TRIPOM
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009

Perioperative exercise programmes

Key points:

- Physical inactivity is the fourth leading risk factor for global mortality
- Prolonged physical inactivity leads to reduced aerobic capacity and loss of muscle mass
- Less than one-third of adults currently undertake the recommended levels of physical activity
- Preoperative exercise should be encouraged and can improves the body's ability to withstand the physiological demand of major surgery and reduce the risk of adverse postoperative outcomes
- Successful prehabilitation relies on co-ordinated team working between patients and perioperative teams across primary and secondary care

MCQs –

1 Regular exercise leads to

- Decrease in plasma triglyceride levels
- Decrease in plasma LDL-cholesterol
- Decrease in plasma HDL-cholesterol
- Protection against atherosclerosis
- Reduction in stroke risk by 25-30%

2 Regular physical activity is protective against which of the following cancers?

- Colorectal cancer
- Lung cancer
- Postmenopausal breast cancer
- Endometrial cancer
- Brain cancer

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3 Current recommendations for physical activity in 19-64 year olds include

- At least 30 minutes of daily activity
- 150 minutes of moderate intensity activity per week
- 150 minutes of vigorous intensity activity per week
- Activities to work on balance and co-ordination on at least 2 days per week
- Strength training exercises on at least 2 days per week

4 With regards to preoperative exercise training

- High intensity interval programmes have been shown to improve fitness more than moderate continuous exercise
- Exercise training results in an improvement in fitness in all people
- Preoperative exercise training before joint arthroplasty significantly improves quality of life
- Preoperative exercise programmes for lung cancer patients reduces their total length of hospital stay
- Neoadjuvant chemoradiotherapy can reduce preoperative fitness levels by up to 19%

5 Tests to assess physical fitness in preoperative patients include

- Timed get up and go test
- Cardiopulmonary exercise testing
- Incremental shuttle walk test
- Six-minute walk test
- Dukes activity status index

Lack of activity destroys the good condition of every human being, while movement and methodical physical exercise save it and preserve it.

Plato [4th century BC]

Hippocrates (c. 460 – c. 370 BC) was a Greek physician often referred to as the 'Father of modern medicine'. Along with creating the Hippocratic Oath he is also credited with the quote "Walking is a man's best medicine". He was not the only person of this era to recognise the benefit of physical activity as the above quote from Plato the Greek philosopher demonstrates. It is now known that walking and other forms of exercise are important for both the prevention and treatment of disease. However, it took many

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centuries for Hippocrates' idea to be proven and become an integral part of patient health.

Exercise in the past

Dr William Heberden, an eminent English physician in the 18th century, noted the case of a patient with angina pectoris whose symptoms improved by chopping wood for half an hour a day.[i] Despite this observation, patients with acute coronary syndrome were prescribed total bed rest and patients became fearful that exertion would lead to a heart attack. This advice continued through the 1930s.

In the 1940s it was slowly recognised that mobilisation helped prevent complications of bed rest without increasing the risk of acute coronary events. In the 1950s Professor Jeremiah Morris, a Scottish epidemiologist, undertook the first observation studies that investigated physical activity and heart disease amongst London Transport employees. He compared two groups of workers, bus conductors who were active all day walking up and down the buses and bus drivers who spent long hours sat down and inactive. He found that the inactive bus drivers had significantly higher rates of coronary heart disease than the active bus conductors.[ii] Although this seems obvious given what is known about physical activity now, at the time these findings were revolutionary.

In 1962 Professor Ralph Paffenbarger, a researcher in the field of physical activity epidemiology, founded the landmark College Alumni Health Study. This used periodic questionnaires over several decades to look at physical activity levels, illnesses and deaths in more than 50,000 people who had graduated from Harvard University or the University of Pennsylvania. He found that regardless of whether people had hypertension, smoked or were at the extremes of body habitus, the mortality rate was lower in the more physically active.[iii]

Current guidelines on physical activity levels

The works of Morris and Paffenbarger have significantly influenced the developments of guidelines regarding physical activity and health. In 1995, the expanding evidence base for exercise and its benefit on health led to the publication of the first set of guidelines on exercise prescription.[iv] These guidelines have now been refined and developed to incorporate specific recommendations and add in advice for older patients (>65 years). The current physical activity guidelines from the Department of Health for adults aged 19-64 years include (Figure 1):[v]

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1 Aim to be active daily. Over a week activity should add up to at least 150 minutes (2½ hours) of moderate intensity exercise in bouts of 10 minutes or more (ideally aim for 30 minutes on at least 5 days of the week).

