validation study specific to men with prostate cancer was conducted and is reported elsewhere [61]. The test consists of stepping up and down from a portable 25 cm step at a fixed rate for 3 minutes, interspaced with a 1-minute rest between two further stages (at incrementally higher rates). This is a relatively low level of exercise that can be adapted for people with disability. Heart rate was monitored during and after the test and used in the determination of cardiopulmonary fitness [62].

Strength
Grip strength (upper-limb strength) was measured using a handheld dynamometer, with participants asked to complete three squeezes per hand, each being held for 5 seconds. The results were recorded and assessed against population norms [63].

The sit-to-stand test (lower-limb strength) assesses the number of repetitions achievable in a set amount of time [64-66]. The score was the total number of stands performed correctly (full standing position attained and fully seated between stands) in 30 seconds compared to population-based reference values.

Participant feedback
Semi-structured interviews were conducted in a sub-sample of 20 men. The interview questions were constructed to gain feedback about their perspectives of the health assessment and how best to frame the lifestyle advice within the computer-generated prescription. Interview participants were selected purposively across low and high performers, as well as across recruitment sites.
Data Analysis

Current health assessment variables such as weight, physical fitness and strength were assessed at baseline and at 3 months using descriptive statistics, means and standard deviations for normally distributed variables, medians and interquartile ranges (IQR) for non-normally distributed variables, and counts and percentages for categorical variables. Results from the Siconolfi step test, grip strength and sit-to-stand tests were used to classify men into one of three categories (low, medium and high) for cardiopulmonary fitness, upper body strength and lower body strength, respectively. Cut-offs were based on age specific normative values. Patient characteristics and treatment factors in relation to cardiopulmonary fitness were examined by regression analysis. Statistical significance was considered at \( P < 0.05 \). The dataset was entered and managed in SPSS version 22 (SPSS Inc, Chicago, USA). Statistical analyses were performed in R version 3.0.2 (R Development Core Team, Austria). The semi-structured interviews were audio recorded and transcribed verbatim. Framework Analysis [67] were used to identify themes.

RESULTS

Participants

Characteristics of the whole sample \( N=83 \) participants and of the 20 (24%) men in the qualitative study are shown in Table 1. Because the participants were a targeted ‘at-risk’ population in need of lifestyle advice, they may not necessarily reflect the wider prostate cancer population. The median age of men was 69 (IQR=9.5) years with a range of 47 – 83. Median Charlson comorbidity index was 6 (IQR=3) so men had multi-morbidity (two or more existing co-morbidities), which could potentially impact their ability to exercise. The 10-year risk of a cardiovascular event (defined by QRisk2) showed that 34 of the 83 (41%) of the sample had a >20% risk score of a cardiovascular event within 10 years, suggesting that this was a population at high risk and in need of lifestyle advice. Participants in the interview subgroup had similar characteristics 11 out of 20 (55%) and there were no statistically significant differences.

Table 1. Demographic and treatment characteristics of study participants

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>PARTICIPANTS N=83 (%)</th>
<th>Interview participants n=20(24%)</th>
<th>P -value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (Years)</td>
<td>68.2 (7.4)</td>
<td>70.1 (7.5)</td>
<td>0.324</td>
</tr>
<tr>
<td></td>
<td>Median (IQR) (years)</td>
<td>69 (9.5)</td>
<td>70 (6.25)</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------------------</td>
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<td>-----------</td>
</tr>
<tr>
<td>RANGE</td>
<td>47 – 83</td>
<td>55 - 83</td>
<td></td>
</tr>
<tr>
<td>AGE GROUPS N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;65</td>
<td>22 (26.5)</td>
<td>4 (20)</td>
<td></td>
</tr>
<tr>
<td>65-75</td>
<td>47 (56.6)</td>
<td>12 (60)</td>
<td></td>
</tr>
<tr>
<td>&gt;75</td>
<td>14 (16.8)</td>
<td>4 (20)</td>
<td></td>
</tr>
<tr>
<td>ETHNICITY N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>80 (96.4)</td>
<td>20 (100)</td>
<td>0.689</td>
</tr>
<tr>
<td>Black British</td>
<td>2 (2.4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1 (1.2)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>EMPLOYMENT STATUS N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retired</td>
<td>19 (22.9)</td>
<td>1 (5)</td>
<td></td>
</tr>
<tr>
<td>Working</td>
<td>54 (65.1)</td>
<td>16 (80)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>10 (12)</td>
<td>3 (15)</td>
<td></td>
</tr>
<tr>
<td>TREATMENT (men may have received several)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>53 (63.9)</td>
<td>8 (40)</td>
<td></td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>26 (31.3)</td>
<td>8 (40)</td>
<td></td>
</tr>
<tr>
<td>Brachytherapy</td>
<td>3 (3.6)</td>
<td>2 (10)</td>
<td></td>
</tr>
<tr>
<td>Hormone therapy</td>
<td>32 (38.5)</td>
<td>9 (45)</td>
<td></td>
</tr>
<tr>
<td>CHARLSON COMORBIDITY INDEX</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>6 (3)</td>
<td>8 (4.5)</td>
<td>0.067</td>
</tr>
<tr>
<td>Missing (%)</td>
<td>17 (20.4)</td>
<td>9 (45)</td>
<td></td>
</tr>
<tr>
<td>SMOKING STATUS N (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smoker</td>
<td>45 (54.2)</td>
<td>13 (65)</td>
<td></td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>27 (32.5)</td>
<td>4 (20)</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>4 (4.8)</td>
<td>1 (5)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>7 (8.4)</td>
<td>2 (10)</td>
<td></td>
</tr>
<tr>
<td>CVD (QRISK2 &gt;20): N (%)</td>
<td>34 (41.0)</td>
<td>11 (55.0)</td>
<td>0.377</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (4.8)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol: mean (SD)</td>
<td>4.3 (1.0)</td>
<td>4.3 (1.2)</td>
<td>0.896</td>
</tr>
</tbody>
</table>
Dietary algorithm

