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STUDY PROTOCOLS

A personalized app to improve quality of life of patients with a stoma: A protocol for a multicentre randomized controlled trial

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Abstract

Aim: Proper education, guidance and support is crucial before and following creation of a stoma. Patients with a stoma and their close relatives need to adapt to and cope with this new – and sometimes unforeseen – situation, which may result in insecurities and a variety of psychosocial problems. Self-efficacy is associated both with a reduction in psychosocial problems and with improved quality of life. The main objective of this study was to investigate whether self-reported quality of life of patients with a stoma can be enhanced by offering personalized and timed guidance, as well as peer contact, in a patient-centred mobile application.

Method: A multicentre, double-blind, randomized controlled trial will be conducted. Consented adults >18 years of age who will receive an ileostomy or colostomy and possess an eligible smartphone will be included. The intervention group will be given the full version of the application (containing personalized and timed guidance, such as operation-specific information and information on the associated care pathway) to install on their smartphone. In addition, the intervention group has access to a protected peer-support platform within the app. The control group will receive a restricted version of the application that contains only generic (non-personalized) stoma-related information. The primary outcome is quality of life, 3 months postoperatively. Secondary outcomes are Patient Reported Outcome Measures (PROMs), such as psychological adaption, as well as number of complications, re-admission and re-operation rates and the length of hospital stay.

Results: Patient enrolment began in March 2021. Data collection was not complete when this protocol was submitted.

Conclusion: We hypothesize that patients with a stoma who are supported by the intervention version of the app will report a significantly higher quality of life than patients with a stoma who are supported by the control version of the app (ie, are not offered personalized and timed guidance and information and do not have access to peer support in the app).

KEYWORDS
app, colorectal, colostomy, digital, ehealth, ileostomy, mhealth, mobile application, mobile health, quality of life, stoma, surgery

The Stoma APPtimize Collaborative Study Group members are present in Appendix A.

INTRODUCTION

It is estimated that over 7000 new stomas are created annually in the Netherlands [1]. The creation of an ileostomy or colostomy may be required for colorectal malignancy or inflammatory bowel disease. For the patient, having a stoma may negatively affect their self-image and daily functioning, which most likely will result in a reduced quality of life [2–4]. Especially in the initial postoperative period, patients must adapt to the new situation. Coping with a stoma may be difficult, resulting in insecurities that can lead to psychosocial problems, such as depression, stress, anxiety, decreased social participation and sexual problems [5]. Patients are also at risk of stoma-related morbidity (the incidence of which varies from 20% to 80%), with peristomal skin problems and leakages being the most common complications [6, 7]. Self-efficacy is associated with a reduction in psychosocial problems and stoma-related morbidities [8, 9]. Hence, patient education and guidance are crucial both pre- and postoperatively. Several educational stoma-care programmes have been described in the literature, all of which have shown positive results in terms of psychosocial skills, self-efficacy and quality of life [10, 11]. However, providing personal and adequate stoma care both in and out hospital settings can be challenging. In general, Dutch patients were only moderately satisfied with the stoma care they received, and several shortcomings were reported in information provision, the postoperative care and contact with fellow peers [12, 13].

A tailored personalized mobile application (app) may be an important and eligible addition to regular stoma care to improve information provision and contact with fellow peers [12, 13]. An app, if properly designed in terms of content and regulations, has great potential to provide support, whenever needed, to patients with a stoma. It is essential that the app provides up-to-date and reliable information which can be consulted and searched at any time, and that the information is presented in a visually attractive way [13]. Reliable and easy to understand information on how to cope with a stoma and what is considered 'normal' and what is not, and the possibility for peer-to-peer contact between patients, may be very important in the perioperative phase, but also to fall back upon later. Access to such information at any time may facilitate acceptance, self-confidence and self-efficacy, and may help a patient regain control over their new situation, possibly resulting in a decreased demand for caregivers. By conducting this double-blind randomized controlled trial (RCT), we aimed to investigate whether personalized and timed guidance, as well as peer contact, in a patient-centred mobile application can significantly improve the quality of life of patients following placement of a stoma compared to patients with no personalized and timed guidance or peer contact.

METHOD

Study setting

The Stoma APPtimize trial is a double-blind multicentre RCT that will be conducted in the Netherlands. APPtimize is a blended word, combining 'APP' and 'timize' from 'application' and 'optimization'. The Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) statement will be followed, and the trial will be reported in accordance with the Consolidated Standards of Reporting Trials of Electronic and Mobile Health Applications and online TeleHealth (CONSORT-EHEALTH) statement. The Stoma APPtimize study will be conducted in accordance with the Declaration of Helsinki. A written informed consent form is required to participate in this study. Approval for this study was obtained from the local Medical Ethics Committee (registration number NL75119.018.20), and the study is registered on the International Clinical Trial Registry Platform (NL8895).

