Study Protocol

WhatsApp-assisted prehabilitation programme for adult patient undergoing elective colorectal cancer surgery – A randomized controlled trial

Principal Investigator: Miss. Sung Hoi Ling Shering, Registered Nurse (Specialty), Department of Surgery, Tseung Kwan O Hospital (TKOH), KEC

Other Co-investigator: Dr. So Winnie Kwok Wei, Professor, The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong

Academic Supervisor: Dr. So Winnie Kwok Wei, Professor, The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong

Site Supervisor: Dr Yu Yin Li, Associate Consultant, Department of Surgery, TKOH, KEC

BACKGROUND

Colorectal cancer is a global health concern and ranks second most prevalent forms of cancer in Hong Kong. The incidence and mortality had increased by a substantial 15.3% and 20.7% over a decade, reaching 5899 and 2298 cases in 2021 (Hong Kong Cancer Registry, 2023). Surgery is still the primary curative option in the management of colorectal cancer. Enhanced Recovery After Surgery (ERAS) protocol, a multimodal coordinated strategy with elements of preoperative education, enhanced surgical and anesthetic approach and postoperative rehabilitation, has been promulgated in the local public hospitals. Although compromising result of shortened general length of stay (LOS) (5 vs 10, $p<0.05$) in ERAS is illustrated, surgical complications such as postoperative ileus (POI) remain unresolved (Wong, 2016). Significant burdens associated with POI including prolonged LOS (median LOS=14), physical deconditioning with extended rehabilitation services (68%), impaired lung function requiring invasive ventilator support (5%) and leading to 2% of mortality (Tseung Kwan O Hospital, 2022). The cause of POI is still inconclusive;

however, it is mediated by surgical approach and cardiopulmonary condition, in which the vulnerabilities could be modified and optimized (Lee et al., 2020; Wells et al., 2022).

Prehabilitation refers to optimization in a single or multi-disciplinary approach of exercises training, nutritional therapy and psychological counseling, with aims to improve physical fitness, strengthen cardiopulmonary function and reduce mental distress, through lifestyle modification and better physiological reserve (Bojesen et al., 2023; Bousquet-Dion et al., 2018; Carli et al., 2020). Exercise training and nutritional counseling have demonstrated to keep physically active and improve nutritional status in reducing risks of postoperative respiratory and wound infections (Lee et al., 2023; Li et al., 2021; López-Rodríguez-Arias et al., 2021; Wang et al., 2022). In the current clinical practices of a local public hospital, the concept of educations in form of preoperative exercises and nutritional counseling outweighs the purposes of actual prehabilitation. Moreover, the accessibility of regular outpatient supervised exercises and in-person nutritional counseling is limited in weekly and biweekly session respectively due to high caseloads of out-patient visits in context of short-handed physiotherapists and dietitian, and colorectal cancer patients are highly recommended to follow the unsupervised exercises and dietary regimen at home. Suboptimal regimen adherence toward these preoperative educations may result in poor surgical outcomes such as prolonged LOS (Barberan-Garcia et al., 2018).

Mobile health (mHealth) has been all the rage in the recent research studies, especially in the pandemic of COVID-19, to deliver barrier-free health interventions at a reduced health cost (Baillot et al., 2017; Duarte-Rojo et al., 2021; Metcalf et al., 2019; van der Meij et al., 2018). Behavior change is the common goal of mHealth interventions impacted on enhanced regimen adherence through self-monitoring,

prompt notification and customized educational content. A systematic review by Jakob et al. (2022) identified that effective behavior change with better regimen adherence contributed by mHealth apps in feature of personalized health content (Edney et al., 2019; Luhanga et al., 2018), positive reminders (Benze et al., 2019; Oftedal et al., 2019), user-friendly apps design (Hendrie et al., 2020; Orlemann et al., 2018) and personal reinforcement (Chen et al., 2017; Svetkey et al., 2015). WhatsApp, one of the mobile apps supporting instant text, voice and video messaging, is widely utilized (77.6%) in Hong Kong (Datareportal, 2024) and identified as effective in delivering health interventions (Ferret et al., 2021). WhatsApp-delivered health promotion programmes have demonstrated positive impacts on healthy lifestyle in sedentary adults (Alghafri et al., 2018; Cavallo et al., 2012; Durmaz et al., 2019) and raising awareness of cancer screening in developing countries (Bradway et al., 2017; Knaul et al., 2018; Pereira et al., 2020).

In this study, concept of prehabilitation encompassing physical training, nutritional therapy and psychological counseling is embedded to align with the current ERAS protocol. mHealth in form of WhatsApp-assisted technology is incorporated into the proposed prehabilitation programme to deliver the health interventions to enhance the regimen adherence and thus patients' outcomes on postoperative complications, LOS and mental well-being.

THEORETICAL FRAMEWORK OF THE PROGRAMME

Poor physical activity and malnutrition are the prognostic factors for postoperative complications and morbidity for colorectal cancer patient undergoing surgical procedure, of which could be modified though preoperative health education and lifestyle modification. Adherence is an essential component for effectiveness of a health promotion programme in the process of behavior change. Given the context

of this programme, concept of prehabilitation refers to a behavior change interventions for colorectal cancer patients to engage in a surgery school in optimizing physical functioning, nutritional status and psychological well-being. To design an evidence-based prehabilitation programme, it is crucial to have a better understanding of how engagement influencing behaviors. Grimmett et al. (2021) reviewed the input of behavioral science in the existing thirteen prehabilitation studies and identified mHealth strategies of skills and knowledge (capability), user-friendly features (opportunity) and prompt notification (motivation) contributing the role of behavior change (Barberan-Garcia et al., 2020; Brahmbhatt et al., 2020; Szinay et al., 2021). Hence, the concept of this proposed programme is underpinned by a theoretical framework of the capability, opportunity, motivation and behaviour (COM-B) model of behavior change developed by Michie et al. (2011) (Figure 1).

