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Implementing a system-wide cancer prehabilitation programme: the journey of Greater Manchester's 'Prehab4cancer'

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Introduction

Patients undergoing major cancer interventions such as major surgical resection, chemotherapy, radiotherapy, and immunotherapy are prone to the adverse effects of their cancer, as well as to the side effects of the treatments designed to cure them. For surgery, despite advancing innovations and the use of more minimal resection techniques, morbidity and mortality rates remain high (1,2), particularly amongst the older and most frail patients, who are more likely to adopt sedentary lifestyles (3,4).

Prehabilitation (commonly known as "Prehab") and supported recovery are increasingly recognised as important by people affected by cancer and healthcare providers internationally (5,6). Following a cancer diagnosis, the prehab process aims to optimise a person's physical, nutritional, and psychological health in the time period before their cancer treatment begins and throughout treatment for non-surgical interventions (7). The core components of a multi-faceted prehab programme include cardiovascular and skeletal muscle fitness training, nutritional management, wellbeing with psychological support, and medical optimisation. This optimisation process supports the patient in preparing for the physiological challenges of their cancer treatments, whilst aiming to shorten recovery time, reduce peri-operative complications and improve compliance with nonsurgical treatments (8).

The most effective prehab programmes provide a holistic approach to promote patient empowerment, adherence and improved experience; which includes a graded, evidence-based exercise prescription to give the best opportunity to improve fitness in the constrained time-period before cancer treatment (9). High-intensity interval training (HIIT) exercise provides an effective, time efficient approach to increasing fitness (needs ref), but any exercise could be viewed as potentially beneficial for patients (10). The rehabilitation side of the programme supports patients' recovery from their cancer interventions and where necessary can be used to prepare them for other treatments (11). Rehabilitation should aim also to support the transition to lifelong exercise and so help in the prevention of future cardiovascular and cancer events (10).

Most supporting evidence for prehab has come from surgical patients undergoing colorectal, lung and oesphago-gastric resections (12-17). There is currently less evidence supporting the use of prehab programmes in hepato-pancreato-biliary surgery but prehab studies in patients undergoing liver resection have shown improvement in pre-operative physical fitness especially in the least fit groups (18). Multi-modal prehab may prove to be particularly important in the surgical

treatment of pancreatic cancer, a diagnosis often associated with cachexia and malnutrition. Recent evidence from ongoing initiatives in Manchester (UK) recommends nutritional assessment and supplementation before and after major pancreas resection (personal communication).

Prehabilitation is likely to be most useful in older cancer patient cohorts, who are more likely to have complex co-morbidities as well as sensory, balance or cognitive impairment with reduced functional abilities (19). Lawrence et al evaluated functional recovery following major abdominal surgery in older patients (mean age 69). In the absence of a prehab or rehab programme, the results showed that eight weeks post-operation only 30% of patients had recovered to preoperative levels and at six months, only 50% had achieved baseline functional ability (20).

This is supported by more recent evidence from the GOSAFE international evaluation and follow-up of older patients (mean age 78) undergoing major oncological surgery which reports on-going decreased functional capacity in 1/3 of colorectal patients at 3 months [21]. The objective of GOSAFE investigators (22) to provide meaningful data to assist clinicians in tailoring care of elderly patients to avoid under or overtreatment appears very pertinent and supports reports from others suggesting that older patients identify good functional recovery as a priority rather than duration of survival and (7,23) highlights quality of life as an important metric for prehabilitation. The development of a prehabilitation programme designed to derive optimal engagement and benefit for older people supports the recent focus from UK national health policy for healthcare innovations to support people to 'age well' (24), with greater consideration given to people experiencing mild, moderate and severe frailty (25).

Rather than relying on chronological age, functional age appears a better predictor of outcomes (26) and this can be measured in a number of ways to allow detection of significant physiological and psychomotor defects. Formal evaluation of older patients' functional capacity would support fitter older patients to undergo more radical treatments, while protecting those who do not possess the required physiological reserve. It may also help to evaluate the outcomes of prehabilitation more effectively and ensure safe delivery of prehab programmes for such patient groups.

The individualised prehab requirements of cancer patients based upon their functional, rather than chronological, age can be considered using the universal-targeted-specialised model endorsed by Macmillan-RCOA (7), (See figure 1). As patient needs increase, the level of support increases providing a 'specialised' healthcare-exercise service provision at the top of the triangle.

Case for change in cancer care Greater Manchester, UK

Although there is growing evidence for the effectiveness of prehab, it has not yet been accepted into core clinical practice by the National Health System. Robust multi-centre trials are underway in the UK (27,28) and internationally (29) with the aim to evaluate prehabilitation care on a much larger scale than was previously conducted to derive the underpinning evidence of effectiveness and efficacy as well as patient acceptance of the interventions.

People in Greater Manchester (GM) diagnosed with cancer tend to be less active and have poor health compared to other UK areas (30). Many have complex unmet health and social care needs throughout their treatment, which can remain for up to six months or more after treatments. Cancer outcomes was one of the composite health metrics that drove the creation of the Greater Manchester Health and Social Care Partnership (GMHSCP) Integrated Care System. In 2015, NHS organisations and councils agreed the GM devolution deal entrusting GM to 'take charge' of its own health and social care budget bringing together the social care and healthcare of its 2.8 million population. [31]

This restructuring of the Greater Manchester (GM) healthcare system has supported innovative transformation projects for patients affected by cancer in GM including: the rapid screening programme for lung cancer, Enhanced Recovery After Surgery Plus (ERAS+) programme for major surgery, the CURE project to support smoking cessation, and prehab for those with cancer through the 'Prehab4Cancer' and recovery programme (32).