Study population

The study population consists of patients scheduled for elective or emergency ileostomy or colostomy. Patients must be 18 years of age or older and possess a smartphone operating either iOS 9 or Android 8.0, or more recent versions. Patients who meet one or more of the following criteria will not be considered for inclusion:

Exclusion criteria:

- A Karnofsky score of ≤ 40
- Unable to understand the Dutch language
- Visual impairment, unless well corrected with visual aids
- Physical disabilities limiting the use of a mobile application, such as Parkinson's disease
- Patients with pre-existing skin conditions, such as pemphigus, para-pemphigus and psoriasis.

Investigational intervention

Content development

We conducted a survey study among members of stoma-related patient associations to assess patients' satisfaction and their specific needs in stoma care [12]. In a focus group interview study, we aimed to gain a deeper understanding of the problems faced by patients and to determine how to improve these problems by using an app [13]. Both studies were used to develop a blueprint for the mobile application. The content of the app is based on the Dutch Ostomy Care Guidelines and on information already available from the patient associations [1]. The blueprint was iteratively evaluated by 'expert' health care providers and patient representatives. In Appendix S1, the definitive version of the blueprint is displayed, illustrating the workflow through the app and its basic layout.

Technical development

The application is developed by a third party. The application works on smartphones compatible with the operating systems either iOS

9 or Android 8.0, or more recent versions. Smartphone applications influencing the diagnosis, treatment and monitoring of diseases are considered as medical devices and need to meet additional quality and safety requirements [14]. The 'Stoma App' application is developed specifically for patients undergoing ileostomy or colostomy surgery with the aim of providing personalized and timed guidance and facilitating peer contact and is therefore considered a medical device. The app is CE-marked (NL-CA002-2020-53630). The app is built to comply with the General Data Protection Regulation and follows the data and security guideline ISO 27001 [15].

Usability testing

The usability of the application was tested by a group of patient, representative of two stoma-related patient associations and the Dutch Ostomy Nurse Association, and health-care providers. The usability and weaknesses of the application were evaluated in several walk-through sessions, and adjustments were made. Furthermore, the application will be monitored continuously during the trial.

Intervention and control groups

Intervention group

Patients in the intervention group use the application immediately after inclusion until 1 year postoperatively or stoma reversal. The main goals of the application are: (1) to provide reliable information, (2) to stimulate self-management and self-confidence, (3) to monitor the progress of self-care and self-management, and (4) to provide support to patients from fellow peers. Figure 1 shows the layout of the application. The information will be provided in an information library, including illustrations and videos, and in a personalized timeline, both based on the Dutch guideline for stoma care [1]. The timeline is personalized based on the type of stoma (ileostomy or colostomy), type of surgery (elective or emergency) and operation indication (malign or benign) and is timed based on the date of the operation and the date of discharge from hospital. As these dates can change due to unexpected circumstances, patients can change these dates when necessary. To prevent the patient from becoming overwhelmed by unnecessary information, the timeline shows information only when it is relevant. All information received by the participant can be recalled at any time. Questions or notifications will be pushed through the application to inform and prompt the patient. The questions also function as a registration tool for fluid intake and stoma output and for the elements of stoma self-care that are fulfilled. This may improve the insight of patients regarding their progress in self-management. Patients will also be able to have peer contact with other patients using the public (restricted) version of the application. A suggestion list of peers, all of whom can be contacted, is generated based on the type of stoma, operation indication, and age and sex of the patient. Only patients with a declaration by their general practitioner, surgeon or ostomy nurse will be given access to the platform in the public version of the application.

Control group

Patients in the control group use the application immediately after inclusion until 1 year postoperatively or until stoma reversal. The control group receive a restricted version of the application that contains generic stoma-related information, which is not personalized and timed. This information is comparable with the standard patient information folders developed by the Dutch Stoma Association and based on the Dutch guideline [1].

Outcomes

The primary outcome is stoma quality of life. As the application is patient-centred, providing personalized and timed guidance and a peer-support platform, the Patient Reported Outcome Measures (PROM's); patient satisfaction and psychological adaption, are considered as important secondary outcomes. Other secondary outcomes are postoperative outcomes, stoma-related problems and number of contacts with the ostomy nurse at the outpatient clinic. Table 1 describes all the study outcomes and how and when they will be measured.