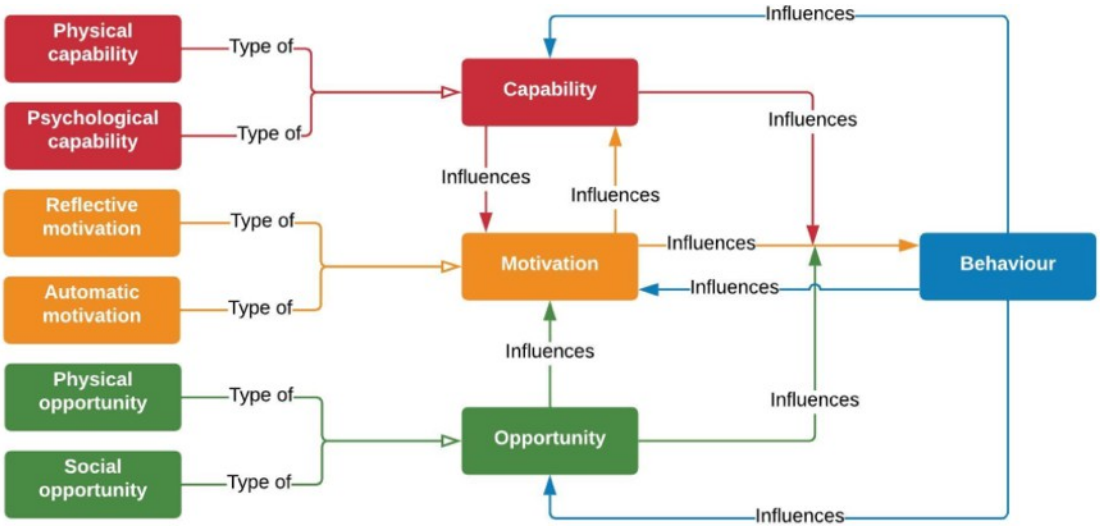

Figure 1. The COM-B model framework

Capability refers to an individual's physical and psychological capability to participate in the activities to achieve the designated outcomes. Given the high penetration of WhatsApp application in Hong Kong social media market, participants are expected to demonstrate a good knowledge of using WhatsApp without hesitation or with minimal guidance (physical capability). In the context of colorectal cancer,

specific educational content towards physical vulnerabilities and dietary advice on cancer-related symptoms promotes the knowledge input. Periodic evidence-based sharing on poor lifestyle increases the awareness on high-risk factors of surgical complications like sedentary lifestyle and complication-induced impacts such as prolonged hospitalization, result in enhancing psychological capabilities with perceived knowledge to perform healthy behavior (Beck et al., 2021; Wang et al. 2022). WhatsApp reminder message provides prompt multimedia reinforcement and supports regular self- monitoring by memory attention with behavior regulation (Banerjee et al., 2021; Mooney et al., 2007).

Opportunity is denoted as physical and social opportunities that influences the engagement. WhatsApp encompasses innovative features of instant text, voice and video message with easy and handy design which creates a better physical opportunity to sustain engagement. These features enhance personalized experiences in a health education with better interaction of communications in multifaceted health interventions on physical activities (e.g. exercises demonstration), psychological therapy (e.g. podcasting of meditation), nutritional advice (e.g. video of cooking recipes). Social influences in form of information exchange and experience sharing promotes the perceived psychological opportunity through practical support (Agasi-Idenburg et al., 2020; Cooper et al., 2022; Parker et al., 2019). Virtual counselling (e.g. podcasting of peer-sharing on experiences and tips towards healthy lifestyle) encourages participants in engagement with the WhatsApp built-in professional support (Agasi-Idenburg et al., 2020; Beck et al., 2021; Wu et al., 2022).

Motivation is defined as automatic and reflective motivation that facilitate the willingness toward engagement. WhatsApp-assisted health intervention with a concrete action with structured timeframe (e.g. 30-minute relaxation breathing

exercises) sustains the regular engagement through setting specific goal (e.g. sleep with at least 6 hours) and enhancing self- confidence (e.g. perform relaxation technique at least once per week) (Beck et al., 2021; Karlsson et al. 2020). In-app reinforcement with positive rewards (e.g. intangible appraisal of badges achievement on adherence to weekly exercises) is essential to motivate their journey (Brahmbhatt et al., 2020; Cooper et al., 2022). Anticipated improvement with progress evaluation also promotes the sustainability of engagement (e.g. maintain the optimal body weight without unintentional weight loss prior to surgery) (Daun et al., 2022; Ferreira et al., 2018)

Given the context of engagement underpinned by COM-B model, WhatsApp-assisted strategies with concrete information of surgery-related complications and benefit of preoperative physical and nutritional enhances, progress reinforcement, and virtual psychological support are incorporated in this prehabilitation protocol (Figure 2).

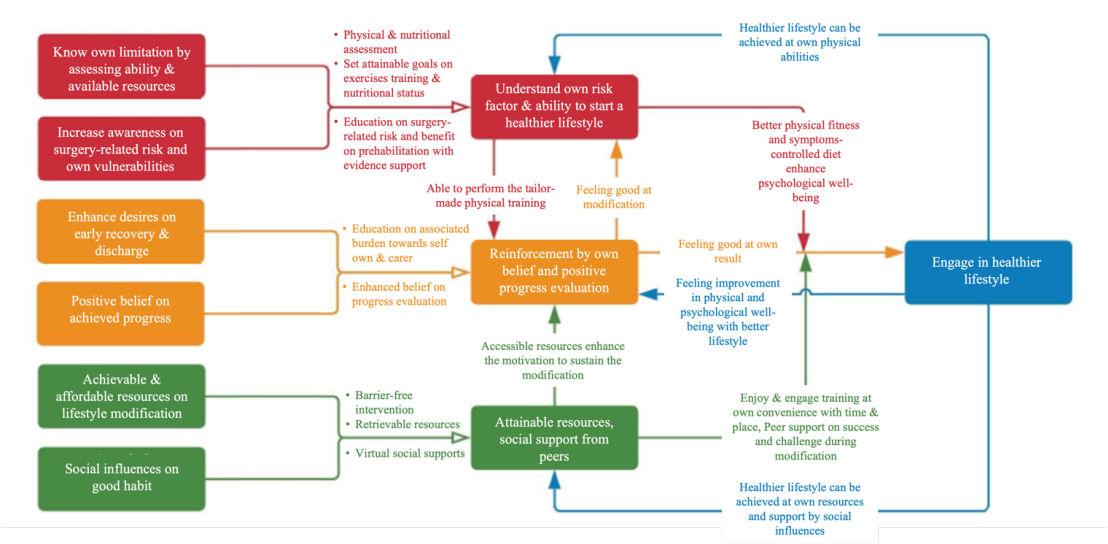

Figure 2. Proposed programmed incorporated with theoretical framework of COM-B model.

TRIAL DESIGN

It is a prospective randomized controlled study (For pilot and a full-scale study)

PRIMARY OUTCOME

Postoperative complication calculated as Comprehensive Complication Index (CCI)

SECONDARY OUTCOMES

Length of hospital stay (LOS); Gastrointestinal recovery; Physical activity; Psychological well-being; Perceptions toward prehabilitation; Sociodemographic characteristics

AIM AND HYPOTHESIS

This study aims to examine the effects of a technology-assisted prehabilitation for reducing postoperative complications and LOS with improved physical activity, nutritional status, gastrointestinal recovery and psychological well-being among patient with colorectal cancer receiving surgery.

It is hypothesized that, compared with usual care, WhatsApp-assisted prehabilitation significantly reduce postoperative complications and LOS, and enhance physical activity, nutritional status, gastrointestinal recovery and psychological well-being with colorectal cancer patients receiving surgery during the postoperative period and after discharge.