Working with partners in Greater Manchester to improve surgical care

The ERAS+ project

Prehab for cancer patients undergoing surgery in GM has evolved from the surgical pathway innovation Enhanced Recovery After Surgery+ (ERAS+) (33), a pre and post-surgery care pathway designed and developed in GM and aimed to reduce pulmonary complications the most common significant complication after major surgery (34). The original implementation of ERAS+ at Manchester Royal Infirmary, demonstrated a 50% reduction in respiratory complications in patients undergoing major surgery and reduced hospital length of stay by 3 days (33).

ERAS+ is built on a traditional enhanced recovery after surgery stepped recovery approach and incorporates the ICOUGH respiratory bundle (35). As a direct innovation it integrates prehab into the ERAS pathway, with the aim of improving patient's fitness before surgery with cardiovascular activity and muscle strengthening recommendations, alongside nutritional support, lifestyle advice and medical optimisation. This embedding of prehabilitation into ERAS is now being recognised as an essential step in major surgical care [8,36].

Patient and family education about the ERAS+ pathway are facilitated through the 'Surgery School' format. Patients are invited with family members, carers and friends to attend the multi-disciplinary education session prior to their surgery. At this 90 minute weekly-facilitated session, healthcare professionals (medical, nursing and Allied Healthcare Professionals) involved in the surgery care pathway 'walk' the patient and their accompanying friends/family members through the ERAS+ innovation with an emphasis on 'training for their surgery'. Using behavioural change methodology, 'Surgery School' is designed to empower patients and families, viewing major surgery preparation as a teachable moment (37,38). Pre-operative cardiovascular exercise, muscle strengthening, smoking cessation, medical optimisation, post-operative pain management are all explained alongside the ICOUGH aims of early mobilisation, good oral healthcare, use of incentive spirometers and early fluids and nutrition. Patients and family members are encouraged to ask MDT members facilitating 'surgery school' any questions they may have, and they are also invited to visit the High Dependency Unit and ward areas where they will be looked after following surgery. This helps to establish realistic expectations, reassurance and 'normalisation' to reduce any potential experience of anxiety a patient may be having in anticipation of their surgery. It was also found to strengthen the partnership between healthcare provider, patients, and their networks of support (unpublished data).

Following its success at Manchester Royal Infirmary Hospital, the ERAS+ platform was adopted by the GMHSCP system for implementation at a further six NHS hospital trust sites within the GM region as the GM ERAS+ programme, supported and funded by a Health Foundation Scaling up Improvement grant (2018-2020) (39).

As part of the initial rolling out of the GM ERAS+ programme and the ambition to facilitate patients getting fitter prior to surgery (prehabilitation), hospital sites began to formulate links with their local GM borough leisure organisation health-focused partners to help consider and develop the delivery of community-based physical activity intervention prehabilitation for surgical patients in their

locality utilising existing exercise referral schemes. These links were formed in parallel with the development of the CAN-Move exercise rehabilitation programme [40], a commissioned exercise referral scheme available for Salford residents recovering from cancer treatments including surgery and oncological interventions. The specialist exercise instructor leading this programme would become the Prehab4Cancer exercise lead.

During a similar timeframe the GM Active board was conceived, bringing together 12 separate leisure and community organisations from across GM, working collaboratively to increase the levels of exercise and physical activity of the GM population. The formation of GM Active enabled relationships formed with individual leisure providers to be expanded to include health-focused representatives from all the GM leisure organisations, a progression which became a 'lever' for the concept of system-wide prehabilitation delivery at scale.

Patients accessing the ERAS+ programme were signposted to local physical activity resources through their ERAS+ teams, during 'pre-op' appointments and 'surgery school' and were encouraged to attend on a voluntary basis. The community-based exercise referral schemes could be accessed by both oncological and non-oncological major surgical patients either free of charge, or with minimal costs, through locally agreed introductory rates. A combination of cardiovascular and resistance-based training was provided to patients, using the existing referral fitness instructors in borough sites who were already delivering pulmonary rehabilitation, falls rehabilitation, pain management, cardiac rehabilitation and in some cases cancer rehabilitation sessions.

Patients entering these preliminary programmes increased their exercise capacity in the preoperative period (unpublished data). There were, however, a number of barriers identified to wider scale adoption including organisation of gym referral and patient appointments; ownership of referral from secondary healthcare; differences in the exercise aspects on offer, variation in cost, which despite being mainly low it remained as a barrier to some patients undertaking the sessions. Importantly, there had not been a large-scale investment in secondary and primary care understanding of the gym prehab sessions and, as such, patients received inconsistent recommendation to engage from key clinicians within their surgical pathways, if any recommendation was made at all. Prehab4Cancer focus groups comprised of People Affected By Cancer (PABC) confirmed this important barrier to engagement. It is therefore essential that surgeons, oncologists, Cancer Nurse Specialists (CNSs) and other key healthcare professionals

advocate engagement in prehab using consistent communication (similar language, explanation of the service, written information and positive affirmation).

Prehab4Cancer design

The evolving relationship of the GM secondary healthcare providers with the GM Active leisure organisation enabled learning to be adopted from the preliminary implementation of prehab in individual boroughs, fostered through the GM ERAS+ programme delivery. This in turn became a catalyst for key representatives from the GM Active board and the ERAS+ programme team to consider the development of a GM system-wide prehab service model for Greater Manchester 'The Prehab4Cancer and Recovery programme' with GM Cancer oversight and supported financially through transformation funding.

The Prehab4Cancer (P4C) programme, with system-wide stakeholders now in place, was co-designed with PABC as patient involvement representatives, alongside cancer surgical pathway healthcare experts and exercise professionals from GM Active. The programme was initiated with an ambition to facilitate two thousand patients to undertake community-based prehabilitation and recovery, close to their residential address, in the eighty-six GM Active leisure facilities across the GM conurbation. Patients would be supported before (prehab) and after (rehabilitation) cancer treatments (including surgery, chemotherapy and radiotherapy), and where applicable during treatment, to have increased physical, nutritional and wellbeing support.