Weight and BMI assessments identified that 51 out of 83 (61.4%) of the men were overweight and 72 of the 83 men (86.7%) had a waist to hip ratio above recommended norms, indicating a high prevalence of central (abdominal) obesity. Men were categorised as normal weight (4 out of 84-6.6%) and needing more protein (6 out of 83-7.2%), overweight/obese (14 out of 83-16.9%) or overweight/obese and needing more protein (55 out of 83-66.2%) (Table 2). Capillary blood tests of cholesterol, in conjunction with BMI showed that 26% of men had a BMI >30 and 72 out of 83 (86.7%) of men with a hip to waist ratio above recommended normal values this reflects characteristics of metabolic syndrome. This is defined as a cluster of metabolic risk factors that increase the risk of developing cardiovascular disease: central adiposity (above normative values of waist circumference); mild hypertension; hyperglycaemia; dyslipidaemia and insulin resistance [68]. This was reflected in the men’s cardiovascular risk scores. Key strategies for managing this are calorie restriction to promote fat loss and the manipulation of macronutrient composition, i.e. reducing fat, carbohydrate intake and increasing protein content to address body composition muscle issues.

Table 2. Components of the assessment that contributed to algorithm classification by BMI classification, waist to hip ratio and strength

<table>
<thead>
<tr>
<th>BMI CLASSIFICATION</th>
<th>PARTICIPANTS N = 83 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (18.5-25 BMI)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Overweight (25-30 BMI)</td>
<td>51 (61.4)</td>
</tr>
<tr>
<td>Obese (&gt;30 BMI)</td>
<td>22 (26.5)</td>
</tr>
<tr>
<td>Missing data</td>
<td></td>
</tr>
<tr>
<td>WAIST TO HIP RATIO</td>
<td></td>
</tr>
</tbody>
</table>
Within normal limits (<0.9) | 11 (13.2)
---|---
Above recommended (>0.9) | 72 (86.7)

**GRIP strength**

Mean (SD) | 38.4 (8.4)
---|---
Missing | 4

**DIETARY ALGORITHM CLASSIFICATION (%)**

Normal weight (Healthy eating) | 4 (4.8)
Normal weight (plus additional protein) | 6 (7.2)
Overweight/ obese | 14 (16.9)
Overweight/ Obese (plus additional protein) | 55 (66.2)

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Exercise algorithm

Cardiopulmonary fitness in 22 of the 83 (26.5%) men was categorised as low (unable to complete the first stage of the Siconolfi step test). The same number of men were classified as having high cardiopulmonary fitness (Table 3). The Siconolfi step test was generally well tolerated by men with no adverse events, though some men experienced minor motor control problems associated with the stepping motion. Strength was low, with 40 or the 83 (48%) men below normative values for upper limb strength and 44 out of the 83 (53%) for lower limb strength (Table 3). It is important to note that discrepancies between upper- and lower-limb strength classifications were commonly observed within individuals, (e.g. a low or moderate classification for lower-limb strength and a high classification for upper-limb strength) indicating the importance of assessing both upper- and lower-body strength and prescribing appropriate resistance training exercises for the different muscle groups.

