Digital medicine in men with advanced prostate cancer – a feasibility study of electronic patient reported outcomes in patients on systemic treatment.

Highlights

- Electronic Patient- reported outcome measures can potentially improve patient care and streamline services.
- Digital access and familiarity is lower in older groups
- Electronic patient-reported outcome measures are feasible in clinic but more challenging from home.
- Strategies to support remote completion are summarised.

Abstract

Aims

Electronic patient reported outcome (ePRO) measures have potential to improve patient care, both at an individual level by detecting symptoms, and at an organisational level to rationalise follow-up. Introduction of ePROs has many challenges including funding, institutional rigidity and acceptability for both patients and clinicians. There are multiple examples of successful ePRO programmes but no specific feasibility studies in those who are less digitally engaged. Prostate cancer is predominantly a disease of older men and digital exclusion is associated with increased age. We assessed the feasibility of ePRO completion in older men receiving treatment for advanced prostate cancer both within the clinic and from home.

Materials and Methods

Men receiving palliative systemic treatment were asked to complete ePROs on a tablet computer in the outpatient department at 0 and 3 months. Participants were also offered optional completion from home. Feasibility was assessed via a mixed methods approach.

Results

On site ePRO completion was acceptable to the majority of patients with 90% finding them easy or straightforward and 80% preferring electronic over paper. Remote completion was more challenging, even for those who accessed email daily and owned a tablet, with only 20% of participants successfully completing ePROs. Barriers to electronic completion can be categorised as technical, attitudinal and medical. Quality of Life and symptom ePRO results were comparable to published data.

Conclusions

On site completion is achievable in this population with limited staff support. However, remote completion requires further work to improve systems and acceptability for patients. Remote completion is critical to add significantly to current clinical care by detecting symptoms or stratifying follow-up.

Key words

Quality of Life, Patient reported outcomes measures, Electronic Patient reported outcome measures, Prostate Cancer.

Introduction

The management of patients with advanced prostate cancer has undergone a revolution over the last decade, with at least 6 new agents licensed (in combination with ongoing androgen suppression) based on improvements in survival derived from pivotal trials. These range from chemotherapy (Docetaxel, Cabazitaxel) (1,2) through novel anti-androgens (Abiraterone, Enzalutamide, Apalutamide) (3,4) to radionucleotides (Radium 223) (5) and immunotherapeutics (Sipilucel –T)(6). Increasingly, evidence supports their use in the 'upfront' setting i.e. in combination with androgen deprivation at first diagnosis of metastatic disease, based on the results from the multi-arm STAMPEDE trial and allied studies (7–11). However, at present there is limited evidence available regarding predictive markers of efficacy to guide treatment choices and much therefore comes down to patient and clinician choice. Crucial to this is the relative effects of these treatments on quality of life, and how they might affect/are affecting the individual patient who may differ from those within the clinical trials.

The collection and reporting of patient reported outcomes (PROs) is established in clinical trials but use in routine clinical care is sparse. PROs can be used to detect unreported symptoms, allow more efficient use of clinic time and potentially replace the need for some routine follow-up appointments (12,13). Challenges exist including institutional rigidity, IT infrastructure, funding and a lack of acceptance by both clinicians and patients of their utility. Many systems that are in place are a collaboration between university and hospital with research resources to support implementation (14). These systems demonstrate however that PRO use in routine care is both possible and acceptable with evidence of improved symptom management, treatment completion and even overall survival (12,15–18).

Unprecedented changes in clinical practice have occurred due to the COVID pandemic with infection control priorities limiting face to face contact. The challenges of adapting to COVID are also an opportunity however to push forward on implementing systems to allow remote assessment of patients in routine clinical care as a mechanism to promote self-care and optimise clinical encounters in a health service under pressure. However, it is critical that patients are not left behind and we need to understand patient experience of electronic PRO completion to target support and identify what intervention is most useful.

Historically PROs have been completed on paper and this impairs rapid interpretation within a clinic appointment. Electronic PROs (ePROs) with real-time analysis allow clinicians to identify areas of concern and trends over time. Successful systems utilise a range of completion options including workstations and tablets in clinic and opportunities to complete questionnaires at home, with tablets being provided in some research settings. ePROs can also overcome some of the pitfalls of paper questionnaires as participants are unable to miss out questions or transpose answers across multiple lines of tick boxes. Despite advantages of ePRO systems there may be challenges in electronic completion for some participants including older people who are more likely to be digitally excluded. An Age UK evidence review (19) reported that 36% of people aged 65+ are offline (lapsed or never users) with only 44% of those aged 75 or older having used the internet in the last 3 months. In addition, older adults are more likely to be "narrow" users (19) and to use desktop or laptop computers, whereas ePROs are often optimised for mobile devices. The age-related risk of digital exclusion is pertinent in prostate cancer populations as 35% of cases are diagnosed in men over 75 (20) and older men predominant even within clinical trials: the mean age in the STAMPEDE docetaxel comparison was 65 (IQR 60-71) (21).

We explored the feasibility of collecting ePROs specifically in a population of older men with prostate cancer, representing a range of digital experience. This was based in an outpatient setting, with a sub-study exploring remote completion. The QoL data collected was benchmarked to published data from larger studies and analysed at an individual patient level to inform decisions about instrument selection for future application in this group.

Methodology

Ethical Approval

The study was conducted in accordance with GCP and the declaration of Helsinki. The sponsor was Brighton & Sussex University Hospitals NHS Trust and the study was approved by the Brighton & Sussex Research Ethics Committee and the HRA (ISCRTN 67560441).