The initial patient cohorts chosen, based upon the current strongest evidence base and reflective of the relationships already in places with GM ERAS+ teams, were colorectal, lung and oesophago-gastric cancer surgery pathways (12-17). It was agreed that all patients resident in GM within these tumour groups and with an offer of curative surgery could additionally be offered 'Prehab4Cancer' as an integral component of their treatment pathway. Additional eligibility criteria included age >18 and being able to safely participate in the exercise programme (41).

Cancer clinical pathway specific subgroups for each surgical cohort worked closely with PABC and members of MDTs from around GM to design the specific surgical P4C pathway for their patients, supported by clinical (medical/therapies/psychological), academic and exercise expertise. Meetings took place on a monthly basis chaired by a clinical lead (surgeon or physician) and supported by the 'Prehab4Cancer' programme and clinical leads. These subgroups informed the co-design and effective implementation of the referral process, patient uptake and adherence to the programme,

clinical considerations for programme delivery specific to tumour group cohorts and consistent communication for patients and family members. The output and ownership from these subgroups appear critical to the success of the programme delivery and would be a recommended component for the development of other prehab programmes being considered.

The project team managing the delivery of P4C consists of a secondary healthcare clinical lead (anaesthetic and critical care consultant, with specialist experience in peri-operative medicine), primary care lead (Macmillan GP), GM Cancer programme lead (specialist occupational therapist with a background in complex rehabilitation and community NHS service leadership) and GM Active programme manager (former CAN-Move manager). The combination of members of this inter-disciplinary team provided oversight of a patient's journey from referral through treatment and into recovery, and a comprehensive understanding of the clinical and holistic needs of cancer patients.

The governance structure (Figure2) which supports the project team and ultimately delivery of P4C includes an overarching steering group reporting into the GMHSCP via the GM Cancer Board, cancer clinical pathway specific subgroups, intervention-specific expert groups and an AHP Advisory board (including dietitians, occupational therapists, physiotherapists, speech and language therapists and PABC).

Attention was particularly given to older patients considered to be high risk or identified to be prefrail/frail, agreeing assessments and interventions which could be graded to such patient cohorts for maximal engagement and safe delivery of the programme. As a result, relatively few patients are excluded from the programme with patients in their 70s, 80s and 90s effectively participating in P4C. This was further supported by education events to wider healthcare professional stakeholders involved in referral to the P4C service and who would be in contact with programme participants.

P4C intervention

The exercise interventions, pathways and outcome metrics (see table 1) for P4C were developed by the authors in partnership with PABC, the expert exercise and pathway subgroups and were aimed to improve patient cardiovascular fitness, muscle strengthening and incorporate nutritional and wellbeing support to complement existing provision within GM cancer patient pathways.

The programme recognises many of the secondary symptoms that cancer patients experience related to their diagnosis and subsequent treatment including fatigue, low mood and feelings of

anxiety (42). It builds on widely understood principles surrounding exercise positively contributing to the reduction of such secondary symptoms, particularly related to mental health (43-45), with the overall aim of providing a holistic pathway to improve patient quality of life, during and after treatment. This in turn supports people with cancer to recover faster from their treatment with motivation for resumed independence and the ability to perform their pre-morbid occupations including returning to work, self-care and other important and personally meaningful activities of daily life.

Participants' wellbeing modality was constructed using the NICE 2004 stepped care model (46) approach to psychological support, highlighted in the Macmillan Prehabilitation Evidence and Insight report from 2017 (47), and accepted as an effective framework to deliver mental wellbeing assessment and intervention.

In addition, by using well-equipped community-based leisure resources, as opposed to hospital gymnasiums, there was also the intention that this would support a secondary programme aim to induce long-term lifestyle behavioural change, supporting patients' adoption of on-going exercise following discharge from the programme.

Through existing partnerships with GM Active, the non-profit organisation UKactive, who represent the fitness and leisure sector partnered with the Prehab4Cancer team. Their research institute's principal investigator provided input to the prehab-intervention design and training of GM Active staff, in addition to the reporting and evaluation of the exercise components. This included careful consideration of the timeframe available for the prehabilitation component (typically 3-4 weeks) and the minimal effective exercise dose that could be provided.

Exercise dose was considered for both cardiovascular and resistance exercise based upon manipulation of the intensity of effort required ('how potent?'), the volume/duration for which it was performed ('how much?'), and also frequency of sessions across each week ('how often?'). Within this, a standardised intervention was developed that enabled individualisation to scale to patient's fitness levels (due to prescription based upon effort i.e. exercise demands relative to patient's current capacity) and enabled flexibility in delivery across the various leisure facilities involved.

An overview of the exercise prescriptions is shown in Table 2. Briefly, both followed progression in terms of the potency of dose prescribed based upon intensity of effort, a concomitant adaptation of

volume/duration in line with this, and fixed frequency of 3x/week sessions. The resistance training component provided a progressive intensity of effort with minimal effective dose as previously delivered for older adults (48-49). The cardiovascular training was adapted from the RE-HIIT (reduced exertion high intensity interval training) protocol providing a tolerable approach to HIIT (50). Exercise selection was deliberately flexible within this prescription to accommodate the varying equipment between sites of delivery, and patient preferences, functional limitations, and injuries. Resistance training included a minimum of 3 exercises performed to target the main large muscle groups of the body (upper body multi-joint push e.g. chest press/overhead press/seated dip; upper body multi-joint pull e.g. pulldown/seated row; and a lower body multi-joint exercise e.g. leg press/deadlift) with additional single-joint exercise included as supplementary where specific functional deficits existed. Similarly, cardiovascular training was performed using an available ergometer (e.g. cycle, treadmill, cross-trainer, stepper, rower, ski-erg, or arm crank).