Trial recruitment

Elective surgery that preoperatively is expected to result in creation of a stoma

Preoperatively, the treating colorectal surgeon or supervised surgical assistant will introduce the Stoma-APPtimize trial; if the patient is interested in participating in the trial, they will be given the Patient Information Form (PIF). At the following outpatient visit, the ostomy nurse will explain the study and address any questions the patient may have after reading the PIF. Patients will be granted at least 24 h to decide whether they want to participate. After providing written informed consent, patients are randomized to either the control group or the intervention group.

Elective surgery that preoperatively was not expected to result in creation of a stoma, or stoma creation in emergency setting

From 12 h after surgery, the treating colorectal surgeon or supervised surgical assistant will explain the Stoma-APPtimize, if the patient is well awake and the clinical condition permits. If the patient is interested in participating in the trial, they will be given the Patient Information Form (PIF) and will be allowed at least 24 h to decide whether they want to participate. After providing written informed consent, patients are randomized to either the control group or the intervention group.

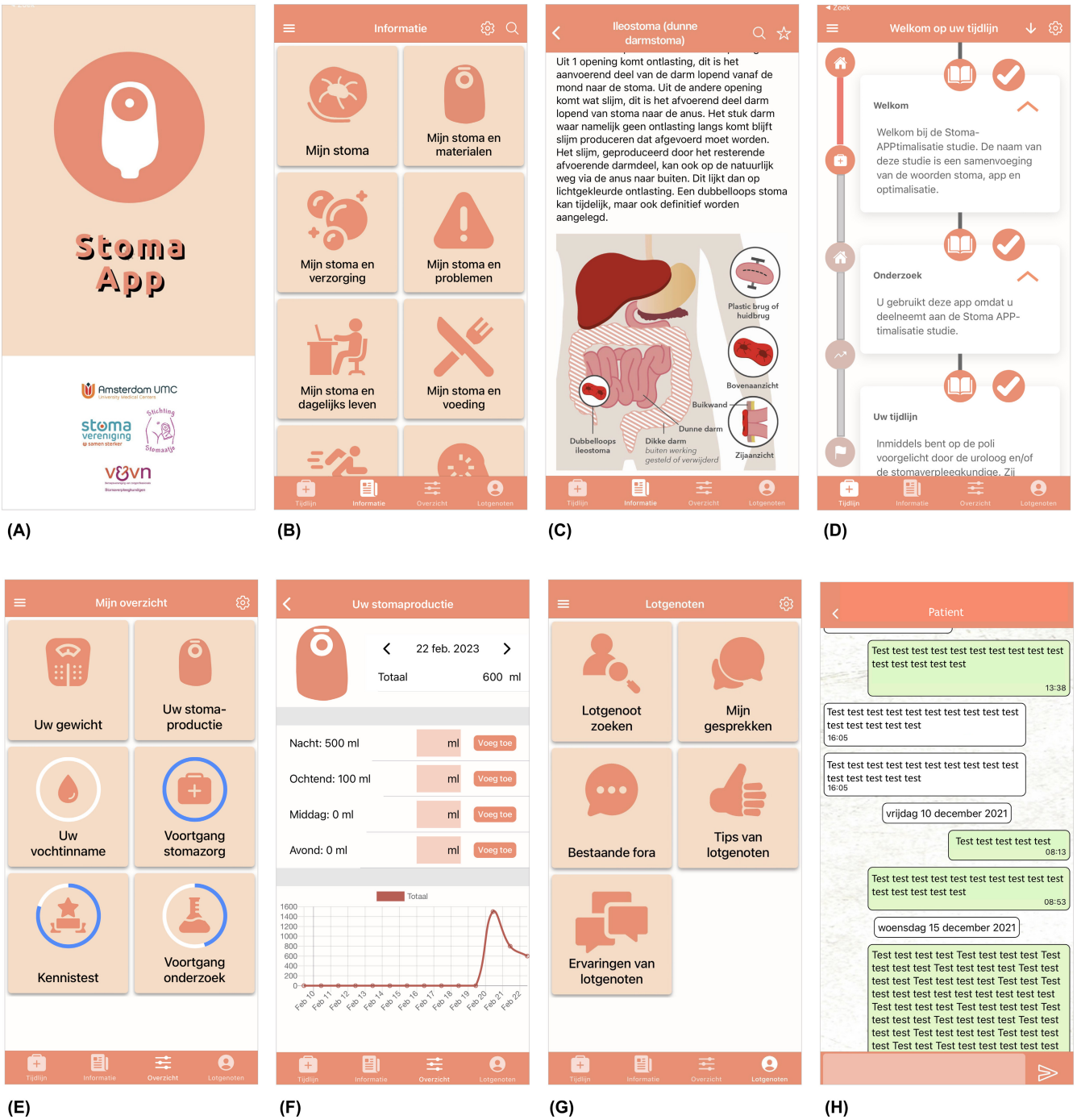

FIGURE 1 Screenshots of the Stoma App (text is shown in the Dutch language). (A) The splash screen that appears when the app is launched shows the participating patient associations and professional associations. (B) The information library containing relevant information. (C) Information about and illustration of an ileostomy. (D) The personalized information timeline; upon reading, text boxes are ticked off and the left bar illustrates progression of the patient in the pathway (in this case, in admission). (E) 'My overview', in which patients can enter their progression in the pathway. (F) Registration of the stoma output. (G) Peer-support platform. (H) One–one peer chat.

Randomization and blinding

After inclusion in the study, the participant will be added to the application system by the ostomy nurse or the coordinating researcher. The system generates a unique personal access code which also randomly allocates participants to either the intervention group or the control group. Allocation will be performed in a 1:1 ratio, with stratification according to indication for surgery (benign or malignant) and type of stoma (ileostomy and colostomy). Random block sizes of two, four and six will be used. Participants and health-care providers will be blinded to the allocation outcomes. The coordinating researcher will provide instructions and is therefore unblinded. Participants will be instructed not to tell other participants or patients about the content of their version of the application.

TABLE 1 Study outcomes and time points.

Variable	Study time points					
	T0	T1	T2	T3	T4	T5
Baseline characteristics						