Patient Eligibility & recruitment

Participants were recruited from uro-oncology clinics in a teaching hospital and 2 district general hospitals across Sussex. Eligible patients were identified from clinic lists and approached by the treating clinician. They either met with the research fellow immediately after the clinic appointment or at a treatment appointment. Eligibility was defined as: prostate cancer not for radical treatment, commencing a new systemic treatment in addition to androgen deprivation therapy. This could be at initial diagnosis ("up front") or on progression to castrate refractory prostate cancer.

Questionnaires

The HrQOL instruments selected were the Euroqol EQ-5D-5L and EORTC QLQC30 and PR25 modules. The EQ-5D-5L is widely used across cancer and non-cancer research, it is brief and allows for calculation of QALYs. The QLQC30 assesses global quality of life and functioning across 5 domains (physical, role, emotional, social and cognitive) and a number of symptoms common across cancer types. The PR25 module covers symptoms and concerns most relevant to prostate cancer and treatment. Representatives from the PCaSo patient support group were involved in testing the online questionnaire platform and assessing acceptability of the platform and questions.

Intervention – see Figure 1.

Baseline demographic/clinical and "computer familiarity" questionnaires were completed on paper prior to accessing the HrQoL questionnaires on a tablet. The researcher was available for support and support requirements were documented. Patient experience was assessed using a bespoke "feasibility" questionnaire covering acceptability of the platform and preferences for future questionnaire completion.

At 3 months, participants completed questionnaires on the tablet, supported by a member of the research team. A feasibility questionnaire was completed in person or by phone.

Participants were offered optional remote completion at additional time points of 1 and 2 months and could also chose to complete the 3-month questionnaire remotely. This could be either via a web-based questionnaire or an app which could be downloaded to the participant's own tablet or mobile.

Analysis

Baseline demographics and digital background were summarised with descriptive statistics. Feasibility assessment utilised a mixed methods approach including analysis of time taken and qualitative analysis of the free text comments. Analysis of QoL PROs was conducted in accordance with the scoring manuals (22). Summary scores, incidence rates and narrative descriptors were used to optimise clinical interpretation. Due to small numbers no significance testing was possible.

Funding

The study was funded by a medical education grant from Sanofi pharmaceuticals and research fellow salary from the Sussex Cancer Fund. The software partner was Vitaccess Ltd. The funders had no role in the study design or conduct.

Results

Baseline characteristics

45 men were offered the study of whom 40 were recruited between September 2016 and March 2017, see Consort Diagram (Figure 2). Mean age was 74 years (range 58-89 years). The most common treatment received were the novel antiandrogens enzalutamide (17) and abiraterone (2); 13 participants received chemotherapy in the form of docetaxel (10, 5 upfront, 5 on progression) or cabazitaxel (3) and 8 radium^{223}.

Participants were pre-classified into "computer familiarity" groups based on email usage. 5 participants did not have an email address, 6 used email weekly or less frequently and 29/40 accessed their email daily. 24 had used a tablet computer before but only 14/40 used a tablet regularly. 19 participants had a smart phone but only 1 used their phone for anything other than text messages and phone calls.

Data completeness

All 40 participants completed the baseline assessment. At 3 months 35 participants completed questionnaires and feasibility data was available for 33 of these participants. There was a failure of data transfer for the QoL questionnaires for 1 participant at baseline and 3 at follow up. There was unreliable access to trust Wi-Fi at some sites and so data upload was delayed in some cases which may have contributed.

Feasibility results

The mean time taken to complete the questionnaires at baseline was 12.2 minutes with 31/39 participants completing the questionnaires within 5-15 minutes. There was no difference at 3 months (mean 12 minutes, 27/32 completing within 15 minutes). Remote completion via web or app took a similar time.

Direct electronic data capture was broadly acceptable for participants. 36/40 found the questionnaires easy or straightforward. All participants reported that they would be happy to complete questionnaires regularly as part of standard clinical care and 32/40 would prefer electronic questionnaires. 4 participants preferred paper completion, with 4 happy with either. Only 3 participants required significant assistance from the research team at the baseline visit. This was due to difficulty seeing the questions on the tablet and using the appropriate pressure to submit answers. All those who used a tablet regularly (14/40) reported no difficulties with using the tablet.

The majority of those who had never used a tablet still found completion straightforward, easy or very easy. See table 1.

At 3 months 28/33 participants found completion easy or straightforward, however 6/33 required support from either a relative/friend or the research team, this was related mainly to visual difficulties with the tablet. 2 participants reported that completing questionnaires was more challenging as they felt unwell.

Remote Completion

33 participants consented to remote completion but only 8 successfully completed questionnaires with indication of attempts by up to 4 other participantsThe baseline characteristics of this group were not markedly different to the study population: the mean age was identical at 74 (range 62-84); 6/8 checked their email daily: a similar proportion to the study population. 6/8 had a tablet computer which is a higher proportion than the study population (14/40), but this did not predict for remote completion and, in fact, only 1 participants used the app on a remote device, the remaining 7 used the web portal. 4 participants who completed questionnaires remotely chose to complete their 3-month questionnaires in clinic. These participants reported that they felt more confident about data reaching the study team when completing on the study tablet and that it was easier than accessing the questionnaires at home.

Experience of remote completion was assessed by phone or in person at 3 months for 33/40 participants. Three themes arose which described the perceived barriers to electronic completion: Process-based – e.g. email going into spam, issues with usernames and passwords; Attitudinal – e.g. concerns about downloading an app; and Medical e.g. fatigue. See Figure 3.