Data from patients attending the leisure facilities in the P4C programme, is collected using the ReferAll data collection system, which has been used in previous work examining exercise referral schemes (51-53). UK Active and GM Active have many years of experience working with the ReferAll system, which has been adapted to allow capture of data relating to both outcome and fidelity of the interventions in line with the Consensus on Exercise Reporting Template (CERT) (54).

The knowledge from the project team and expert groups of the holistic needs of predicted patient cohorts led to areas for continued professional development (CPD) and education. This has included all GM Active fitness instructors involved in service delivery being trained in level 1 stepped-care model (46) communication SAGE and Thyme skills training workshop (55), bespoke nutritional screening (devised by cancer specialist dietitian members of the AHP Advisory Board), exercise prescription, prehabilitation overview and consideration of potential complex needs 'Prehab4Cancer' participants may present with. There is on-going CPD training which includes facilitated reflective peer session with oncology specialist psychologist and programme lead to provide emotional support to staff delivering P4C intervention, as well as weekly education sessions covering topics such as severe and enduring mental health conditions and cognition.

The P4C patient pathway

The starting point for the surgical P4C pathway is the Multi-disciplinary team decision to operate (See figure 3). In phase 1, all patients undergoing colorectal, lung and upper GI cancer surgery are offered 'Prehab4Cancer' without restriction. The patient is then referred through the GM Active 'Prehab4Cancer' on-line referral form (<u>https://www.gmactive.co.uk/prehab4cancer/</u>). Here patient referral information including demographics, diagnosis, relevant past medical history and other specified details is provided by a named healthcare professional referrer to support on-going gymhealthcare liaison and the creation of a ReferAll patient record. Upon receipt of the referral the P4C referral coordinator contacts the patient within 48 hours and arranges attendance at an initial assessment clinic within another 48 hours from telephone contact. This initial assessment clinic will be held at a local leisure facility within 5 miles or 30 minutes travel from the patient's residential postcode. The assessment clinic is facilitated by one of the P4C Specialist Instructors, at one of the 17 assessment clinics held weekly. The specialist instructors are trained in cardiac, pulmonary and cancer rehabilitation as well as qualifications on falls prevention, obesity & diabetes and musculoskeletal disorders to allow them to work with complex patients.

At the initial assessment, a patient is assessed using P4C agreed clinical, physiological, functional and psychosocial metrics (Table 1). Details of their assessments are recorded on the ReferAll system. An exercise prescription is generated in line with the standardised intervention detailed above providing a combination of cardiovascular and resistance exercise with the aim for patients to attend a minimum of three gym sessions per week leading up to surgery and 2-3 sessions per week during neo-adjuvant chemotherapy . Following evaluation, patients are triaged into a targeted (less fit) or universal (fitter) pathway, which offer varying levels of supervision dependent upon patient fitness, nutritional needs, frailty, requirement for psychological support and ability to self-manage their exercise prescription independently in a potentially unfamiliar gym environment. Patients undergoing neo-adjuvant chemotherapy treatments as part of OG or lower GI cancer pathway are automatically entered into the targeted pathway, with the expectance that these patients will deteriorate in their endurance and physiologically during their oncological treatment. These neo-adjuvant prehab pathways last for 2-3 months and continue up until surgery.

In the targeted pathway for patients who require increased levels of support, patients attend for group sessions, with an attending exercise specialist or local instructor. The patient is monitored and HR data, RPE and Borg scales recorded during sessions. The universal patients are provided with a detailed exercise programme to adhere to and educated on achieving their training zones at the gym with additional weekly regular specialist reviews for support. They are given details of the targeted group sessions, which they are invited to attend should they wish to and encouraged to undertake

other gym activities which appeal to them. On non-gym days all patients are encouraged to be active and aim to undertake 30 minutes of moderate physical activity, which can be spread throughout the day, in line with national physical activity advice (10).

Once undertaking the P4C programme, patients are re-assessed using the same outcome metrics prior to surgery following their prehab phase, 4-6 weeks post-surgery when they are deemed physically able to resume engagement in exercise and again finally at the point of discharge from the service following 12 weeks of a recovery programme.

In contrast to the prehab phase, which is deliberately prescriptive for those patients who have completed their treatment following surgery, the recovery phase aims to provide an exercise prescription which is more personalised to patient preference and physical activities which will be more likely to lead to long term behavioural change. P4C specialist instructors utilise the relationship they have developed with patients, as well as their local knowledge of available community resources to engage participants in physical activity they will be motivated to continue to do, whilst supporting their recovery from major surgery. Beyond the 12 weeks funded recovery phase, patients can be transitioned to other exercise referral schemes or subsidised, independent gym access dependent on the patient's ongoing needs and the borough they live in.

For patients who require further adjuvant therapies following surgery (OG and Lung adjuvant chemotherapy), their rehabilitation adopts a similar prescriptive nature to their prehab, which will be on-going through their post-op treatment. When this is completed, they will be offered transition to a recovery phase programme.

'Specialised' P4C pathways aimed at those most high-risk patients experiencing sarcopenia and/ or moderate/severe frailty and subsequent higher risk of complications through surgery or other curative oncological treatment are now in development in GM. We are working with sports medicine and academic colleagues to explore the potential pathway, staffing groups (including AHPs working with specialist fitness instructors) and interventions that will help optimise this groups of patients.