Prior to the full-scale RCT, a pilot study will be conducted to assess the feasibility, acceptability and preliminary effectiveness of the WhatsApp-assisted prehabilitation program.

METHOD AND ANALYSIS

DESIGN

A single with assessor-blind, double-armed randomized controlled trial (RCT)

design approach will be conducted. Randomization will be done using a computer-generated random sequence to ensure allocation concealment. Participants will be randomly assigned to intervention group with WhatsApp-assisted prehabilitation program and control group with standard preoperative program under ERAS protocol (Figure 3).

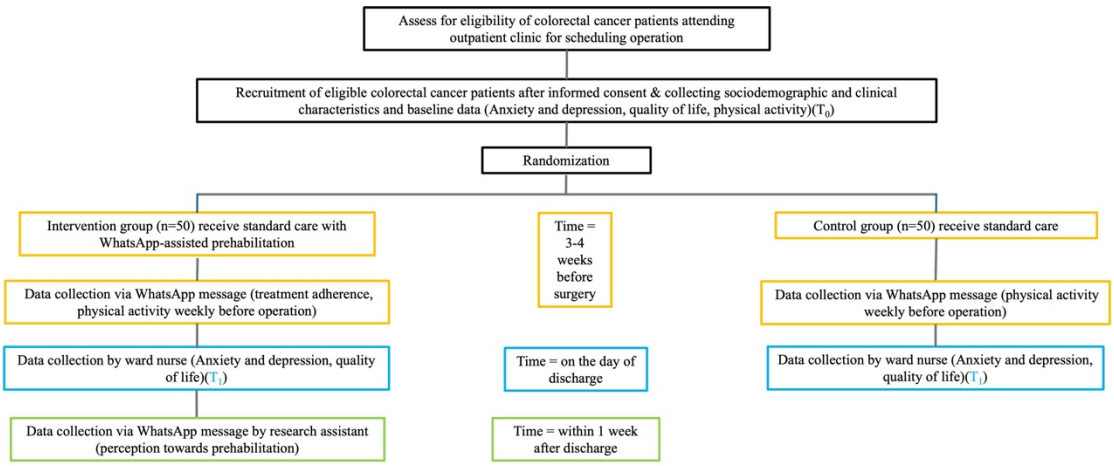

Figure 3. The flow of study procedure.

PARTICIPANTS (For pilot and a full-scale study)

Participants will be recruited in the Department of Surgery in Tseung Kwan O Hospital by convenience sampling. The study hospital is a local tertiary care hospital in Hong Kong and study department provides services care to adult patients with gastrointestinal cancer.

Inclusion Criteria: Patients (1) aged over 18, (2) scheduled for elective colorectal cancer surgery as primary treatment, (3) possess a smart technology with internet plan or WIFI access, (4) able to use WhatsApp application with read, write and interact, (5) can understand Chinese (Cantonese) and follow instructions.

Exclusion Criteria: Patients with (1) expected surgery date less than 21 days, (2) identified cognitive disorder, (3) respiratory disease or (4) musculoskeletal problems, that is, showed difficulties in understanding the study procedures, providing

informed consent or following instructions, in their medical records, (5) requiring neoadjuvant therapy. Participants will be also excluded if their surgery is cancelled (as judged by surgeon or patient refused operation) after randomization.

SAMPLING SIZE

Sample size calculation was based on guidelines of pilot RCT (Julious, 2005; Lancaster et al., 2004; Whitehead et al., 2014), the need to assess feasibility and estimate variability and the context of the main study's sample size planning. The pilot study with a sample size of 24 participants (12 per arm) will be conducted to evaluate the feasibility and preliminary effectiveness of the WhatsApp-prehabilitation program. This sample size is sufficient to evaluate the recruitment, attrition, outcome measurement while accounting for potential attrition of 20%. This will also align to the main study's effect of primary outcome of comprehensive complication index. From Molennar et al. (2023) multicenter RCT study, the odd ratio was 0.47 with outcome incidence at 0.37. In our population from the study hospital (2022-2023), the incidence was 0.33 with mean of CCI at 22. Using power analysis software G*Power 3.1 and considering a decrease of the CCI by 30% as clinically meaningful with anticipating attrition rate of 20%, it is estimated total of 100 patients (50 per arm) would be sufficient for a double-group RCT with 80% power at two-sided with a level of significance at 5% in the full-scale study.

RANDOMIZATION AND BLINDING (For pilot and a full-scale study)

This study consists of two groups: an intervention group that receives the digital prehabilitation with standard care and a control group that receives the standard care only. A computer-based randomization will be utilized to allocate patients into either one group. Eligible participants will be randomly assigned in a 1:1 ratio to either control group or intervention group. Block randomization was

performed through a computer-generated sequence, and serial and opaque with sealed envelopes will be prepared in by independent staff not involved in clinical care or screening or assessment, in which will be used to conceal the sequence until the intervention as assigned at the outpatient preoperative clinic. Participant cannot request to change to other group.

Given the nature of digital approach of intervention, it is difficult to conduct a double- blinded trial in this study. However, single blinded with outcome assessor will be conducted in both groups.

CONTROL (STANDARD CARE) (For pilot and a full-scale study)

Participants in the control group will receive the standard care without digital intervention prior to surgery. Standard care involves physical training, dietary and psychological advice. In addition, it may take approximate 10-15 minutes in doing the questionnaires at day of recruitment [Baseline (T0)], weekly before operation and on the day of discharge(T1).

INTERVENTION (PREHABILITATION WITH STANDARD CARE) (For pilot and a full-scale study)

In addition to standard care, participants will receive digital approach of WhatsApp-assisted prehabilitation programme and then start the home-based training for about 3-4 weeks prior to the surgery. The WhatsApp-assisted prehabilitation includes exercises training, dietary advice and psychological support. In support by the existing RCTs studies, prehabilitation duration ranges from 2 to 4 weeks, considering the current clinical setting, it is recommended at least 3-week intervention should be conducted. Contents will contain elements of physical training (e.g. aerobic and resistance exericses) and psychological therapy (e.g. meditation) will be delivered through WhatsApp at three sessions (day 1, 3 & 5) per

week for 30 minutes and 15 minutes respectively, educational information associated with colorectal cancer surgery and prehabilitation(e.g. high risks factors towards surgical complications) and dietary advices (e.g. recipes) will be delivered on weekly basis (day 1) as follows:

WhatsApp-assisted intervention – Week 1 (Day 1)

Component	Information provision, animation-assisted exercises, psychological support
Content	- Information related to surgery and prehabilitation - Animation-assisted demonstration on exercises (30 mins) - Dietary advice (e.g. low residue diet) - Psychological reinforcement (e.g. positive belief on anticipated goal)
Length of session	45-60 minutes
Format	Individual

WhatsApp-assisted intervention – Weekly (Day 3)

Component	Animation-assisted demonstration, psychological support
Content	- Animation-assisted demonstration on exercises (30 mins) - Psychological reinforcement/ relaxation technique
Length of session	30-45 minutes
Format	Individual

WhatsApp-assisted intervention – Weekly (Day 5)

Component	Animation-assisted demonstration, psychological support
Content	- Animation-assisted demonstration on exercises (30 mins) - Psychological reinforcement/ relaxation technique
Length of session	30-45 minutes
Format	Individual

In addition, it may take approximate 10-15 minutes in doing the questionnaires

at day of recruitment [Baseline (T0)], weekly after intervention and on the day of discharge(T1).