QoL results

QoL results at baseline are summarised in table 2. As expected in a population of patients with progressive disease but deemed fit to commence treatment there is an appreciable symptom burden but participants do not report high levels of disability. For example although the majority of participants reported some problem with mobility (51% EQ5D) or physical functioning (85% QLQC30) this was generally of a low grade such that the calculated score for physical functioning was 74/100, indicating a good level of function.

There was good concordance across the different instruments where there is overlap. For example: the EQ-5D-5L and the EORTC QLQ C30 both give a measure of overall health status and this was similar at 68 (range 13-97, SD 19.8) for the EQ-5D-5L visual analogue score and 64 (range 17-100, SD 21.1) for the Global health status score (EORTC QLQ C30).

Most patients reported problems with pain, captured by both the EQ5D and QLQC30, although for the majority of participants this was mild. Anxiety and depression or impact on emotional functioning was also reported by the majority of participants. The PR25 instrument detected high incidence of urinary and hormone treatment-related symptoms although with low average severity (score of 23/100 and 14/100).

QoL change at 3 months

At 3 months mean Overall/Global health was similar to baseline (66 vs 68 EQ5D; 60 vs 64 QLQ), however, these aggregate figures do not necessarily represent the experience of the individual participant. Paired data from the EQ5D VAS shows a diverse patient experience: using a change of >10 as a threshold for clinical meaningful change 11/31 patients had no change; 12/31 rated their health as worse and 8/31 as improved. See Figure 4.

The EORTC instruments also demonstrated a variety of patient experiences at 3 months. Table 3 summarises these changes with a threshold of 10 as a clinically meaningful difference for the individual. There is diversity in the results: more patients showed improvement in emotional functioning and this is mirrored by a reduction in those reporting anxiety or depression symptoms on the EQ5D from 56% to 34%. In contrast fatigue and global health status were more likely to be static or worse. The prostate cancer-specific symptoms were unchanged for most patients which is not surprisingly given that most patients were already established on GnRH analogues at baseline and so already had hormone treatment-related side effects and their new systemic treatments were unlikely to impact on urinary and bowel symptoms. It is disappointing however that pain was not improved for more patients whether by the impact of their treatment on disease (particularly Radium) or by improved analgesia.

Discussion

We have demonstrated the feasibility of on-site direct electronic data capture in this population of older patients, a significant proportion of whom had limited experience of mobile devices. Our study was well received with 89% uptake; published studies show a wide range of uptake with lower uptake seen in mixed on treat/follow-up populations compared to those on treatment. The PROMPTCARE system had 20% uptake in the feasibility phase and only 16% of those invited were enrolled in the controlled trial (17,23). Whereas the eRAPID RCT in systemic therapy had 73% uptake in eligible patients (18) and the landmark study by Basch and colleagues, which demonstrated an overall survival advantage, had a 90% uptake (15).

ePRO interventions in routine care often lack the resources to support recruitment of patients: the TRIGGER project was a Macmillan & Royal College of Radiologists pilot in three sites aiming to introduce a short ePRO for patients receiving pelvic radiotherapy. There was a wide range of uptake (12-39%) and study conclusions suggest that asking staff to incorporating this into existing workloads was a significant barrier (24).

The baseline results from this population fit within the reference values for prostate cancer (all stages) and stages II-IV, with the exception of fatigue which is worse in this study population (score of 39 vs 26.9 for all stages & 26.2 for stage II-IV) (25). Our PRO results across all instruments are also consistent with the published results from both registry data and clinical trials in similar populations (26,27). Availability of longitudinal PRO data for the individual patient reveals granularity of experience which is not generally presented in aggregate trial data and has potential to provide data to support decision-making in the clinic. Whilst PROs can contribute to the evidence base for decision-making in patient care, both at an individual and aggregate level, there are potential weaknesses. Reporting bias can occur by patients consciously or sub-consciously adjusting responses, as they might in a consultation. This may be reduced when PROs are completed at home and separated temporally from clinic visits where decisions are being made. Longitudinal PRO collection can allow for patients' inherent optimistic or pessimistic outlook to be accounted for by considering change in responses rather than absolute values. At an aggregate level care needs to be taken when censoring for missing or incomplete data as this is likely to be informative rather than random. Non-completion might reflect that the patient is too unwell to complete questionnaires, or conversely, that they are too busy getting on with life depending on the clinical context.

Remote completion was more challenging for the participants in this study with technical, attitudinal and medical barriers. Technological issues, e.g. registration emails going into spam, have already been addressed in more mature systems – for example the e-RAPID team provide log in details on a post card (28). Electronic PRO projects who have reported feasibility have excluded those without home internet access but the experience of those who have access but may not be regular users has not been explored. Some research studies have capacity to provide a study tablet for those without hardware (29,30) but this is not the case for PRO use in routine care. Tackling attitudinal barriers is more complex and it is notable that a number of participants who successfully completed questionnaires remotely nevertheless elected to do their 3-month questionnaires at the hospital. Other groups have described the importance of real time feedback to users so that they can be confident that their responses have been detected, this is likely to overcome concerns about data being lost. The potential for family and friends to facilitate digital access was raised by several participants who either offered relatives email addresses or reported that they relied upon the support of others to access the PRO at home.

The COVID pandemic may have accelerated digital adoption by those who either were previous not connected or were connected but not engaged. A small qualitative study reported broadly positive experiences in 30 adult participants who were previously narrow or never users, with increases in both social (e.g. zoom) and practical use (31). However, COVID may also have impacted negatively upon the support available to those who are hesitant about digital technology with the closure of public spaces e.g. libraries and the inability to see family and friends (32).