Evaluation of Prehab4Cancer

Since it launched in April 2019, at the time of writing, over 600 patients from across the GM conurbation have participated in the P4C programme. Of colorectal patients (n=331), average age of

patients entering P4C is 67 (35-91), 60% are male with over 47% of patients in P4C over the age of 70 and from all boroughs in GM. For lung (n=258) the average age of patients entering P4C is 69, with 47% male and more than 57% of patients over the age of 70, with again representation from all over GM. Approximately 80% of people referred agree to attend their initial assessment and 95% of those attending this appointment engage in the programme, demonstrating acceptability for people diagnosed with cancer in GM. Initial participant feedback focus groups held at 6 months into the programme have generated consistently positive support for P4C.

The high uptake rates from phase 1 cohorts will enable the second phase of patients undergoing major surgical procedures including hepato-pancreato-biliary surgery, head and neck and urology cancer diagnoses to commence in advance of the project's planned delivery timeline along with lung cancer patients on non-surgical treatment pathways accessing the programme.

Despite evidence for the efficacy of prehab and rehabilitation in controlled settings, robust evaluation of its 'real world' effectiveness is needed. By early 2021, P4C will have supported ~2,000 patients to participate in freely accessible community-based prehab and recovery programmes across the GM region. Its successful implementation in GM presents a potential best practice 'Whole Population' model, adaptable for all appropriate cancer patients in the UK. This work would, to our knowledge, represent the first large scale evaluation of a treatment pathway focused around cancer prehab and rehabilitation within a 'real world' context (i.e. within the context of usual day to day delivery of care) as opposed to within a controlled research context (i.e. a randomised controlled trial). Thus, we will generate evidence regarding the 'real world' effectiveness of Prehab4Cancer's implementation that might support the sustainability and extension of the current programme, as well as the transferability and scalability of similar models of care delivery to be adopted by other local and combined authority areas in the UK.

During P4C implementation, all patients referred into the service, and meeting the inclusion criteria, will have been offered the intervention. The majority of participants would be classed as older adults (over 65 years old), with many in their 70s, 80s and 90s. This will allow us to evaluate the role of prehabilitation in older patients who have traditionally been absent from cancer intervention trials (56-57).

Throughout the programme, intervention fidelity and patient outcomes will be measured and digitally captured including survival rates, surgical complications, hospital readmissions, treatment

recovery, physiological and functional measures, and quality of life (QOL) patient reported outcomes (PROMs). This dataset, in combination with historic 'legacy' datasets representing usual care models, will enable the evaluation to take place and allow a pragmatic evaluation of Prehab4Cancer.

Conclusion

The introduction of ERAS+ in 2015 as a new pathway in Greater Manchester (GM) including a prehabilitation advice and support package, in-hospital best care surgical model, and post-hospital recovery supporting patients, has already led to rapid improvements in post-surgical complications and costs (unpublished GM ERAS+ data).

With the addition of P4C, GM Cancer is the first regional system in the UK to introduce delivery of system-wide, large scale physical activity supported multi-modal prehabilitation and recovery interventions as a standard of care for cancer patients. P4C to date has focused on robust co-design, development, and implementation of an effective service model with attention paid to stakeholder engagement. This has led to receipt of high numbers of referrals from across GM for the all the cancer groups involved. Prehab in older and more frail patients will be reviewed in the evaluation of the current P4C model, which will help in the design of the specialised prehabilitation models for patients in GM.

The successful implementation of the P4C pathway in GM presents a best practice model that might be adopted by other local and combined authority areas nationally. However, robust evaluation is needed to evidence its effectiveness, 'value for money' and to help maximise its impact to influence the case for national adoption of prehabilitation service delivery.

References:

1.Pearse RM. Global patient outcomes after elective surgery: prospective cohort study in 27 low-, middle- and high-income countries. Br J Anaesth 2016;117(5):601-9.

2.Tjeertes E, Ultee KHJ, Stolker RJ et al. Perioperative complications are associated with adverse long-term prognosis and affect the cause of death after general surgery. World J Surg 2016 40:2581-2590.

3.**Richards** SJG, Frizelle FA, Geddes JA et al. Frailty in surgical patients. Int J Colorectal Dis. 2018 Dec;33(12):1657-1666.

4.**Sadiq** F, Kronzer VL, Wildes TS et al Frailty Phenotypes and Relations With Surgical Outcomes: A Latent Class Analysis. Anesth Analg. 2018 Oct;127(4):1017-1027.

5.Thorsen L, et al. Cancer patients' needs for rehabilitation services. Acta Oncol. 2011;50(2):212–222

6.Silver J. Cancer Rehabilitation and Prehabilitation May Reduce Disability and Early Retirement, Cancer 2014 (120), Issue14: 2072-2076

7.MacMillan Cancer Support, Royal College of Anaesthetists, and the National Institute for Health Research. *Prehabilitation for people with cancer: Principles and guidance for prehabilitation within the management and support of people with cancer.* 2019. https://www.macmillan.org.uk/about-us/healthprofessionals/resources/practical-tools-for-professionals/prehabilitation.html

8.Carli F, Gillis C and Scheede-Bergdahl C. Promoting a culture of prehabilitation for the surgical cancer patient. Acta Oncologica, 56:2, 128-133

9.**Tew** GA, Ayyash R, Durrand J et al. Clinical guideline and recommendations on pre-operative exercise training in patients awaiting major non-cardiac surgery. Anaesthesia. 2018 Jun;73(6):750-768

10.Department of Health and Social Care (2019) *UK Chief Medical Officers' Physical Activity Guidelines* London: Dept. of Health and Social Care.

11.Faithfull S, Turner L, Poole K et al Prehabilitation for adults diagnosed with cancer: A systematic review of long-term physical function, nutrition and patient-reported outcomes. Eur J Cancer Care (Engl). 2019 Jul;28(4)

12.Piraux E, Caty G, Reychler G Effects of preoperative combined aerobic and resistance exercise training in cancer patients undergoing tumour resection surgery: A systematic review of randomised trials.. Surgical Oncology 27 (2018) 584-594.