DEVELOPMENT AND VALIDATION

The content theme of WhatsApp message is developed and designed by a panel of healthcare team involving surgeon, nurse, and allied health professionals. Information comprises of impacts of colorectal cancer surgery with relevant statistics and identifying the common misconceptions towards colorectal cancer and preoperative optimization through multimedia interaction and active manner. Expert panel of multidisciplinary health professionals in the study hospital will also validate the final content.

IMPLEMENTATION(For pilot and a full-scale study)

The study is mainly delivered through a digital platform through WhatsApp. Designated trained research assistants are responsible for the digital prehabilitation programme and it is expected to commence approximately four weeks prior to the scheduled colorectal cancer surgery. Basic training of using WhatsApp function such as video or voice playing and message texting will be provided to all participants at the first approach in the outpatient clinic after randomization. The designated WhatsApp message will be delivered three time per week (Monday, Wednesday and Friday) in the morning session. The purposes of WhatsApp-assisted interventions are to enhance the cognitive understanding in surgery-related risks and complication with structured knowledge on beneficial impacts in preoperative physical and nutritional strengthening through multimedia interaction. The message also provides prompts and cues to action with promoting adherence to exercises intervention and reinforcing the sustainability through progress measures and emotional support. Psychological supportive podcasting shares experience and skills on lifestyle modifications, in

which enhances the competency and positive commitment in behavioral changes.

Participants will also receive the message to evaluate the progress of the training on the same day of the intervention in the evening by the trained research assistants.

FIDELITY OF INTERVENTION

The fidelity of the intervention is ensured by recruiting three part-time research assistants (RA1, RA2, RA3) with background of current studying in nursing programme, of proficiency in using WhatsApp function. The principal investigator will provide one day training to RAs in (1) site visit of study venue; (2) introduction and evidence of benefit of prehabilitation; (3) application of WhatsApp; (4) procedure of intervention; (5) knowledge about confidentiality and privacy. A standardized manual will be used to guide the delivery of WhatsApp intervention. In addition, the message delivered will be randomly selected by principal investigator to assess the compliance with intervention protocol at least one session per month. Regular monthly meeting with RA will be provided in the first three month of commencement of study to maintain effective communication, clarify misunderstanding and solve the problem encountered.

OUTCOME MEASUREMENTS

The outcome measures will be collected by trained research assistants, who are not involved in clinical care, delivery of intervention and allocation of participants.

Primary Outcomes

Postoperative complications

Comprehensive complication index (CCI) is our primary outcome in this study. It is a validated and reliable calculated index used to measure the postoperative complications regarding to the severities (Amaro-Gahete et al., 2022; Slankamenac et al., 2014). It is more comprehensive and sensitive in colorectal cancer surgery and

the scales ranges from 0 (no complication) to 100 (death associated with complication) (Tamini et al., 2021). The online version of CCI will be utilized from a certified online platform (www.assessurgery.com) and the relevant data will be collected by the study investigator from the hospital record and translated into CCI through the calculator.

Secondary Outcomes

Length of hospital stay (LOS)

Length of hospital stay (LOS) will be measured in number of days in hospital from the day of operation to discharge. This outcome data will be retrieved by the designated nurse from the hospital record.

Gastrointestinal recovery

Gastrointestinal recovery will be measured as time to first flatus (in hours), time to first bowel (in hours), occurrence of associated events (reinsertion of nasogastric tube, gastrograffin study), to identify the impacts of POI. Data will be collected by a designated nurse and project assistant(s).

Physical activity

Physical activity (PA) will be assessed by International Physical Activity Questionnaire Short Form (Chinese version) (IPAQ-SF) at baseline, weekly before operation and upon discharge. Sedentary lifestyle contributes to lower functional status after surgery, which associated with postoperative complication such as chest infection and prolonged length of stay due to optimal patients' recovery (Collins et al., 1999; Santa Mina et al., 2015). Recent systematic review revealed that higher preoperative activity level was associated to shortened length of stay and improved quality of life among cancer patient receiving surgery (Steffens et al., 2018). In addition, low physical activity has been demonstrated relationship with increased

postoperative complication in gastrointestinal cancer surgery (Tatematsu et al., 2013; Whelan et al., 2021; Yanagisawa et al., 2020). IPAQ-SF (Chinese version) is a validated and reliable tool that has been widely used to assess the physical activity for cancer patients receiving surgery in research studies with good reliability of intraclass correlation coefficient ranging from 0.81-0.89 (Craig et al., 2003; Deng e al., 2008). Data will be collected by training research assistant and designated nurse.

Psychological well-being

Psychological well-being in terms of anxiety and depression and quality of life (QoL) will be measured. The Chinese version of Hospital Anxiety and Depression Scale (C-HADS) and the Short Form 12 Health Survey (SF-12 version 2 (Hong Kong)) are both widely used validated tools with high reliability of Cronbach's alpha at 0.85 and 0.84 with good internal consistency respectively. Data will be collected by project assistant(s) at baseline and on day of discharge day by case nurses.

Perception towards prehabilitation

Patient-report perception towards digital prehabilitation will be collected after discharge through WhatsApp platform by research assistant(s) with a 5-point-likert-scale survey validated by an expert panel in the study department. Survey in content of usability (5- point Likert-scale), satisfaction (5-point Likert-scale), acceptability (5-point Likert-scale) will be assessed. Adherence to interventions by percentage (self-reported on progress evaluation) will be also evaluated.

Sociodemographic characteristics

Sociodemographic characteristics will be collected by the trained research assistant(s) with a simple interview on the day of recruitment, involving gender, sex, medical history, diagnosis of cancer, marital status, anthropometric measures, educational background, smoking status, history of surgery or chemotherapy or

radiation therapy, exercises habit, use of supplements, current physical or psychological illness.

DATA COLLECTION PROCEDURES

A colorectal surgeon working in the study department will screen for eligibility for all patients scheduling for colorectal cancer surgery. If the patients meet the inclusion criteria, the surgeon will refer them to the designated trained research assistant(s). The trained research assistant (RA4) will introduce the study purposes and explain the intervention procedures will an information sheet. If patients agree to join the study, the trained research assistant will obtain the written informed consent and then acquire the sociodemographic characteristics and perform baseline assessment (T0) of patients before randomization. Patients in the control group will receive the standard care while those in the intervention group will receive the digital prehabilitation plus standard care according to the allocation.