The burden of symptoms had an impact on questionnaire completion. Any patient who is struggling with fatigue or other symptoms may find completing PROs, whether paper or electronic, a burden. The numbers in this study were too small to assess for an association between global health status or fatigue and PRO completion rates or times. The LAPCD study reported that response rates were lower in the elderly, those with socioeconomic deprivation and patients with more advanced disease supporting the idea that even for paper questionnaires those who are most in need may be less able to access help via PRO instruments (27).

The provision of tailored advice to patients based on their responses and the reference to questionnaire responses by clinicians is also reported to increase patient perception of value of completing questionnaires (18). It is critical that PROs can be integrated into clinical systems to allow for efficient use by clinicians and this has required significant work in the systems that are currently in place (14). If PROs are seen to be useful for clinical care then patients are more likely to overcome technological, attitudinal or medical barriers to achieve completion.

A reduction in face- to- face consultations accentuates the need to support ePRO completion in all patients, we have not found a simple screening question to predict those who are in need of support, for example 23/29 participants who checked their email daily and 8/14 who used a tablet regularly did not achieve remote completion. Opinions are divided about whether providing alternative formats (paper/phone completion) actually reduces engagement with online completion in those who are connected but not familiar. Potential interventions to support ePRO completion are summarised in table 4.

Future Directions

1. **My Clinical Outcomes – establishing PROs in routine practice**

Brighton and Sussex University Hospitals NHS Trust are incorporating remotely completed ePROs into routine care for patients receiving treatment for "treatable but not curable" cancer using the *My Clinical Outcomes* platform. These PROs are used as a tool to highlight patients with increasing symptom burden, or who are struggling on treatment to clinicians and CNS teams, to facilitate earlier follow-up and targeted interventions or referrals onto appropriate services. This has been developed as part of a 2 year pilot project in Enhanced Supportive Care, funded by NHSI Specialist Commissioning.

2. **Prostate Cancer PSA Follow-up Stratification**

This pilot project in East Sussex is using PROs alongside PSA measurement to stratify follow-up. This programme makes use of physician associates to coordinate remote follow-up and reduce both telephone & face to face appointments. Questionnaire selection has been informed by this feasibility study. PROs will be available both on paper and electronically as per patient preference. Uptake of electronic questionnaires will be supported and monitored although it is anticipated that ePROs may be more readily adopted in patients with early disease.

Conclusions

On site electronic PRO completion is feasible for most patients but significant support will be needed to facilitate remote completion for patients who are less digitally able, including options of telephone or paper completion. Establishment of PRO completion in routine clinical care needs funding and attention to ensure patient inclusion. In general terms it is likely that those who are currently receiving treatment are likely to be both more willing and more able to complete PRO instruments than those who are currently not receiving treatment. If electronic PROs are to form a part of healthcare resource rationalisation by replacing some routine follow-up then it is imperative to find strategies to widen participation across patient groups.

Tables & Figures

Table 1: Feasibility of questionnaire completion: study population & by previous tablet use.

Ease of completion	All n=40	No tablet use n=16	Infrequent tablet use n=10	Regular tablet use n=14
Very Easy	5	14	8	14
Easy	23			
Straight forward	8			
Difficult	3	2	2	0
Very Difficult	1			

Table 2: QoL results at baseline

Instrument	**Domain**	**Calculated Score (Range 1- 100 Function score high = good function Symptom score high = high symptom burden**	**% reporting problems**
EQ-5D-5L			
	Overall Health (VAS scale)	68	
	Mobility		51
	Self care		13
	Usual Activities		44
	Pain/discomfort		74
	Anxiety/depression		56
EORTC QLQ C30			
	Global Health Status	64	
	Physical Functioning	74	85
	Role Functioning	74	64
	Emotional Functioning	74	92
	Cognitive Functioning	80	62
	Social Functioning	82	49
	Fatigue	39	95
	Pain	28	64
	Insomnia	29	69
EORTC PR25			
	Urinary Symptoms	23	89
	Incontinence Aid (n=11)	6	9
	Bowel Symptoms	10	56
	Hormone treatment-related symptoms	14	87
	Sexual Activity	5	100

Table 3: Change in QoL at 3 months

Instrument	Domain	Improved	No difference	Worse
EORTC QLQ C30				
	Global Health Status	4	15	12
	Physical Functioning	5	16	10
	Role Functioning	8	14	9
	Emotional Functioning	15	14	2
	Cognitive Functioning	7	13	11
	Social Functioning	6	16	9
	Fatigue	9	9	13
	Pain	10	14	7
	Insomnia	10	17	4
EORTC PR25				
	Urinary Symptoms	7	24	0
	Incontinence Aid	0	3	0
	Bowel Symptoms	6	25	0
	Hormone treatment-related symptoms	5	20	6
	Sexual Activity	1	25	5

Table 4 Potential Interventions to support ePRO completion.