General characteristics	x					
Disease-related characteristics	x					
Postoperative outcomes						
Length of hospital stay			x			
Overall morbidity			x	x	x	x
Complications			x	x	x	x
Re-operations			x	x	x	x
Re-admission			x	x	x	x
In-hospital mortality			x	x	x	x
Number of outpatient visits			x	x	x	x
Self-reported problems			x	x	x	x
Patient Reported Outcome Measures						
Mobile proficiency (MDPQ-16)	x					
General quality of life (WHOQol)	x		x			x
Stoma quality of life (Stoma-QoL)		x	x	x	x	x
Disability (WHODAS2)	x			x	x	x
Psychosocial adaption (OAI-23)		x	x	x	x	x
Patient satisfaction questionnaire						x

Abbreviations: OAI-23, Ostomy Adjustment Inventory-23; MDPQ-16, 16-question version of the Mobile Device Proficiency Questionnaire; Stoma QoL, Stoma Quality of Life Tool; T0, At informed consent; T1, 2 weeks after surgery; T2, 1 month after surgery; T3, 3 months after surgery; T4, 6 months after surgery; T5, 12 months after surgery or end of follow-up; WHODAS2, World Health Organization Disability Assessment Schedule 2.0; WHOQoL, World Health Organization Quality of Life assessment tool.

Data collection

Data from the intervention and control groups will be mostly automatically collected and stored in a database. Self-reported questionnaires and reminder push notifications to fill them in will be sent automatically. Some data, such as baseline characteristics or clinical outcomes, will be retrieved from the electronic health record by the coordinating researcher and entered into electronic case report forms. Trial findings will be stored in accordance with local data protection regulations. A data protection impact assessment was included in the protocol.

Sample size calculation

The quality of life of patients with stomas has been well described in the literature. In the study by Sier et al., the study population and the data analyses share similarities with the study proposed here [16]. In the study by Sier et al., patients received additional stoma care, in terms of home visits by a stoma nurse. The results from the study by Sier et al. were used as the best estimated reference values to calculate the optimal sample size in the present study. The average quality-of-life score in the study by Sier et al., measured using the stoma quality-of-life tool (Stoma-QoL), was 63.4 (SD = 10.5) for the intervention group and 56.6 (SD = 10.9) for the control group. We assumed that a patient-centred application would be of greatest benefit in the immediate postoperative phase, when patients need to learn how to cope with a stoma. We hypothesize that the QoL of patients in the group allocated Stoma-APPtimize would increase with 5.0 point, compared with 56.6 in the control group. Using a sample size calculation with 90% power, a two-sided alpha of 0.05 and an SD of 10.7, we estimated that 98 participants per study group are needed. A loss to follow-up rate of 10% was also estimated. Therefore, the total target sample size was set at 208 participants ((2 × 98)/0.9 = 208).