During the intervention period, progress evaluation on treatment adherence from the intervention group will be collected by trained research assistant weekly. Trained research assistant will also collect the data of physical activity level weekly from both intervention and control group.

On the day of discharge, a set of data (anxiety and depression, quality of life) (T1) will be collected from the patients by nurses working in the study unit, who are blinded to the subject allocation. Designated nurse in the study team will collect the clinical data from the medical record (CCI, LOS, gastrointestinal recovery) after discharge.

After discharge, trained research assistant(s) (RA1, RA2, RA3) will collect the data of perception towards prehabilitation through WhatsApp message.

DATA MANAGMENET

To protect patient privacy, all research data would be handled in line with HA/Hospital's policy in handling/storage/destruction of patients' medical records. All collected data will be kept strictly confidential and for research purposes only. Anonymity will be ensured for all data collected, with the whole investigator team, the employed research staff and IRB/REC have exclusive access to the datasets. Integrity and reliability of data derived will be ensured. The storage period will be 6 years including the period of study. A new electronic device (Smartphone) and a new SIM card will be purchased for this study. This SIM card will be verified and completed with the real name registration under study investigator according to the Telecommunication (Registration of SIM Cards) Regulation in Hong Kong and the phone number of this SIM card will be used to register for the WhatsApp Business Account. During these periods, the electronic device (mobile) used for digital intervention and the informed consent will be kept in a specific locked cabinet. The electronic device is also encrypted with a password and the password will be changed regularly in every 3 months. Trusted and encrypted network is used to deliver the WhatsApp intervention. After completion of aforesaid storage period, the mobile SIM card and the WhatsApp account will be destroyed and reset. All hard copy of data will also be discarded as confidential waste 6 years after the completion of study. The Principal Investigator, and the coordinating investigator will be responsible for safekeeping of the personal data and study data during and after the study.

PATIENTS AND PUBLIC INVOLVEMENT

Patients and the public will not be involved in the study design nor development of interventions. Only participants in the intervention group will receive the WhatsApp message to explore their perceptions in content of satisfaction,

usefulness and acceptability towards the interventions. However, all study participants will receive a plain language summary of the results after the completion of study as part of the knowledge translation approach.

DATA ANALYSIS

All analyses will be performed using IBM SPSS statistics (Version. 29) with level of significance set at 0.05 (2-tailed). Descriptive statistics will be used to summarize baseline characteristics and outcome measures. Normality of continuous variables will be assessed based on their skewness and kurtosis statistics and normal Q-Q plots. Appropriate transformations will be made on skewed continuous variables to render them normally distributed. Homogeneity of baseline characteristics between groups will be assessed by using independent t-test, Mann-Whitney U test, chi-squared test or Fisher's exact test. Those baseline characteristics showing statistically significant difference between groups ($p<0.05$) will be considered as potential confounding covariates and adjusted in subsequent outcome analyses. The outcomes of LOS and CCI will be compared between groups using multiple regressions with adjustment for the potential confounding covariates identified above. GEE models will be used to compare the repeated measure outcomes (e.g. QoL) across study time points between groups with adjustment for the covariates. The occurrence of associated events will be compared by using logistic regression with adjustment for the covariates.

ETHICS AND DISSEMINATION

The research team will protect participants' rights and safety by adhering to local laws, the Hong Kong Personal Data (Privacy) Ordinance, institutional policies, Declaration of Helsinki, and the International Conference on Harmonization – Good Clinical Practice (ICH- GCP). Ethical approval will be obtained from Central

Institutional Review Board (IRB). Principal investigator passed CUHK CRMO Online training for Declaration of Helsinki & GCP Workshop for Investigator and Site Personnel (2.0) (recognised by TransCelerate BioPharma). Permission to use the indicated instruments will be obtained from the original authors.

Agreement will be made in advance with personnel in charge of the study venues for arranging participants recruitment. A colorectal surgeon working in the study department will screen for eligibility for all patients scheduling for colorectal cancer surgery. If the patients meet the inclusion criteria, the surgeon will refer them to the designated trained research assistant(s). The trained research assistant (RA4) will introduce the study purposes and explain the intervention procedures will a detailed information sheet including the study purpose and all potential benefits and risks regarding to the study intervention. If patients agree to join the study, the trained research assistant will obtain the written informed consent. All study participants will be rewarded a value of HK$100 voucher for the travel and time expenses in this study.

All collected data will only be used for research. Patients will be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without giving any reason, loss of benefit or impacts on the care they are receiving. Anonymity will be always ensured, and the findings will only be published as part of the fulfillment of thesis dissertation and in a peer-reviewed journal in local and international conference journals. Any protocol modification will be communicated to the local research ethics committees in a timely manner.

DISCUSSION

Leveraging technology in health interventions has been rapidly spreading. This multifaceted innovative approach incorporating technology to provide opportunities

for all patients in accessing barrier-free health interventions at their convenience and result in better patients' outcome. In addition, the incidence of colorectal cancer (CRC) still demonstrates an upward trend and the complexity of care becomes demanding. Prehabilitation could improve the physiological reserve among CRC patients, of promoting physical activity, faster recovery and reducing complications and psychological distress. However, the benefits of leveraging technology in prehabilitation programme to enhance patients' outcomes of postoperative complications, LOS and mental health remains limited Therefore, this study aims to evaluate the feasibility and effect of digital prehabilitation delivered by WhatsApp, where an novel and convenient intervention for colorectal cancer patients undergoing surgery at any time and place. The result will provide insights of the use of digital approach. To our knowledge, this is the very first trial of digital prehabilitation for CRC patients in Hong Kong public hospitals. Therefore, it provides positive contribution and acts as an important quality benchmark for patients' outcomes. The findings will also generate knowledge on the optimalization of care provided to CRC patients prior to surgery and assist to develop a structured and effective health system in our community. This innovation may have implications to other research studies and extends the potential clinical practices to related subspecialities such as gastric cancer. The study engages different stakeholders with universities, health organization and patients and provides a high quality of knowledge exchange during the process.

FUNDING AND INSURANCE

This project is funded by the Y. K. Pao Foundation Centre for Nursing Excellence in Chronic Illness Care, The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong. The study will not consume any

resources from the Hospital Authority and the subjects will not be charged for the study. All study participants will be rewarded a value of HK$100 one-off voucher for the travel and time expenses in this study.

The issue of insurance is not applicable in this study.

CONFLICT OF INTERETST

No direct conflict of interest to declare.