2 Alternatively, the same benefits can be achieved by 75 minutes of vigorous intensity activity spread across the week or combinations of moderate and vigorous intensity activity.

3 Physical activity to improve muscle strength should be undertaken on at least two days a week.

4 Everyone should minimise the amount of time spent being sedentary for extended periods.

These guidelines are based on advice from the World Health Organisation (WHO) alongside the UK National Institute for Clinical Excellence (NICE). This advice is the same for adults over the age of 65 with the addition of adding in physical activity to improve balance and co-ordination on at least two days of the week for those at risk of falls. Alongside this, there has been an increase in public awareness of the benefits of regular exercise and increasing activity levels.

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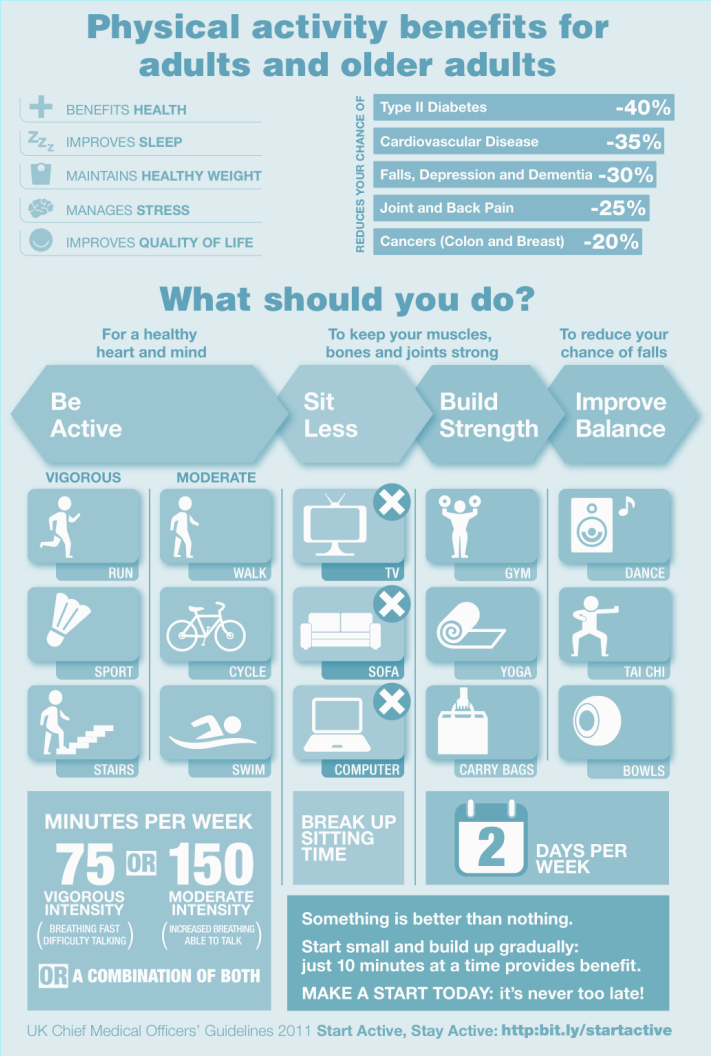

Figure 1: Physical activity guidelines and benefits (DOH 2011)

Why does physical inactivity matter?

Sedentary behaviour is defined as activity involving an energy expenditure of less than 1.5 metabolic equivalents (METS). Typically, sedentary behaviour involves lying or sitting down. The average UK adult is estimated to spend approximately 60% of their day sedentary with over 50% of people being inactive for 5 hours or more at a time.[vi] There is a clear association between inactivity and major comorbid disease with sedentary

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individuals having an increased risk of two to three times of cardiovascular disease, diabetes, obesity, malignancy and mortality.[vii] The benefits of exercise and increasing activity levels are widely recognised across a broad range of medical conditions[viii] [ix] and particularly so for elderly patients.[x]

Sedentary behaviour is associated with reduced aerobic fitness. This is particularly important as VO_2 max (the maximal rate of oxygen uptake - a marker of aerobic capacity) declines naturally by approximately 10% per decade after 30 years of age.[xi] Alongside this, ageing is accompanied by a progressive loss of lean muscle mass, or sarcopenia – a component of the increasingly recognised 'frailty syndrome'.[xii] These changes all together significantly compromise the ability of patients to withstand major physiological insults such as major surgery. Consequently, the World Health Organisation have identified physical inactivity as the fourth leading risk factor for global mortality.[xiii]

These changes can be offset through regular exercise and are minimised in patients who are habitually active. Evidence is emerging that sarcopenia and skeletal muscle deconditioning associated with ageing can be improved by a combination of aerobic and strength training.[xiv] In the perioperative setting there is increasing interest and increasing evidence in preoperative (prehabilitation) and postoperative (rehabilitation) optimisation of physical fitness with the aim to improve outcomes after surgery.