Table 3. Assessments that informed algorithm tailoring of physical activity advice, through grip strength sit to stand and Siconolfi step test

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>PARTICIPANTS N = 83 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRIP STRENGTH ALGORITHM CLASSIFICATION N (%)</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>40 (48.2)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------</td>
</tr>
<tr>
<td>High</td>
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**SIT TO STAND ALGORITHM CLASSIFICATION N (%)**

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<table>
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<tbody>
<tr>
<td>Low</td>
<td></td>
<td>44 (53)</td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td>24 (28.9)</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td>11 (13.2)</td>
</tr>
</tbody>
</table>

**SICONOLFI STEP TEST ALGORITHM CLASSIFICATION N (%)**

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<table>
<thead>
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</thead>
<tbody>
<tr>
<td>Low (Stage &lt;1)</td>
<td></td>
<td>22 (26.5)</td>
</tr>
<tr>
<td>Moderate (Stage 2)</td>
<td></td>
<td>34 (41)</td>
</tr>
<tr>
<td>High (Stage 3)</td>
<td></td>
<td>22 (26.5)</td>
</tr>
</tbody>
</table>

**Safeguarding**

Safety was assessed via QRisk2, blood pressure and capillary blood tests for cardio metabolic risk factors. Men above the norms for these parameters were referred for further medical review as part of safety procedures. These variables were included in the computer algorithm to alert pharmacists of high risk men and integrated into the pharmacy software to create a general practitioner notification.

If at the pharmacy as assessment, one or more of the following findings were of concern:

- QRISK 2 score over 20%
- Total Cholesterol/HDL ratio over 4.0
- Blood Glucose over 7mmol/l
- Blood Pressure over 140mmHg systolic /90mmHg diastolic
- A health issue that has been raised by the participant that may need investigating further

**Qualitative analysis: participant perspectives and beliefs**

Some interviewees saw assessment as a catalyst for behaviour change, whereas others were sceptical about links between exercise, diet and prostate cancer. For others, the assessment was reassuring, and the prescription reinforced known lifestyle behaviours (Table 5). Six men strongly believed in the
benefits of positive lifestyle behaviours and said they felt capable of making these changes. These men were stimulated by the health assessment, which focused their attention on improving their health and fitness and incentivised them in anticipation of the re-assessment and active tracking of their progress, this was seen in their changes in scores over time.

All men interviewed were confident that they knew what positive lifestyle behaviours they needed to make to improve their health but to move from “knowing the right thing to do” to “doing it” required an external stimulus. Interviewees talked about the moment that had stimulated them to increase physical activity or improve their diet. For some, simply knowing that this research project involved a comprehensive health and fitness assessment inspired them to make changes. For others, they described how the experience of undergoing the assessment raised their awareness, focused their attention on their strength and fitness and stimulated them to act. Health behaviour change was triggered by experiencing the tests as “difficult to do” or understanding that their performance was below their own expectations or normative values.

Despite the positive impact on health behaviours for many men, four interviewees recounted that while they were interested in the project and were happy to have been assessed, their underlying health beliefs meant that the health assessment had made no impact on their lifestyle behaviours. For these men, assessment of their health status was experienced in the context of a personal “feeling of wellness” and ability to function rather than as a means of seeking any objective physiological measure of health or fitness, and they tended to normalise being overweight or unfit as an inevitable part of older age. They went on to rationalise that lifestyle changes were therefore not necessary or would be ineffective. Whilst these men explained that they were fully aware of positive lifestyle behaviours they should adopt (such as improving their diet or exercising regularly) they described how it was either unnecessary (referring to their underlying health beliefs, or fatalistic outlook), or not possible (referring to previous difficulties making lifestyle changes).

How data informed the development of the algorithm

Figure 2 presents the fundamental components of the personalised lifestyle programme and depicts how the algorithm was used to integrate results from the exercise and anthropometric data. Using this algorithm, an individualised exercise and dietary programme was designed for each man using test scores for cardiopulmonary fitness, upper- and lower-body strength, and body composition parameters. The algorithm decision tree for dietary advice draws data from the physical fitness and strength assessments to provide dietary information for improving strength, based on nutritional
review and analysis [68]. The algorithm categories put men into weight reduction, healthy eating and/or increased protein requirement. By categorising men as low, moderate or high for fitness variables, and as either Group 1 or Group 2 for body composition variables (with PLUS indicating the need for additional protein intake to help increase skeletal muscle mass), a tailored programme could be created to address specific needs. For example, an appropriate algorithm for a man with low cardiopulmonary fitness and low upper- and lower-body strength, who was also overweight would be prescribed: CPF1/LBS1/UBS1/WMC (Group 2)/PLUS. The algorithm for physical activity was built on recommendations for enhancing physical activity for cancer survivors and provided advice that promoted cardiorespiratory fitness, moving more and strength building (Figure 3).
Figure 2. Algorithm decision tree for personalised prescription of dietary advice