Data analyses

Statistical analyses of differences between the two groups will be performed using SPSS for Windows version 26 (SPSS Inc.). Data will be analysed according to the intention-to-treat protocol and any missing data will be imputed. Continuous data will be reported as mean and standard deviation for a normal distribution and as median and 95% CI for a non-normal distribution. Whether the data follows a normal distribution will be determined by visual inspection of the histograms and by analysing the data using the Kolmogorov–Smirnov test. The analysis will be performed using linear regression. Values of $p < 0.05$ will be considered statistically significant. Categorical data will be displayed as numbers and percentages and analysed using the chi-square test.

Prognostic factors

The following baseline characteristics will be collected preoperatively: sex, age, American Society of Anesthesiologists (ASA) classification, body mass index, alcohol intake, smoking, Karnofsky scores, operation indication, comorbidity and mobile device proficiency.

Potential confounders

Major per- and postoperative complications, prolonged hospital stay, readmission and comorbidities are considered as potential confounders. Health care personnel are instructed to register all potential confounders in the electronic health record. The coordinating researcher will screen potential confounders during follow-up of the participants.

Trial discontinuation and withdrawal

The participants will be informed of their right to withdraw from the trial at any time and without any explanation. There will be no

further follow-up of participants who have withdrawn, and data that have already been collected will be used. The follow-up of participants will end upon the reversal of their stoma (anastomosis of the intestine and stoma closure). After stoma closure surgery, participants will be invited to complete the questionnaires 12 months after surgery or at the end of follow-up. In the app participants will register themselves when their stomas are reversed. Participants who did not receive an ileostomy or a colostomy during surgery will be withdrawn from the study and replaced with a new participant.

Dissemination of trial results

The results of the Stoma APPtimize trial will be published in peer-reviewed scientific journals and presented at scientific conferences. Also, stoma-related patient organizations will be informed about the results of the trial.

DISCUSSION

Providing adequate stoma care enables patients to cope better with their stoma and therefore it is essential for improving their quality of life. Although the importance of stoma care has been reported, it falls short in several aspects. Innovative mobile applications have significant potential to overcome these shortcomings. To our knowledge, the Stoma APPtimize trial is the first study to evaluate a patient-centred mobile application that is truly based on patients' needs and desires. This is also the first study in which the control group used a (restricted) version of an app.

Self-efficacy and patient engagement can be improved by using mobile apps [17, 18]. A Chinese app specifically developed for stoma patients improved patient-related outcomes, such as self-efficacy, whereas a Turkish app did not improve any outcomes [17, 19]. However, both apps have different functionalities and are less extensive than our app. In our opinion, the Stoma APPtimize trial is the only study that has conducted a proper process for the design and development of a stoma mobile application. Before development, we assessed the problems experienced in stoma care, in addition to patients' specific needs and desired functionalities. The target group and stakeholders were involved in the development of the app to guarantee its usability and relevance. Moreover, to optimize its future implementation in standard care, the app is provided by ostomy nurses via the trial and publicized by patient and professional associations.

CONCLUSION

We hypothesize that patients supported by the intervention version of the mobile app 'Stoma App' are better supported and have more self-efficacy in their stoma care, and therefore will have a better quality of life than patients with a stoma who are supported by the control version of the app (and not offered personalized and timed guidance and information, or have access to peer support in the app). By simulating patient self-efficacy, other clinical outcomes might also benefit.

AUTHOR CONTRIBUTIONS

Sebastiaan L. van der Storm: Conceptualization; funding acquisition; writing – original draft; methodology; writing – review and editing; software; visualization; investigation; validation; project administration. **Willem A. Bemelman:** Conceptualization; writing – review and editing; supervision. **Susan van Dieren:** Methodology; writing – review and editing. **Marlies P. Schijven:** Supervision; methodology; conceptualization; funding acquisition; writing – review and editing; visualization; software.

FUNDING INFORMATION

This study is carried out with a subsidy of the Dutch patient association "Stomach Liver Intestine Foundation". The funder has no influence on the content or execution of the project.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The future Stoma APPtimize trial data will be available from the corresponding author on reasonable request.

ETHICS STATEMENT

This protocol has been approved by the by the Medical Ethics Committee Amsterdam UMC and is registered at "Toetsingonline" (Registration number NL75119.018.20). Written informed consent will be obtained from all participants by the coordinating researcher.