REFERENCE

Agasi-Idenburg, C. S., Koning-van Zuilen, M., Westerman, M. J., Punt, C. J., Aaronson, N. K., & Stuiver, M. M. (2020). “I am busy surviving”-views about physical exercise in older adults scheduled for colorectal cancer surgery. *Journal of Geriatric Oncology*, *11*(3), 444-450.

Alghafri, T. S., Alharthi, S. M., Al-Farsi, Y., Alrawahi, A. H., Bannerman, E., Craigie, A. M., & Anderson, A. S. (2018). ‘MOVEdiabetes’: a cluster randomized controlled trial to increase physical activity in adults with type 2 diabetes in primary health in Oman. *BMJ Open Diabetes Research and Care*, *6*(1), e000605.

Baillot, A., Boissy, P., Tousignant, M., & Langlois, M. F. (2017). Feasibility and effect of in-home physical exercise training delivered via telehealth before bariatric surgery. *Journal of Telemedicine and Telecare*, *23*(5), 529-535.

Banerjee, S., Semper, K., Skarparis, K., Naisby, J., Lewis, L., Cucato, G., Mills, R., Rochester, M., & Saxton, J. (2021). Patient perspectives of vigorous intensity aerobic interval exercise prehabilitation prior to radical cystectomy: a qualitative focus group study. *Disability and Rehabilitation*, *43*(8), 1084–1091.

Barberan-Garcia, A., Ubré, M., Roca, J., Lacy, A. M., Burgos, F., Risco, R., Momblán, D., Balust, J., Blanco, I., & Martínez-Pallí, G. (2018). Personalised Prehabilitation in

High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. *Annals of Surgery*, *267*(1), 50–56.

Beck, A., Vind-Thaysen, H., Hasselholt-Soegaard, C., Blaakaer, J., & Seibaek, L. (2021). What matters to you? An investigation of patients' perspectives on and acceptability of prehabilitation in major cancer surgery. *European Journal of Cancer Care*, *30*(6), e13475.

Benze, G., Nauck, F., Alt-Epping, B., Gianni, G., Bauknecht, T., Ettl, J., Munte, A., Kretzschmar, L., & Gaertner, J. (2019). PROutine: a feasibility study assessing surveillance of electronic patient reported outcomes and adherence via smartphone app in advanced cancer. *Annals of Palliative Medicine*, *8*(2), 104–111.

Bojesen, R. D., Dalton, S. O., Skou, S. T., Jørgensen, L. B., Walker, L. R., Eriksen, J. R., Grube, C., Justesen, T. F., Johansen, C., Slooter, G., Carli, F., & Gögenur, I. (2023). Preoperative multimodal prehabilitation before elective colorectal cancer surgery in patients with WHO performance status I or II: randomized clinical trial. *British Journal of Surgery Open*, *7*(6), 134.

Bousquet-Dion, G., Awasthi, R., Loiselle, S. È., Minnella, E. M., Agnihotram, R. V., Bergdahl, A., Carli, F., & Scheede-Bergdahl, C. (2018). Evaluation of supervised multimodal prehabilitation programme in cancer patients undergoing colorectal resection: a randomized control trial. *Acta Oncologica*, *57*(6), 849-859.

Bradway, M., Carrion, C., Vallespin, B., Saadatfard, O., Puigdomènech, E., Espallargues, M., & Kotzeva, A. (2017). mHealth Assessment: Conceptualization of a Global Framework. *JMIR mHealth and uHealth*, *5*(5), e60.

Brahmbhatt, P., Sabiston, C. M., Lopez, C., Chang, E., Goodman, J., Jones, J., McCready, D., Randall, I., Rotstein, S., & Santa Mina, D. (2020). Feasibility of Prehabilitation Prior to Breast Cancer Surgery: A Mixed-Methods Study. *Frontiers in Oncology*, *10*, 571091.

Carli, F., Bousquet-Dion, G., Awasthi, R., Elsherbini, N., Liberman, S., Boutros, M., Stein, B., Charlebois, P., Ghitulescu, G., Morin, N., Jagoe, T., Scheede-Bergdahl, C., Minnella, E. M., & Fiore, J. F. (2020). Effect of Multimodal Prehabilitation vs Postoperative Rehabilitation on 30-Day Postoperative Complications for Frail Patients Undergoing Resection of Colorectal Cancer: A Randomized Clinical Trial. *JAMA surgery*, *155*(3), 233-242.

Cavallo, D. N., Tate, D. F., Ries, A. V., Brown, J. D., DeVellis, R. F., & Ammerman, A. S. (2012). A social media-based physical activity intervention: a randomized controlled trial. *American Journal of Preventive Medicine*, *43*(5), 527–532.

Chen, Y. S., Wong, J. E., Ayob, A. F., Othman, N. E., & Poh, B. K. (2017). Can Malaysian young adults report dietary intake using a food diary mobile application? A pilot study on acceptability and compliance. *Nutrients*, *9*(1), 62.

Collins, T. C., Daley, J., Henderson, W. H., & Khuri, S. F. (1999). Risk factors for prolonged length of stay after major elective surgery. *Annals of surgery*, *230*(2), 251–259. https://doi.org/10.1097/00000658-199908000-00016

Cooper, M., Chmelo, J., Sinclair, R. C. F., Charman, S., Hallsworth, K., Welford, J., Phillips, A. W., Greystoke, A., & Avery, L. (2022). Exploring factors influencing uptake and adherence to a home-based prehabilitation physical activity and exercise

intervention for patients undergoing chemotherapy before major surgery (ChemoFit): a qualitative study. *BMJ Open*, *12*(9), e062526.

Craig, C. L., Marshall, A. L., Sjöström, M., Bauman, A. E., Booth, M. L., Ainsworth, B. E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J. F., & Oja, P. (2003). International physical activity questionnaire: 12-country reliability and validity. *Medicine and science in sports and exercise*, *35*(8), 1381–1395. https://doi.org/10.1249/01.MSS.0000078924.61453.FB

Datareportal. (2024). Digtal 2024: Hong Kong. Retrieved from https://datareportal.com/reports/digital-2024-hong-kong

Daun, J. T., Twomey, R., Dort, J. C., Capozzi, L. C., Crump, T., Francis, G. J., Matthews, T. W., Chandarana, S. P., Hart, R. D., Schrag, C., Matthews, J., McKenzie, C. D., Lau, H., & Culos-Reed, S. N. (2022). A Qualitative Study of Patient and Healthcare Provider Perspectives on Building Multiphasic Exercise Prehabilitation into the Surgical Care Pathway for Head and Neck Cancer. *Current Oncology (Toronto, Ont.)*, *29*(8), 5942–5954.