The challenge faced by surgical patients

Approximately 4 million major surgical procedures are performed in the UK annually at a cost of over £16 billion.[xv] Additionally surgical interventions have almost doubled in both men and women aged over 75 years in the last two decades.[xvi] Surgery is associated with a significant burden of perioperative morbidity and mortality that represents a significant public health challenge particularly in older patients. Life expectancy is continuing to rise and an increasing proportion of older patients are presenting for surgery with multiple comorbidities. Studies have shown that the presence of a single post-operative complication increases the risk of mortality for up to 10 years after surgery, independent of any other comorbidities[xvii] and that high risk patients make up a small group yet they account for 80% of all deaths following surgery.[xviii] In 1993, Older and colleagues first identified that low fitness levels are associated with an increase in mortality rates in elderly patients after surgery.[xix] Since then this observation has been replicated on numerous occasions.

Major surgery represents a major stressor and the subsequent inflammatory response has a profound effect on the physiological function of the body. Surgical patients may

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often be relatively sedentary partly secondary to their comorbidities and partly due to their lifestyle. Physical deconditioning, distinct from clinical disease, may contribute to or be the cause of their reduced functional capacity. The degree of functional impairment predicts the postoperative outcome and patients with lower aerobic fitness have significantly increased risks of adverse postoperative events ranging from major morbidity, mortality, longer hospital stays and reduced long-term quality of life. It has been recognised in multiple studies that being unfit increases complications rates and contributes to poorer outcomes with strong evidence supporting the association between measured cardiovascular fitness and postoperative outcome.[xx] [xxi] [xxii] Any associated comorbidities or frailty compound this increased risk. Physiological age therefore has a clearer association with perioperative outcome than chronological age.

Assessment prior to major surgery should include looking at a number of factors that impact on the perioperative outcome. Amongst others these include comorbidities, physical activity status, smoking, nutrition, alcohol intake, independence, evidence of frailty or cognitive dysfunction and polypharmacy. Accurately defining physical activity status remains a challenge. Subjective reporting by the patient is complicated by often significant discrepancies and overestimation of physical activity levels.[xxiii] Where possible, an objective assessment of physical fitness is recommended. There are a number of independently validated tests that can be used including timed stair climbing, the 6-minute walk test, the incremental shuttle walk test and cardiopulmonary exercise testing (CPET). CPET has the largest evidence base and is covered in detail in the CPET tutorial.

Preoperative Exercise

Aerobic fitness can be defined as the coordinated capacity of the cardiovascular, respiratory and musculoskeletal systems to boost the delivery and handling of oxygen within the body. The association between perioperative outcome and physical fitness has resulted in a large amount of research relating to exercise interventions and to evaluate whether such interventions correlate with an improved outcome. This is termed prehabilitation. Although the exact definition of prehabilitation is flexible it can be thought of as "the process of enhancing the functional capacity of the individual to enable them to withstand a stressful event".[xxiv] [xxv] There is a common theme of early intervention with the aim to improve outcome. Preoperative exercise programmes fall into this category. It goes without saying that there is the need for simultaneous integrated prehabilitation strategies to optimize other unhealthy lifestyle factors such as smoking, alcohol intake and nutrition. It is beyond the scope of this tutorial to cover them all and they have been discussed in detail in the prehabilitation tutorial.

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Exercise training has been well documented as feasible and safe in patients with a spectrum of severe cardiac and pulmonary conditions. It has been shown to improve physical fitness and clinical outcomes in patients with ischaemic heart disease[xxvi xxvii], cardiac failure[xxviii], stroke[xxix], intermittent claudication[xxx] and COPD.[xxxi] It has also been shown that being physically active and fitter reduces the risk of a variety of chronic diseases including obesity, osteoporosis, type 2 diabetes, depression, colorectal cancers, breast cancer and kidney cancer.[xxxii]

A structured preoperative exercise programme should increase functional capacity and therefore functional reserve meaning patients are better able to cope with the subsequent physiological stress of surgery. The theoretical rationale is that this will then lead to a faster recovery even in the presence of complications, along with a faster return to functional 'normality' compared to inactive patients. Figure 2 demonstrates that a prehabilitated patient who has improved their pre-operative functional status is better able to cope with the major physiological insult of surgery. They experience a faster recovery with a more rapid return to functional independence even in the presence of postoperative complications. This is probably more relevant in high-risk patients particularly sedentary individuals, the elderly or frail.