PATIENT CONSENT STATEMENT

Oral and written consent will be obtained.

TRIAL REGISTRATION

International Clinical Trial Registry Platform (ICTRP), NL8895, prospectively registered on the 27th of August 2020.

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REFERENCES

1. V&VN Stomaverpleegkundingen. Richtlijn Stomazorg Nederland. [Accessed 2021 August 12]. Available from: https://www.venvn.nl/media/rekjq2s4/richtlijn-stomazorg-nederland.pdf?fileticket=r_6xShh5UsU%3d&portalid=1
2. Sharpe L, Patel D, Clarke S. The relationship between body image disturbance and distress in colorectal cancer patients with and without stomas. J Psychosom Res. 2011;70(5):395–402.

3. Bekkers MJ, van Knippenberg FC, van den Borne HW, Poen H, Bergsma J, van BergeHenegouwen GP. Psychosocial adaptation to stoma surgery: a review. J Behav Med. 1995;18:1–31.
4. Schiergens TS, Hoffmann V, Schobel TN, Englert GH, Kreis ME, Thasler WE, et al. Long-term quality of life of patients with permanent end ileostomy: results of a Nationwide cross-sectional survey. Dis Colon Rectum. 2017;60(1):51–60.
5. Ayaz-Alkaya S. Overview of psychosocial problems in individuals with stoma: a review of literature. Int Wound J. 2019;16(1):243–9.
6. Bakx R, Busch OR, Bemelman WA, Veldink GJ, Slors JF, van Lanschot JJ. Morbidity of temporary loop ileostomies. Dig Surg. 2004;21:277–81.
7. Formijne Jonkers HA, Draaisma WA, Roskott AM, van Overbeeke AJ, Broeders IA, Consten EC. Early complications after stoma formation: a prospective cohort study in 100 patients with 1-year follow-up. Int J Colorectal Dis. 2012;27:1095–9.
8. Bekkers MJ, van Knippenberg FC, van den Borne HW, van Berge-Henegouwen GP. Prospective evaluation of psychosocial adaptation to stoma surgery: the role of self-efficacy. Psychosom Med. 1996;58:183–91.
9. O'Connor G. Teaching stoma-management skills: the importance of self-care. Br J Nurs. 2005;14:320–4.
10. Danielsen AK, Burcharth J, Rosenberg J. Patient education has a positive effect in patients with a stoma: a systematic review. Colorectal Dis. 2013;15:e276–83.
11. Faury S, Koleck M, Foucaud J, M'Bailara K, Quintard B. Patient education interventions for colorectal cancer patients with stoma: a systematic review. Patient Educ Couns. 2017;100(10):1807–19.
12. van der Storm SL, Hensen N, Schijven MP. Patient satisfaction with stoma care and their expectations on mobile apps for supportive care. Colorectal Dis. 2023. https://doi.org/10.1111/codi.16658
13. van der Storm SL, van Knippenberg SEM, Eskes AM, Schijven MP. Supporting stoma patients' self-efficacy with a mobile application. Submitted.
14. Shuren J, Patel B, Gottlieb S. FDA regulation of mobile medical apps. JAMA. 2018;320(4):337–8.
15. European Parliament. Regulation (EU) 2016/679 of the European parliament and of the council [Internet]. 2016 [cited 2023 Mar 20]. Available from: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A02016R0679-20160504&qid=1532348683434
16. Sier MF, Oostenbroek RJ, Dijkgraaf MGW, Veldink GJ, Bemelman WA, Pronk A, et al. Home visits as part of a new care pathway (iAID) to improve quality of care and quality of life in ostomy patients: a cluster-randomized stepped-wedge trial. Colorectal Dis. 2017;19(8):739–49. https://doi.org/10.1111/codi.13630
17. Barello S, Triberti S, Graffigna G, Libreri C, Serino S, Hibbard J, et al. eHealth for patient engagement: a systematic review. Front Psychol. 2016;6:2013. https://doi.org/10.3389/fpsyg.2015.02013
18. Wang QQ, Zhao J, Huo XR, Wu L, Yang LF, Li JY, et al. Effects of a home care mobile app on the outcomes of discharged patients with a stoma: a randomised controlled trial. J Clin Nurs. 2018;27(19–20):3592–602. https://doi.org/10.1111/jocn.14515
19. Yiğitoğlu ET, Şendir M. Effect of a mobile patient education application on adjustment to stoma and development of peristomal skin lesions: a quasi-experimental study. Wound Manag Prev. 2021;67(12):30–40.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX A

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