13.**Barberan**-Garcia A, Ubré M, Roca J et al. Personalised Prehabilitation in High-risk Patients Undergoing Elective Major Abdominal Surgery: A Randomized Blinded Controlled Trial. Ann Surg. 2018 Jan;267(1):50-56.

14.West MA, Loughney, Lythogoe D, et al. Effect of prehbailitation on objectively measured physical fitness after neoadjuvant treatment in preoperative rectal cancer patients: a blinded interventional pilot study. Br J Anaesth 2014; 114(2):244-51.

15.Hughes MJ, Hackney RJ, Lamb PJ et al. Prehabilitation Before Major Abdominal Surgery: A Systematic Review and Meta-analysis. World J Surg (2019) 43:1661-1668.

16.Vermillion SA, James A, Dorrell RD et al. Preoperative exercise therapy for gastrointestinal cancer patients: a systematic review. Systematic Reviews (2018) 7:103.

17.Vagvolgyi A, Rozgonyi Z, Kerti M et al Effectiveness of pulmonary rehabilitation and correlations in between functional parameters, extent of thoracic surgery and severity of post-operative complications: randomised clinical trial.. J Thorac Dis 2018 ;10(6) :3519-3531.

18.Dunne DF, Jack S, Jones RP et al. Randomized clinical trial of prehabilitation before planned liver resection. Br J Surg. 2016 Apr;103(5):504-12.

19.Pergolotti M, et al. The prevalence of potentially modifiable functional deficits and the subsequent use of occupational and physical therapy by older adults with cancer. J Geriatr Oncol. 2015;6:194-201.

20.Lawrence VA, Hazuda HP, Cornell JE et al. Functional independence after major abdominal surgery in the elderly. J Am Coll Surg. 2004; 199:762-772

21.Saur NM, Montroni, Ugolini G et al. Outcomes that matter to patients? the geriatric oncology surgical assessment and functional recovery after surgery (GOSAFE) study: subgroup analysis of 440 patients undergoing colorectal cancer surgery. Journal of Geriatric Oncology. 2019 (10), Issue 6, Supplement 1, Page S11

22.Montroni I, Rostoft S, Spinelli A et al. GOSAFE - Geriatric Oncology Surgical Assessment and Functional rEcovery after Surgery: early analysis on 977 patients. J Geriatr Oncol. 2020 Mar;11(2):244-255.

23.Bachini M, Moravek C, Lindsey SC, Fleshman J, Rocha FG, Maithel SK (2019) The patient perspective to cancer care: Aligning physician expectations with patients' wishes. *HPB*, *21*(*1*).

24.NHS Long Term Plan 2019 <u>https://www.longtermplan.nhs.uk/wp-content/uploads/2019/08/nhs-long-term-plan-version-1.2.pdf</u>

25.NHS RightCare Frailty Toolkit 2019 <u>https://www.england.nhs.uk/rightcare/wp-content/uploads/sites/40/2019/07/frailty-toolkit-june-2019-v1.pdf</u>

26.**Schmidt** M, Eckardt R, Altmeppen S et al. Functional impairment prior to major non-cardiac surgery is associated with mortality within one year in elderly patients with gastrointestinal, gynaecological and urogenital cancer: A prospective observational cohort study. J Geriatr Oncol. 2018 Jan;9(1):53-59

27.**The Wessex** Fit-4-Cancer Surgery Trial [Westfit Trial] <u>https://clinicaltrials.gov/ct2/show/NCT03509428</u>

28.PREPARE-ABC http://www.uea.ac.uk/prepare-abc

29.Rooijen S, Carli F, Dalton S et al Multimodal prehabilitation in colorectal cancer patients to improve functional capacity and reduce postoperative complications: the first international randomized controlled trial for multimodal prehabilitation. BMC Cancer (2019) 19:98 7-11

30.GM Cancer (2017) Need to be completed

31.Bougeard AM, Moore J Delivering perioperative care in integrated care systems. Clin Med (Lond). 2019 Nov;19(6):450-453.

32.GM Cancer 2020 annual report – Anna P was going to create a URL from the GM Cancer website for me for this – it will be available to access before the article is published – I can chase her tomorrow.

33.**Moore JA**, Conway DH, Thomas N et al. Anaesthesia. Impact of a peri-operative quality improvement programme on postoperative pulmonary complications 2017 Mar;72(3):317-327.

34. Fernandez-Bustamante A, Frendl G, Sprung J et al

Postoperative Pulmonary Complications, Early Mortality, and Hospital Stay Following Noncardiothoracic Surgery: A Multicenter Study by the Perioperative Research Network Investigators. JAMA Surg. 2017 Feb 1;152(2):157-166.

35. Cassidy MR, Rosenkranz P, McCabe K et al. I COUGH: reducing postoperative pulmonary

complications with a multidisciplinary patient care program JAMA Surg. 2013 Aug;148(8):740-5.

36. Carli F, Bousquet-Dion G, Awasthi R, et al. 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 Surg.* Published online January 22, 2020. doi:10.1001/jamasurg.2019.5474

37.Lawson P and Flocke SA. Teachable moments for health behavior change: a concept analysis. Patient Educ Couns. 2009 July; 76(1): 25–3.

38.Grocott, M.P.W., Plumb, J.O., Edwards, M. *et al.* Re-designing the pathway to surgery: better care and added value. *Perioper Med* **6**, 9 (2017)

39.Moore, J. (2019) *Improving surgical care for patients and their families in Greater Manchester – ERAS+ GM.* London: The Health Foundation. Available at: <u>https://www.health.org.uk/improvement-projects/improving-surgical-care-for-patients-and-their-families-in-greater-manchester-%E2%80%93</u> Accessed 27.02.20.