- **Normal Weight**
  - BMI <30kg/m²
  - And/or Waist Circumference < 102cm
  - And/or Waist: Hip Ratio < 0.9

- **Overweight Weight/Obes**
  - BMI >30kg/m²
  - And/or Waist Circumference > 102cm
  - And/or Waist: Hip Ratio > 0.9

- **Strength**
  - Grip Strength < lower confidence interval for age norms
  - And/or Sit to Stand < lower confidence interval for age norms

- **Non-weight loss**
- **Weight Management**
- **Group 1**
- **Group 2**
- **Group 1 PLUS**
- **Group 2 PLUS**

**Outcomes**

- **Reduced Cardiovascular Risk**
  - (Improvement in QRisk2)
- **Improved strength**
  - (Improvement in Grip Strength and Sit to Stand test)

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**Figure 3. Algorithm decision tree for personalised prescription of exercise advice**

- **Upper body strength**
  - Grip strength ( categorisation based on confidence intervals for age-matched norms)
  - Resistance exercises (Resistance bands)

- **Lower body strength**
  - Sit to stand ( categorisation based on confidence intervals for age-matched norms)
  - Resistance exercises (Resistance bands)

- **Cardiopulmonary fitness**
  - Stairclimber step test (0:1 stage = low; 2 stage = medium; 3 stage = high)
  - Structured aerobic exercise and/or purposeful physical activity

- **Intervention groups**
  - High Group
  - Moderate Group
  - Low Group

**Outcomes**

- **Maintenance of flexibility and muscle strength**
- **Progressive resistance training to improve upper- and lower-body strength**
- **Progressive aerobic exercise training (e.g. walk/jog/run/swim/ cycle/) to increase cardiopulmonary fitness**
- **Purposeful brisk walking programme using progressive pedometer step-count targets**
DISCUSSION

In this study, we determined measurement and thresholds for health, strength and cardiopulmonary fitness of men with prostate cancer that informed our computer-based algorithm. We identified men diagnosed with prostate cancer who were at higher risk of cardiovascular disease and multi-morbidity. These men needed a lifestyle intervention as 41% had high levels of predicted risk for cardiovascular disease within the next 10 years but also referral back to their primary care teams for further management. Higher risk men were obese (22%) and had muscle weakness (50%) that could increase the risk of functional incapacity and falls. Our results are consistent with previously reported data for men receiving ADT [69], although only 32 out of 83 (38.5%) of men in our cohort had received ADT. This suggests that a broader range of men could benefit from lifestyle intervention than that recommended in NICE guidance for men receiving ADT. The assessment data underpinning the algorithm were used to define cardiopulmonary fitness, strength and cardiovascular health safely using objective measurements that could be conducted in a community pharmacy.

Recommendations for the safe design and content of an exercise prescription originate from the ASCM Cancer Survivorship and Exercise Guidelines [70]. This document recommends that the prescription should be individualised, according to survivors’ pre-treatment aerobic fitness, cancer treatment, medical comorbidities and any ongoing side-effects of treatment. For men with prostate cancer they recommend an evaluation of muscle strength and wasting, and a medical assessment prior to exercise referral for those with cardiac conditions (secondary to cancer or not) or bone metastasis. For men undertaking walking programs, flexibility or resistance training, aerobic exercise testing is not required.

Interviews with participants showed personalised feedback on health and fitness from the first assessment acted as a catalyst for behaviour change by provoking realisation of how they compared to healthy men of a similar age. There is growing evidence that using such assessments to develop tailored interventions which provide personally relevant messages induces favourable perceptions from individuals [71]. The use of algorithms in conjunction with health assessments can aid clinical decisions, helping treatment-related adjustments to be introduced to the lifestyle prescription [72], but also in adapting treatment to make it more specific to the individual [73]. As we observed in our
study, age and treatment-related adverse effects, such as those from ADT, were significant factors in low levels of fitness. By comparing health assessment data with normative values, we could create an algorithm for personalised lifestyle prescription based on body composition parameters, upper- and lower-body strength and cardiopulmonary fitness.