Stage	Clinical Input	System design features
Introduction	Introduced by trusted clinician	Stratified induction on first use depending on comfort
	Appropriate timing of introduction	Provision of login details on paper and via email
		User guide on paper and electronically
Use	Value reinforced by reference to results in clinic consultations	Intuitive interface
	Staff familiar with system from patient perspective to trouble shoot issues	Automatic completion confirmation
	Clinical resourcing to deal with issues reactively outside of clinical appointments	User–friendly presentation of longitudinal results for clinician & patient
		Provision of targeted self-management resources
Widening access	Prospective identification of patients who are less able to complete	Adjustable font size/read aloud options
	Retrospective identification of non-completers and support e.g. by phone	Provision of tablet/data allowance

Figure 1: Study Schematic

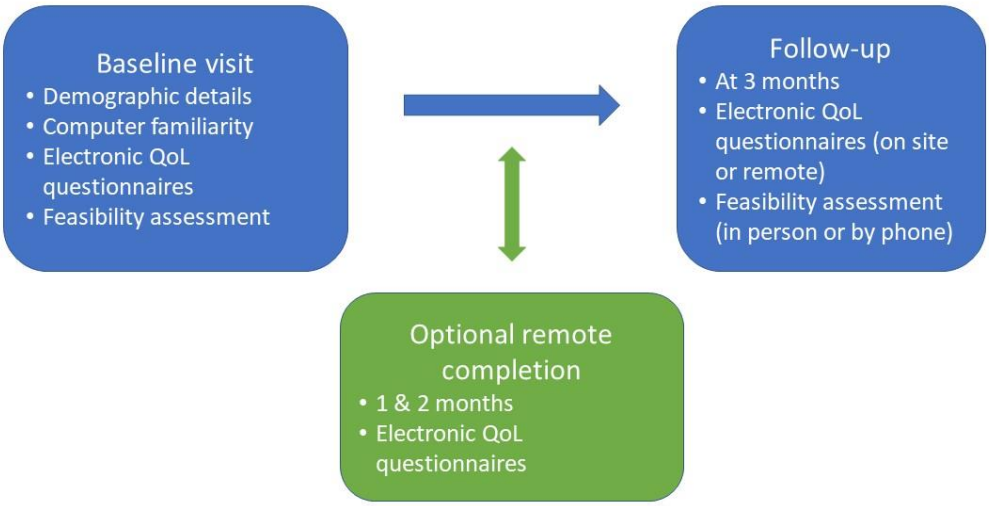


Figure 2: Consort Diagram

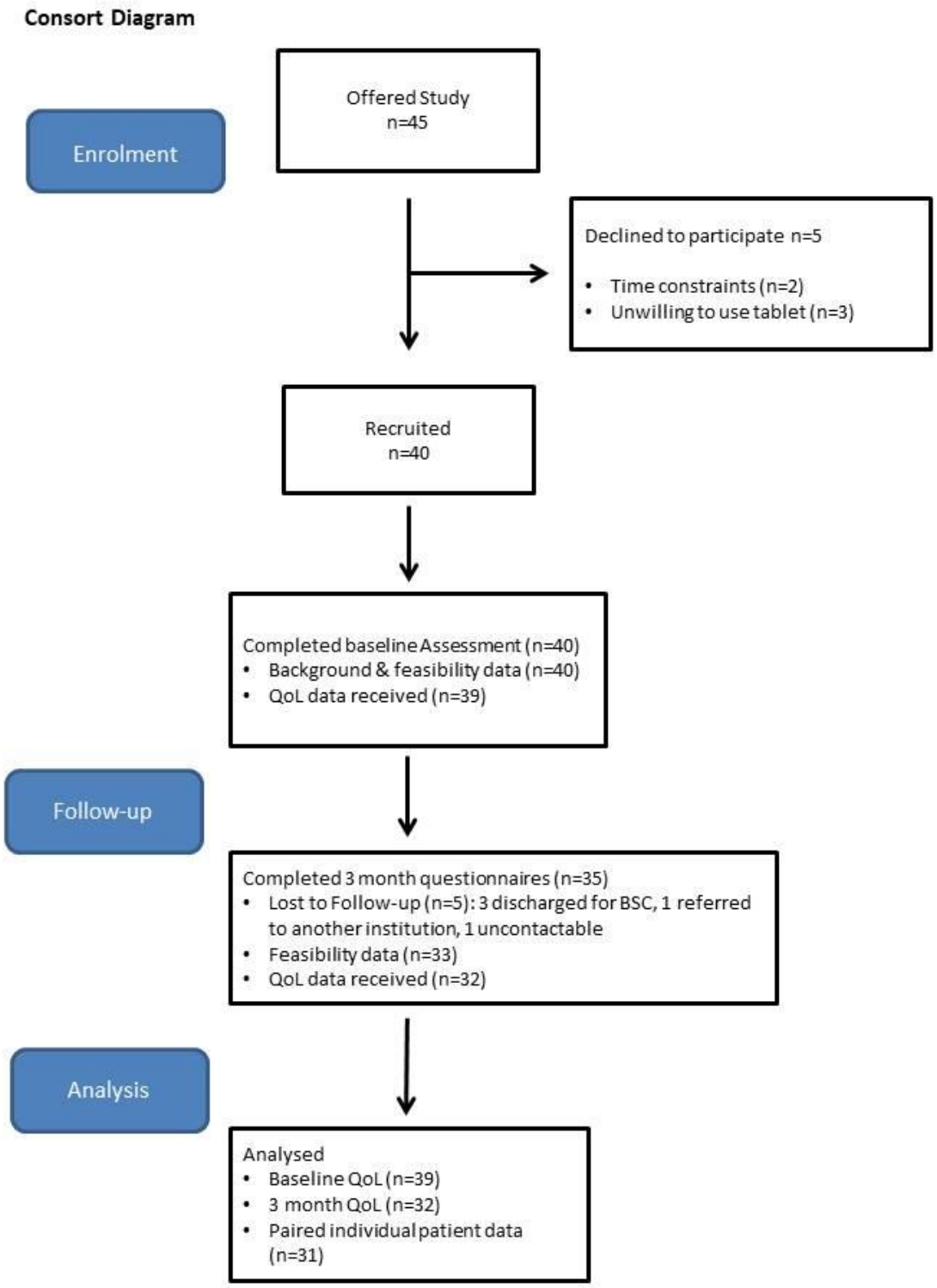


Figure 3: Barriers to electronic completion

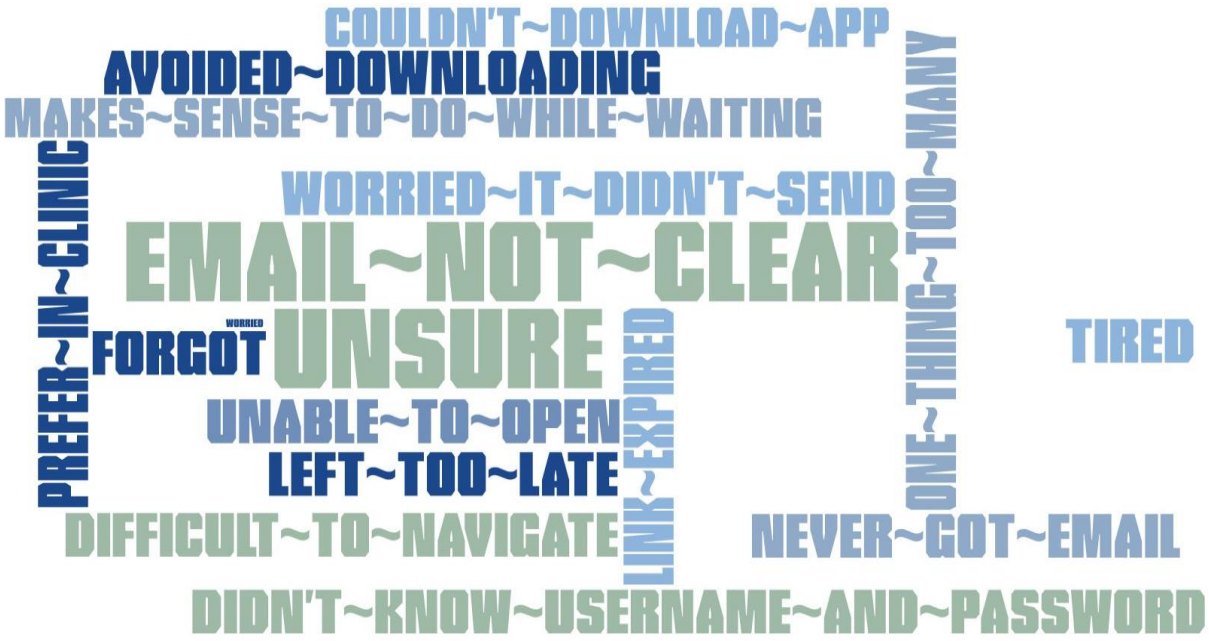
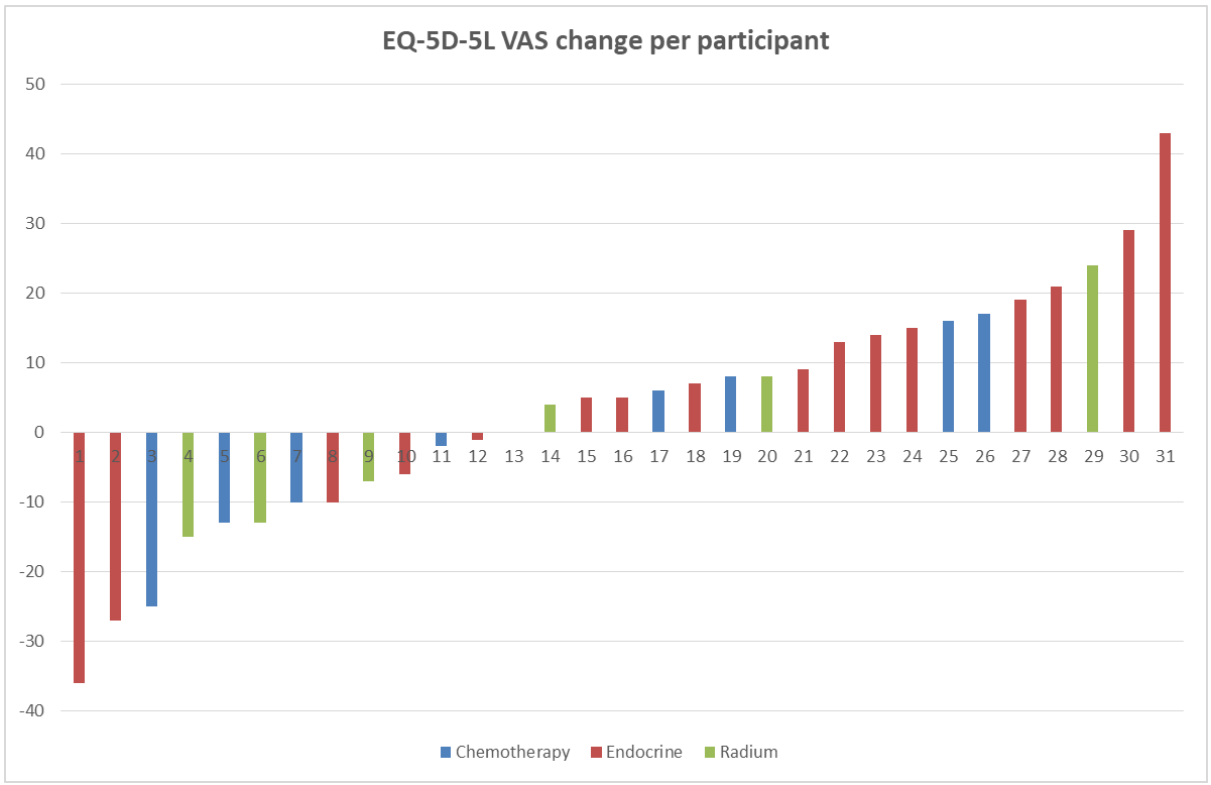