40.ref https://www.salfordcommunityleisure.co.uk/can-move

41.Prehab4Cancer eligibility criteria <u>https://www.gmactive.co.uk/wp-</u> content/uploads/2019/04/Referral-Information-Pack-web.pdf 42. Stark D, Kiely M, Smith A et al **Anxiety disorders in cancer patients: their nature, associations, and relation to quality of life.** J Clin Oncol. 2002 Jul 15;20(14):3137-48.

43.Gordon BR, McDowell CP, Lyons M, Herring MP (2017) The Effects of Resistance Exercise Training on Anxiety: A Meta-Analysis and Meta-Regression Analysis of Randomized Controlled Trials. *Sports Medicine*, *47(12)*, 2521-2532.

44.Gordon BR, McDowell CP, Hallgren M, Meyer JD, Lyons M, Herring MP (2018) Association of Efficacy of Resistance Exercise Training With Depressive Symptoms: Meta-analysis and Meta-regression Analysis of Randomized Clinical Trials. *The Journal of the American Medical Association Psychiatry* 75(6), 566-576.

45.Chekroud SR, Gueorguieva, R, Zheutlin, AB, Paulus, M, Krumholz, HM, Krystal JH (2018) Association between physical exercise and mental healthin 1-2 million individuals in the USA between 2011 and 2015: a cross-sectional study. *The Lancet Psychiatry*, *5*(*9*), 739-746.

46.Stepped care model – 2004 <u>https://www.nice.org.uk/guidance/cg23/documents/cg23-</u> <u>depression-nice-guideline-marked-up-with-proposed-amendments2</u>

47.Macmillan Prehabilitation Evidence and Insight report (2017), <u>https://www.macmillan.org.uk/_images/prehabilitation-evidence-and-insight-review_tcm9-</u> <u>335025.pdf</u>

48.Steele J, Raubold K, Kemmler W, Fisher J, Gentil P, Giessing J. The effects of 6 months of progressive high effort resistance training methods upon strength, body composition, function, and wellbeing of elderly adults. *Biomed Res Int* 2017;2017;2541090

49.Fisher JP, Steele J, Gentil P, Giessing J, Westcott WL. A minimal dose approach to resistance training for the older adult; the prophylactic for aging. *Exp Gerontol* 2017;99:80-86

50.Metcalfe RS, Babraj JA, Fawkner SG, Vollaard NB. Towards the minimal amount of exercise for

improving metabolic health: beneficial effects of reduced-exertion high-intensity interval training.

European Journal of Applied Physiology. 2012;112(7):2767-2775

51.Rowley N, Steele J, Wade M, Copeland RJ, Mann S, Liguori G, Horton E, Jimenez A. Are exercise referral schemes associated with an increase in physical activity? Observational findings using individual patient data meta-analysis from The National Referral Database. *J Phys Act Health* 2020; In press

52.Steele J, Wade M, Polley M, Copeland RJ, Stokes S, Mann S. The National Referral Database: An initial overview. *SportRxiv* 2019; https://doi.org/10.31236/osf.io/rgywq

53.Wade M, Mann S, Copeland RJ, Steele J. Effect of exercise referral schemes upon health and wellbeing: initial observational insights using individual patient data meta-analysis from the National Referral Database. *J Epidemiol Commun Health* 2020;74:32-41

54.Slade SC, Dionne CE, Underwood M, *et al* Consensus on Exercise Reporting Template (CERT): Explanation and Elaboration Statement. *British Journal of Sports Medicine* 2016;**50:**1428-1437.

55.Connolly M, Perryman J, McKenna Y, Orford J et al. SAGE & THYME: A model for training health and social care professionals in patient-focussed support. Patient Education and Counseling 2010; 79: 87-93.

56.**Ethan B.** Ludmir, ¹; Walker Mainwaring, BA²; Timothy A. Lin, BA^{1,2}Factors Associated With Age Disparities Among Cancer Clinical Trial Participants. *JAMA Oncol.* 2019;5(12):1769-1773.

57.Cancer Research UK (2018) *Advancing cancer, advancing years: Improving cancer treatment and care for an ageing population* London: CRUK