Deng, H. B., Macfarlane, D. J., Thomas, G. N., Lao, X. Q., Jiang, C. Q., Cheng, K. K., & Lam, T. H. (2008). Reliability and validity of the IPAQ-Chinese: the Guangzhou Biobank Cohort study. *Medicine and science in sports and exercise*, *40*(2), 303–307. https://doi.org/10.1249/mss.0b013e31815b0db5

Duarte-Rojo, A., Bloomer, P. M., Rogers, R. J., Hassan, M. A., Dunn, M. A., Tevar, A. D., Vivis, S. L., Bataller, R., Hughes, C. B., Ferrando, A. A., Jakicic, J. M., & Kim, W. R. (2021). Introducing EL-FIT (Exercise and Liver FITness): A Smartphone App to Prehabilitate and Monitor Liver Transplant Candidates. *Liver transplantation: official*

publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society, *27*(4), 502–512.

Durmaz, S., Ergin, I., Durusoy, R., Hassoy, H., Caliskan, A., & Okyay, P. (2019). WhatsApp embedded in routine service delivery for smoking cessation: effects on abstinence rates in a randomized controlled study. *BMC Public Health*, *19*, 1-12.

Edney, S., Ryan, J. C., Olds, T., Monroe, C., Fraysse, F., Vandelanotte, C., Plotnikoff, R., Curtis, R., & Maher, C. (2019). User Engagement and Attrition in an App-Based Physical Activity Intervention: Secondary Analysis of a Randomized Controlled Trial. *Journal of Medical Internet Research*, *21*(11), e14645.

Ferreira, V., Agnihotram, R. V., Bergdahl, A., van Rooijen, S. J., Awasthi, R., Carli, F., & Scheede-Bergdahl, C. (2018). Maximizing patient adherence to prehabilitation: what do the patients say? *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, *26*(8), 2717–2723.

Ferret, J. C. F., Branco, B. H. M., dos Santos, L. P. G., Rocco, F., & Bernuci, M. P. (2021). WhatsApp-assisted health education intervention: a systematic review. *International Journal for Innovation Education and Research, 9*(9), 56-72.

Grimmett, C., Bradbury, K., Dalton, S. O., Fecher-Jones, I., Hoedjes, M., Varkonyi-Sepp, J., & Short, C. E. (2021). The role of behavioral science in personalized multimodal prehabilitation in cancer. *Frontiers in Psychology*, *12*, 634223.

Hendrie, G. A., Hussain, M. S., Brindal, E., James-Martin, G., Williams, G., & Crook, A. (2020). Impact of a mobile phone app to increase vegetable consumption and variety in adults: large-scale community cohort study. *JMIR mHealth and uHealth*, *8*(4), e14726.

Hong Kong Cancer Registry. (2023). Statistics of the most common cancers – Top Five Cancers by Age. https://www3.ha.org.hk/cancereg/topfive.html

Hughes, M. J., Hackney, R. J., Lamb, P. J., Wigmore, S. J., Christopher Deans, D. A., & Skipworth, R. J. E. (2019). Prehabilitation Before Major Abdominal Surgery: A Systematic Review and Meta-analysis. *World journal of surgery*, *43*(7), 1661–1668. https://doi.org/10.1007/s00268-019-04950-y

Jakob, R., Harperink, S., Rudolf, A. M., Fleisch, E., Haug, S., Mair, J. L., Salamanca-Sanabria, A., & Kowatsch, T. (2022). Factors Influencing Adherence to mHealth Apps for Prevention or Management of Noncommunicable Diseases: Systematic Review. *Journal of Medical Internet Research*, *24*(5), e35371.

Julious, S. A. (2005). Sample size of 12 per group rule of thumb for a pilot study. *Pharmaceutical Statistics: The Journal of Applied Statistics in the Pharmaceutical Industry*, 4(4), 287-291. https://doi.org/10.1002/pst.185

Karlsson, E., Dahl, O., Rydwik, E., Nygren-Bonnier, M., & Bergenmar, M. (2020). Older patients' attitudes towards, and perceptions of, preoperative physical activity and exercise prior to colorectal cancer surgery-a gap between awareness and action. *Supportive care in cancer: official journal of the Multinational Association of Supportive Care in Cancer*, *28*(8), 3945–3953.

Knaul, F. M., Arreola-Ornelas, H., Rodriguez, N. M., Méndez-Carniado, O., Kwete, X. J., Puentes-Rosas, E., & Bhadelia, A. (2018). Avoidable mortality: The core of the global cancer divide. *Journal of Global Oncology*, *4*, 1-12.

Lancaster, G. A., Dodd, S., & Williamson, P. R. (2004). Design and analysis of pilot studies: recommendations for good practice. *Journal of evaluation in clinical practice, 10*(2), 307–312. https://doi.org/10.1111/j..2002.384.doc.x

Lee, M. J., Vaughan-Shaw, P., Vimalachandran, D., & ACPGBI GI Recovery Group. (2020). A systematic review and meta-analysis of baseline risk factors for the development of postoperative ileus in patients undergoing gastrointestinal surgery. *The Annals of The Royal College of Surgeons of England*, *102*(3), 194-203.

Lee, S. Y., Lee, J., Park, H. M., Kim, C. H., & Kim, H. R. (2023). Impact of preoperative immunonutrition on the outcomes of colon cancer surgery: results from a randomized controlled trial. *Annals of Surgery, 277*(3), 381-386.

Li, D., Fang, Y., & Su, S. (2021). Effect of nursing team-led pre-rehabilitation strategy on patients with colorectal cancer. *Jounral of Qilu Nursing,* 27, 11-13.

López-Rodríguez-Arias, F., Sánchez-Guillén, L., Aranaz-Ostáriz, V., Triguero-Cánovas, D., Lario-Pérez, S., Barber-Valles, X., Lacueva, F. J., Ramirez, J. M., & Arroyo, A. (2021). Effect of home-based prehabilitation in an enhanced recovery after surgery program for patients undergoing colorectal cancer surgery during the COVID-19 pandemic. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*, *29*(12), 7785–7791.

Luhanga, E. T., Hippocrate, A. A. E., Suwa, H., Arakawa, Y., & Yasumoto, K. (2018). Identifying and evaluating user requirements for smartphone group fitness applications. *IEEE Access*, *6*, 3256-3269.

Metcalf, M., Glazyrine, V., Glavin, K., Dahlgren, A., Michael, C., Bechtel, M., Bishop, D., DeRuyter, M., Mirza, M., Taylor, J., Wyre, H. W., Hamilton-Reeves, J. M.,

Holzbeierlein, J. M., & Lee, E. K. (2019). The Feasibility of a Health Care Application in the Treatment of Patients Undergoing Radical Cystectomy. *The Journal of Urology*, *201*(5), 902–908.

Michie, S., van Stralen, M. M., & West, R. (2011). The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implementation Science: IS*, *6*, 42.