Figure 4: Change in EQ-5D-5L VAS score at 3 months



References

1. De Bono JS, Oudard S, Ozguroglu M, Hansen S, MacHiels JP, Kocak I, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: A randomised open-label trial. Lancet [Internet]. 2010 Oct 2 [cited 2020 Dec 10];376(9747):1147–54. Available from: https://pubmed.ncbi.nlm.nih.gov/20888992/

2. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, et al. Docetaxel plus Prednisone or Mitoxantrone plus Prednisone for Advanced Prostate Cancer. N Engl J Med [Internet]. 2004 Oct 7 [cited 2020 Dec 10];351(15):1502–12. Available from: https://pubmed.ncbi.nlm.nih.gov/15470213/

3. de Bono JS, Logothetis CJ, Molina A, Fizazi K, North S, Chu L, et al. Abiraterone and Increased Survival in Metastatic Prostate Cancer. N Engl J Med [Internet]. 2011 May 26 [cited 2020 Dec 10];364(21):1995–2005. Available from: https://pubmed.ncbi.nlm.nih.gov/21612468/

4. Scher HI, Fizazi K, Saad F, Taplin M-E, Sternberg CN, Miller K, et al. Increased Survival with Enzalutamide in Prostate Cancer after Chemotherapy. N Engl J Med [Internet]. 2012 Sep 27 [cited 2020 Dec 10];367(13):1187–97. Available from: https://pubmed.ncbi.nlm.nih.gov/22894553/

5. Parker C, Nilsson S, Heinrich D, Helle SI, O'Sullivan JM, Fosså SD, et al. Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer. N Engl J Med [Internet]. 2013 Jul 18 [cited 2020 Dec 10];369(3):213–23. Available from: https://pubmed.ncbi.nlm.nih.gov/23863050/

6. Kantoff PW, Higano CS, Shore ND, Berger ER, Small EJ, Penson DF, et al. Sipuleucel-T Immunotherapy for Castration-Resistant Prostate Cancer. N Engl J Med [Internet]. 2010 Jul 29 [cited 2020 Dec 10];363(5):411–22. Available from: https://pubmed.ncbi.nlm.nih.gov/20818862/

7. James ND, de Bono JS, Spears MR, Clarke NW, Mason MD, Dearnaley DP, et al. Abiraterone for Prostate Cancer Not Previously Treated with Hormone Therapy. N Engl J Med [Internet]. 2017 Jul 27 [cited 2020 Dec 10];377(4):338–51. Available from: https://pubmed.ncbi.nlm.nih.gov/28578639/

8. James ND, Sydes MR, Clarke NW, Mason MD, Dearnaley DP, Spears MR, et al. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): Survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. Lancet [Internet]. 2016 Mar 19 [cited 2020 Dec 10];387(10024):1163–77. Available from: https://pubmed.ncbi.nlm.nih.gov/26719232/

9. Fizazi K, Tran N, Fein L, Matsubara N, Rodriguez-Antolin A, Alekseev BY, et al. Abiraterone plus Prednisone in Metastatic, Castration-Sensitive Prostate Cancer. N Engl J Med [Internet]. 2017 Jul 27 [cited 2020 Dec 10];377(4):352–60. Available from: https://pubmed.ncbi.nlm.nih.gov/28578607/

10. Kyriakopoulos CE, Chen YH, Carducci MA, Liu G, Jarrard DF, Hahn NM, et al. Chemohormonal therapy in metastatic hormone-sensitive prostate cancer: long-term survival analysis of the randomized phase III E3805 chaarted trial. J Clin Oncol [Internet]. 2018 Apr 10 [cited 2020 Dec 10];36(11):1080–7. Available from: https://pubmed.ncbi.nlm.nih.gov/29384722/

11. Davis ID, Martin AJ, Stockler MR, Begbie S, Chi KN, Chowdhury S, et al. Enzalutamide with Standard First-Line Therapy in Metastatic Prostate Cancer. N Engl J Med [Internet]. 2019 Jul 11 [cited 2020 Dec 10];381(2):121–31. Available from: https://pubmed.ncbi.nlm.nih.gov/31157964/

12. Velikova G, Booth L, Smith AB, Brown PM, Lynch P, Brown JM, et al. Measuring quality of life in routine oncology practice improves communication and patient well-being: A randomized controlled trial. J Clin Oncol. 2004;22(4):714–24.

13. Detmar SB, Muller MJ, Schornagel JH, Wever LDV, Aaronson NK. Health-related quality-of-life assessments and patient-physician communication: A randomized controlled trial. J Am Med Assoc. 2002 Dec 18;288(23):3027–34.

14. Absolom K, Holch P, Warrington L, Samy F, Hulme C, Hewison J, et al. Electronic patient self-Reporting of adverse-events: Patient information and advice (eRAPID): A randomised controlled trial in systemic cancer treatment. BMC Cancer. 2017 May 8;17(1).

15. Basch E, Deal AM, Kris MG, Scher HI, Hudis CA, Sabbatini P, et al. Symptom monitoring with patient-reported outcomes during routine cancer treatment: A randomized controlled trial. J Clin Oncol. 2016 Feb 20;34(6):557–65.