The study of exercise and physical activity interventions in cancer populations has increased substantially in recent years, with a review and meta-analysis of systematic reviews concluding that exercise is safe and efficacious [11]. Despite the heterogeneity of the populations included in the reviews (i.e. differences in cancer type, age, timing in the cancer trajectory, etc.), exercise prescription in many studies was relatively similar. Prescriptions consisted of either supervised or home-based endurance training or endurance plus resistance training, prescribed at a moderate intensity (50-70% of a predetermined cardiopulmonary fitness parameter, typically age predicted heart rate maximum or reserve) for 2-3 sessions per week and 10-50 min per exercise session for 12 to 15 weeks. Few of these studies identify if or how the exercise programmes were modified specifically to meet individual needs. Generic prescriptions have benefits but may not realise the full therapeutic potential of a tailored-lifestyle prescription. Sasso et al. [74] defined a framework for prescription in exercise oncology, identifying the key tenants as individualisation, progressive overload, specificity and recovery, which build on the essential baseline assessment. Specificity builds in adaptations to comorbidities and treatment-induced adverse effects as part of the lifestyle prescription but needs guidelines as to how to adapt lifestyle interventions.

Despite the wealth of evidence for the importance of weight management and physical activity, cancer survivors’ engagement with health behaviours and adherence to lifestyle advice is remarkably poor. Studies that identify how to adapt a nutrition prescription for men with prostate cancer are rarely evidenced [68, 75, 76] and reliance on clinical expertise to recognise the needs of individuals is problematic in terms of standardising approaches that can be adopted by community teams. Furthermore, the UKs Longitudinal Study of Ageing found that the proportion of cancer survivors who engaged in self-reported MVPA at least one a week fell from 13% at diagnosis to less than 9% after cancer treatment [77]. In future research, there is a need to investigate how best to communicate behaviour change messages to men via lifestyle interventions in a way that empowers them to act. Theoretical frameworks to guide Digital Behaviour Change Interventions (DCBI) and computer tailoring should inform the language used for messaging in both prescription and feedback processes [53, 78]. Our interview data show that for some men, the health assessment per se was the trigger for behaviour change, while for others, existing health beliefs needed to be challenged before change can happen.
The need for more cancer healthcare professionals to develop skills in the provision of evidence-based lifestyle advice is exemplified by the lack of interventions for managing the adverse effects of ADT [48]. Surveys in the UK suggest that few cancer survivors are provided with such advice when diagnosed [79] or during and after cancer therapy [80, 81]. Recent studies show that very few cancer patients exercise at the recommended level, despite international guidelines recommending its provision as part of routine follow-up care [82-84]. Improved multi-morbidity management in this population through targeted lifestyle change beyond prostate cancer outcomes, which could help to mitigate the adverse impacts of treatment on functional mobility, falls and fractures, as well as cardio metabolic risk, would augment any secondary prevention benefits that may be possible.

A limitation of this study was its selection of a higher risk population more in need of intervention, which may have introduced an element of bias in the algorithm. A strength of study is that the computer algorithm was created from personal physiological and qualitative data as a means of prescribing tailored-lifestyle advice to meet the specific needs of men with prostate cancer. This goes beyond lifestyle interventions which are only based on generic guidelines. The algorithm is flexible in being able to accommodate additional assessment data for further adaptation of the prescription as the evidence-base develops.

CONCLUSION
We have developed a computer algorithm that uses simple, safe and validated assessments to provide tailored lifestyle advice which addresses specific areas of cardiovascular risk, strength and physical fitness in men with prostate cancer. Lifestyle advice is tailored to each man by the algorithm using their assessment results (see supplementary material for example prescription) to inform a more targeted prescription for weight loss, improving muscle strength and cardiovascular fitness. The algorithm uses data from a short assessment battery to provide a picture of current health and functional status, allowing advice to be tailored to existing health and performance levels. This computer-based algorithm that can be integrated into existing software platforms used by primary care and pharmacy service providers and importantly, allows the advice to be generated in real time at the point of care. Such an assessment can act as the first step in testing and implementing tailored, evidence-based, interventions and could also help to engage a broader healthcare team to optimise the therapeutic potential of lifestyle interventions.
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Contributions

SF, AL & BG drafted the manuscript. All authors contributed to the manuscript, data analysis and interpretation. SF was the principal investigator. AL undertook the analysis and developed the computer-based algorithm. KP was project manager and coordinated data collection, qualitative analysis and ethical approvals. JS and RM provided expertise in exercise assessments and interventions, and in defining the cut-points for classification of fitness levels. JA, expertise in prostate cancer treatment, BG and LT provided expertise in nutrition.

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Ethical approval

The study was approved by the UK National Research Ethics Service REC 14/LO/0495 IRAS project ID 148309. All participants provided informed written consent.

Data Sharing Statement

Data from this study is available upon request.
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