Mooney, M., Fitzsimons, D., & Richardson, G. (2007). "No more couch-potato!" Patients' experiences of a pre-operative programme of cardiac rehabilitation for those awaiting coronary artery bypass surgery. *European Journal of Cardiovascular Nursing*, *6*(1), 77–83.

Oftedal, S., Burrows, T., Fenton, S., Murawski, B., Rayward, A. B., & Duncan, M. J. (2019). Feasibility and preliminary efficacy of an m-Health intervention targeting physical activity, diet, and sleep quality in shift-workers. *International Journal of Environmental Research and Public Health*, *16*(20), 3810.

Orlemann, T., Reljic, D., Zenker, B., Meyer, J., Eskofier, B., Thiemt, J., Herrmann, H. J., Neurath, M. F., & Zopf, Y. (2018). A Novel Mobile Phone App (OncoFood) to Record and Optimize the Dietary Behavior of Oncologic Patients: Pilot Study. *JMIR Cancer*, *4*(2), e10703.

Parker, N. H., Lee, R. E., O'Connor, D. P., Ngo-Huang, A., Petzel, M. Q. B., Schadler, K., Wang, X., Xiao, L., Fogelman, D., Simpson, R., Fleming, J. B., Lee, J. E., Tzeng, C. D., Sahai, S. K., Basen-Engquist, K., & Katz, M. H. G. (2019). Supports and Barriers to Home-Based Physical Activity During Preoperative Treatment of Pancreatic Cancer: A Mixed-Methods Study. *Journal of Physical Activity & Health*, *16*(12), 1113–1122.

Pereira, A. A. C., Destro, J. R., Bernuci, M. P., Garcia, L. F., & Lucena, T. F. R. (2020). Effects of a WhatsApp-delivered education intervention to enhance breast cancer knowledge in women: Mixed-methods study. *JMIR mHealth and uHealth*, *8*(7), e17430.

Santa Mina, D., Scheede-Bergdahl, C., Gillis, C., & Carli, F. (2015). Optimization of surgical outcomes with prehabilitation. *Applied physiology, nutrition, and metabolism, 40*(9), 966–969. https://doi.org/10.1139/apnm-2015-0084

Steffens, D., Beckenkamp, P. R., Young, J., Solomon, M., da Silva, T. M., & Hancock, M. J. (2019). Is preoperative physical activity level of patients undergoing cancer surgery associated with postoperative outcomes? A systematic review and meta-analysis. *European journal of surgical oncology: the journal of the European Society of Surgical Oncology and the British Association of Surgical Oncology*, *45*(4), 510–518. https://doi.org/10.1016/j.ejso.2018.10.063

Svetkey, L. P., Batch, B. C., Lin, P. H., Intille, S. S., Corsino, L., Tyson, C. C., Bosworth, H. B., Grambow, S. C., Voils, C., Loria, C., Gallis, J. A., Schwager, J., & Bennett, G. G. (2015). Cell phone intervention for you (CITY): A randomized, controlled trial of behavioral weight loss intervention for young adults using mobile technology. *Obesity*, *23*(11), 2133–2141.

Szinay, D., Perski, O., Jones, A., Chadborn, T., Brown, J., & Naughton, F. (2021). Perceptions of Factors Influencing Engagement With Health and Well-being Apps in the United Kingdom: Qualitative Interview Study. *JMIR mHealth and uHealth*, *9*(12), e29098.

Tatematsu, N., Park, M., Tanaka, E., Sakai, Y., & Tsuboyama, T. (2013). Association between physical activity and postoperative complications after esophagectomy for cancer: a prospective observational study. *Asian Pacific journal of cancer prevention: APJCP*, *14*(1), 47–51. https://doi.org/10.7314/apjcp.2013.14.1.47

Tseung Kwan O Hospital. (2022). *Patient's median length-of-stay and postoperative complications, ERAS colorectal surgery* [Unpublished raw data]. Hospital Authority.

van der Meij, E., Anema, J. R., Leclercq, W. K. G., Bongers, M. Y., Consten, E. C. J., Schraffordt Koops, S. E., van de Ven, P. M., Terwee, C. B., van Dongen, J. M., Schaafsma, F. G., Meijerink, W. J. H. J., Bonjer, H. J., & Huirne, J. A. F. (2018). Personalised perioperative care by e-health after intermediate-grade abdominal surgery: a multicentre, single-blind, randomised, placebo-controlled trial. *Lancet*, *392*(10141), 51–59.

Wang, R., Yao, C., Hung, S. H., Meyers, L., Sutherland, J. M., Karimuddin, A., Campbell, K. L., & Conklin, A. I. (2022). Preparing for colorectal surgery: a qualitative study of experiences and preferences of patients in Western Canada. *BMC Health Services Research*, *22*(1), 730.

Wang, X. Y., Gu, Y. F., Chen, H., Zhang, L., Dai, X. J., Tang, A, J., Hu, X. M., Wu, Q. (2022). Effect of preoperative trimodal prehabilitation on rehabilitation of elderly patients with colorectal cancer. *Chinese Nursing Research*, 18, 3233-3238.

Wells, C. I., Milne, T. G., Seo, S. H. B., Chapman, S. J., Vather, R., Bissett, I. P., & O'Grady, G. (2022). Post-operative ileus: definitions, mechanisms and controversies. *ANZ Journal of Surgery*, *92*(1-2), 62-68.

Whelan, M., van Aswegen, H., Roos, R., Fabian, J., & Bebington, B. (2021). Preoperative physical activity and functional performance levels are predictors of acute postoperative outcomes in a private South African colorectal cancer cohort. *The South African journal of physiotherapy*, *77*(1), 1526. https://doi.org/10.4102/sajp.v77i1.1526

Whitehead, A. L., Sully, B. G., & Campbell, M. J. (2014). Pilot and feasibility studies: is there a difference from each other and from a randomised controlled trial?. *Contemporary clinical trials, 38*(1), 130–133. https://doi.org/10.1016/j.cct.2014.04.001

Wong, Y. W. (2016). *Multidisciplinary Approach of Colorectal Cancer Surgery to Decrease Length of Stay, Early Experience of ERAS program in Tseung-Kwan O Hospital*.
https://www.ha.org.hk/haconvention/hac2016/proceedings/downloads/SPPE1018.pdf

Wu, F., Laza-Cagigas, R., & Rampal, T. (2022). Understanding Patients' Experiences and Perspectives of Tele-Prehabilitation: A Qualitative Study to Inform Service Design and Delivery. *Clinics and Practice*, *12*(4), 640–652.

Yanagisawa, T., Sugiura, H., Tatematsu, N., Horiuchi, M., Migitaka, S., & Itatsu, K. (2020). Preoperative Sedentary Time Predicts Postoperative Complications in Gastrointestinal Cancer. *Asian Pacific journal of cancer prevention: APJCP*, *21*(11), 3405–3411. https://doi.org/10.31557/APJCP.2020.21.11.3405