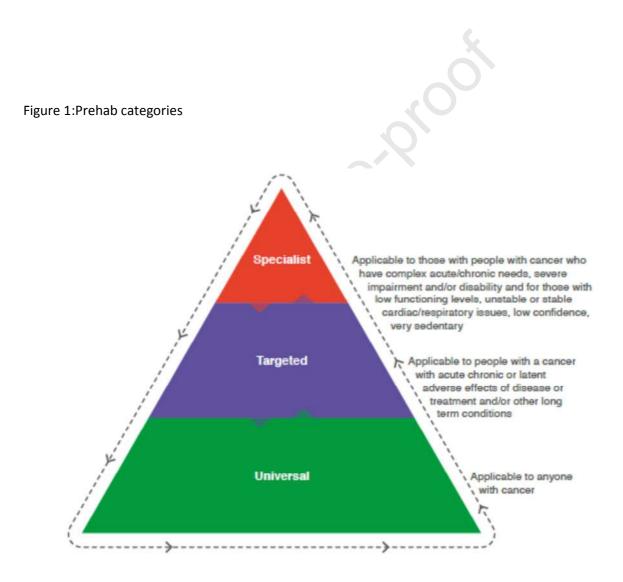


Table 1: P4C outcome metrics

Туре:	Outcome Measure:			
Physiological measures:				
Functional dynamic test	6 Minute Walk Test (6MWT)			
	Incremental Shuttle Walk Test (ISWT)			
Weight	To be measured in kilograms.			
Height	To be measured in metres.			
Heart Rate/BP	Resting heart rate/BP. Plus recording heart rate range during sessions.			
Oxygen saturation Levels	Recorded at rest and throughout the 6MWT/ISWT			
Resistance	Rep max percentage programming.			
	Heaviest weight you can lift for 10 consecutive exercise repetitions. Quad, Core, Shoulder.			
Grip Strength	Hand Grip Strength (dynamometer) measured in kg			
Bespoke nutritional screening a	assessment takes into account Body Mass Index (BMI), weight trend (loss			
	low solid food (IDDSI food and drink descriptors) and hand grip strength.			
Patient Reported Outcome Measu	res (PROMs):			
General Health and Wellbeing	EQ-5D-5L			
(Quality of Life - QOL)	Descriptive system of health-related quality of life states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) each of which can take one of five responses. The responses record five levels of severity (no problems/slight problems/moderate problems/severe problems/extreme problems) within a particular EQ-5D dimension. International Physical Activity Questionnaire-Short Form (IPAQ – SF)			
	 The IPAQ assesses physical activity across a comprehensive set of domains including: a) Leisure time physical activity, b) Domestic and gardening activities, c) Work-related physical activity, d) Transport-related physical activity. N.B. Developed and tested for use in adults (age range 15 to 69 years), 			
Physical Activity	not validated in older adults.			
	https://sites.google.com/site/theipaq/background			

Journal Pre-proof				
Cancer-specific QOL	EORTC QLQ-C30 (version 3)			
	This is a QOL questionnaire targeted to the management of chronic illness. It is included in the NHS England recommended Living with and Beyond Cancer/Personalised Care QOL metrics. It asks more extensive QOL questions which go beyond the EQ-5D.			
Frailty (Activities of Daily Living)	Rockwood Clinical Frailty Scale			
Disability	World Health Organisation Disability Assessment Schedule 2.0 (WHODAS 2.0)			
	This self-administered questionnaire asks about difficulties related to health conditions that impact on someone's ability to do their daily activities.			
Efficacy	Self-Efficacy for Exercise Scale			
	This supports action planning to identify barriers to engagement as the patient accesses the programme whilst also focusing on confidence levels and general self-efficacy of the patient to engage in exercise.			
Patient Reported Experience Measure(s) (PREMs):				
Participant Experience	NHS Family and Friends Test			
	Bespoke 'Prehab4Cancer' participant experience survey			

Table1: examples of cardiovascular and resistance training dose prescription used in P4C programme

Table 2. Examples of cardiovascular and resistance training exercise dose prescription. Note: Most patients received 3 weeks and progression is built around this length of time between diagnosis and surgery. Exercise past this time continues to progress or maintains at week 3 prescription.

	Resistance training			Cardiovascular training			
	Week 1	Week 2	Week 3		Week 1	Week 2	Week 3
How potent? Intensity of effort	nRM RP-E/D	sdRM RP-E/D	~MF RP-E/D	How potent? Intensity of effort	12-13 RPE Borg Scale*		18+ RPE Borg Scale*
How much? Repetitions Load Sets (Rest-sets)	15-18 reps ~50-60%1RM 2 2-4 mins	8-12 reps n/a 2 2-4 mins	8-12 reps n/a 1 n/a	How much? Duration Speed/Power Bouts	30 mins n/a 1	20 mins n/a 1	(RE-HIIT*) 10-20 secs n/a 2
<u>How often?</u> Frequency	3x/week	3x/week	3x/week	<u>How often?</u> Frequency	3x/week	3x/week	3x/week

<u>Decision Rules</u> Starting level Progression	~50-60%1RM (Brzycki formula*) From week 2; + <10% load if >12 reps before set end point achieved	<u>Decision</u> <u>Rules</u> Starting level Progression	Determined by initial fitness (i.e. RPE) Based upon changing fitness (i.e. RPE)				
Resistance training intensity of effort based upon set endpoints and rating of perceived effort (48,52); nRM = not repetition maximum; sdRM = self-determined repetition maximum; MF = momentary failure; 1RM = one repetition maximum; RP – E/D = rating of perceived effort (effort/discomfort); RE-HIIT = reduced exertion – high intensity interval training (see Metcalfe et al., 2012)							

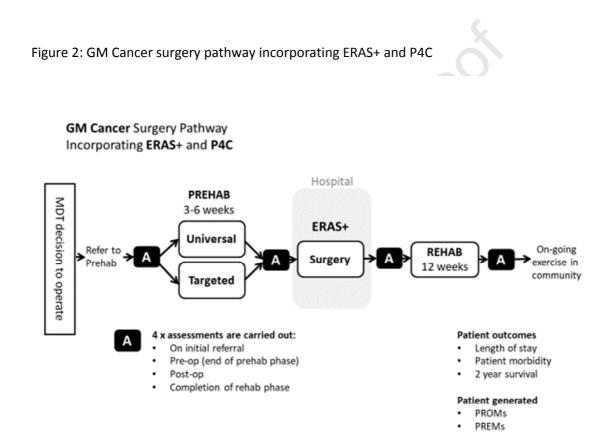
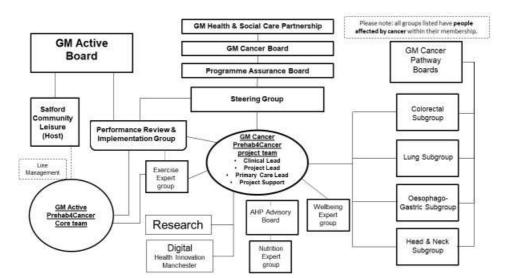


Figure 3: P4C Governance Structure



Prehab4Cancer Governance Structure

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Please find attached invited review article for special article of EJSO

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Yours Sincerely

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