16. Basch E, Deal AM, Dueck AC, Scher HI, Kris MG, Hudis C, et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment [Internet]. Vol. 318, JAMA - Journal of the American Medical Association. American Medical Association; 2017 [cited 2020 Nov 13]. p. 197–8. Available from: https://pubmed.ncbi.nlm.nih.gov/28586821/

17. Girgis A, Durcinoska I, Arnold A, Descallar J, Kaadan N, Koh E-S, et al. Web-Based Patient-Reported Outcome Measures for Personalized Treatment and Care (PROMPT-Care): Multicenter Pragmatic Nonrandomized Trial. J Med Internet Res. 2020 Oct 29;22(10):e19685.

18. Absolom K, Warrington L, Hudson E, Hewison J, Morris C, Holch P, et al. Phase III Randomized Controlled Trial of eRAPID: eHealth Intervention During Chemotherapy. J Clin Oncol [Internet]. 2021 Jan 8 [cited 2021 Feb 1];JCO.20.02015. Available from: https://pubmed.ncbi.nlm.nih.gov/33417506/

19. AGEUK. Digital Inclusion Evidence Review 2018. 2018.

20. Prostate cancer statistics | Cancer Research UK [Internet]. [cited 2020 Oct 8]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/prostate-cancer#heading-Zero

21. Clarke NW, Ali A, Ingleby FC, Hoyle A, Amos CL, Attard G, et al. Addition of docetaxel to hormonal therapy in low- And high-burden metastatic hormone sensitive prostate cancer: Long-term survival results from the STAMPEDE trial. Ann Oncol [Internet]. 2019 Dec 1 [cited 2021 Feb 1];30(12):1992–2003. Available from: https://pubmed.ncbi.nlm.nih.gov/31560068/

22. EORTC QLQ-C30 Scoring Manual The EORTC QLQ-C30. 2001.

23. Girgis A, Delaney GP, Arnold A, Miller AA, Levesque J V, Kaadan N, et al. Development and Feasibility Testing of PROMPT-Care, an eHealth System for Collection and Use of Patient-Reported Outcome Measures for Personalized Treatment and Care: A Study Protocol. JMIR Res Protoc [Internet]. 2016 Nov 24 [cited 2020 Nov 12];5(4):e227. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27884813

24. Macnair A, Sharkey A, Le Calvez K, Walters R, Smith L, Nelson A, et al. The Trigger Project: The Challenge of Introducing Electronic Patient-Reported Outcome Measures Into a Radiotherapy Service [Internet]. Vol. 32, Clinical Oncology. Elsevier Ltd; 2020 [cited 2020 Nov 24]. p. e76–9. Available from: https://doi.org/10.1016/j.clon.2019.09.044

25. Scott NW, Fayers PM, Aaronson NK, Bottomley A, De Graeff A, Groenvold M, et al. EORTC QLQ-C30 Reference Values This manual presents reference data for the QLQ-C30 based upon

data provided by EORTC Quality of Life Group Members and other users of the QLQ-C30 Sprangers on behalf of the EORTC Quality of Life Group EORTC Quality of Life Group. 2008.

26. Kuppen MCP, Westgeest HM, Van Den Eertwegh AJM, Coenen JLLM, Van Moorselaar RJA, Van Den Berg P, et al. Health-related Quality of Life and Pain in a Real-world Castration-resistant Prostate Cancer Population: Results From the PRO-CAPRI Study in the Netherlands. Clin Genitourin Cancer [Internet]. [cited 2020 Oct 8];18(3):233–53. Available from: https://doi.org/10.1016/j.clgc.2019.11.015

27. Downing A, Wright P, Hounsome L, Selby P, Wilding S, Watson E, et al. Quality of life in men living with advanced and localised prostate cancer in the UK: a population-based study. Lancet Oncol [Internet]. 2019 Mar 1 [cited 2020 Oct 8];20(3):436–47. Available from: https://pubmed.ncbi.nlm.nih.gov/30713036/

28. Warrington L, Absolom K, Holch P, Gibson A, Clayton B, Velikova G. Online tool for monitoring adverse events in patients with cancer during treatment (eRAPID): Field testing in a clinical setting. BMJ Open. 2019 Jan 1;9(1).

29. Wintner LM, Giesinger JM, Zabernigg A, Rumpold G, Sztankay M, Oberguggenberger AS, et al. Evaluation of electronic patient-reported outcome assessment with cancer patients in the hospital and at home eHealth/ telehealth/ mobile health systems. BMC Med Inform Decis Mak. 2015 Dec 23;15(1).

30. Taarnhøj GA, Lindberg H, Dohn LH, Omland LH, Hjøllund NH, Johansen C, et al. Electronic reporting of patient-reported outcomes in a fragile and comorbid population during cancer therapy - A feasibility study. Health Qual Life Outcomes. 2020 Jul 11;18(1).

31. Digital Exclusion Research 2020: Understanding the impact of COVID-19 on digital exclusion. [Internet]. [cited 2021 Feb 8]. Available from: http://www.broadbanduk.org/wp-content/uploads/2020/10/Broadband-Stakeholder-Group-Digital-Exclusion-2020-Final-report.pdf

32. Covid-19 is increasing digital inequality: We need human connectivity to close the digital divide | Oxford Law Faculty [Internet]. [cited 2021 Feb 8]. Available from: https://www.law.ox.ac.uk/research-and-subject-groups/oxfordshire-digital-inclusion-project/blog/2020/04/covid-19-increasing