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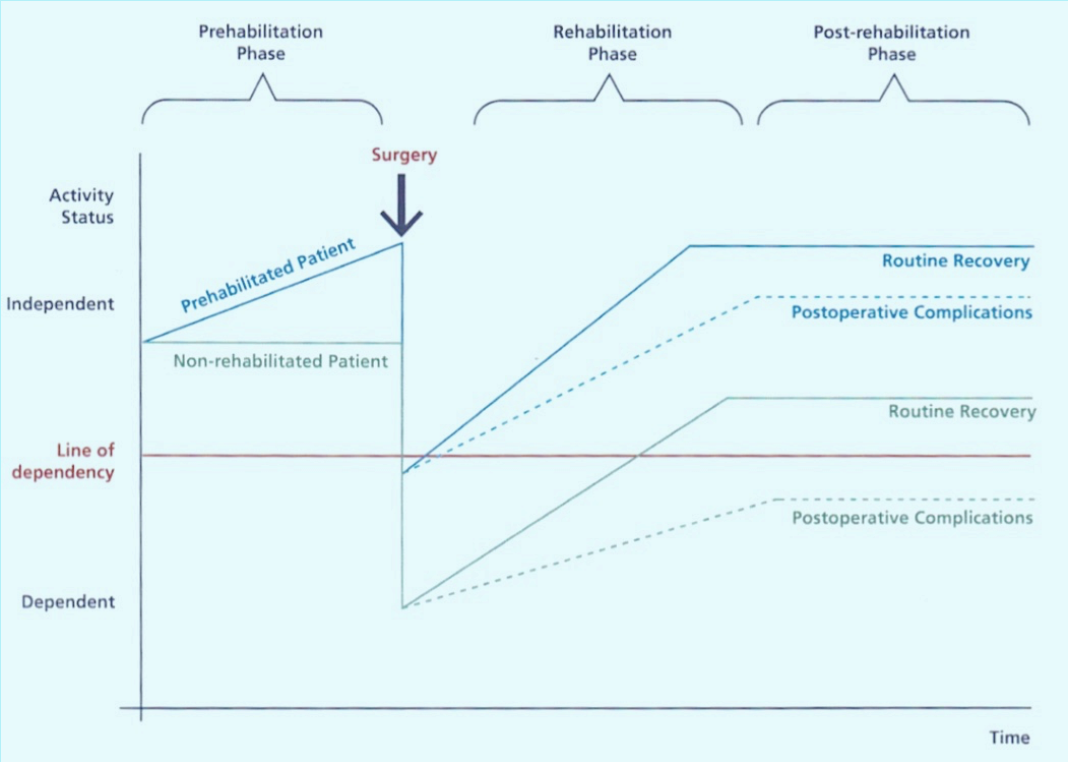

Figure 2: Rationale for preoperative exercise and prehabilitation (reproduced from Preoperative Association Guidelines 2017)

Evidence to support preoperative exercise

While there is extensive evidence that improving functional capacity and being fitter predicts postoperative outcome, there is less evidence on the basis of interventions to improve exercise capacity. There are several trials and schemes in place around the UK and interrogating the clinical trials database identifies 51 trials evaluating prehabilitation and specifically exercise in various surgical patient populations.[xxxiii] Substantial new data should be available in the near future.

There have been many small trials and systematic reviews published looking at preoperative exercise. Two studies looking at lung cancer patients found that preoperative exercise training both improves lung function before surgery and reduces hospital length of stay, postoperative pulmonary complications and forced vital capacity post lung resection.[xxxiv] [xxxv] In 2016 a systematic review looking at preoperative exercise in colorectal cancer patients found evidence that preoperative exercise increases

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functional fitness and to a lesser extent objectively measureable cardiorespiratory fitness prior to colorectal cancer resection. However, it found no clear evidence that this improvement in fitness translated into reduced perioperative risk or improved outcomes. It concluded that there appeared to be difficulties in transferring promising results seen in a research setting into significant clinical improvements.[xxxvi] This mirrors the findings of another review published in 2016 which found that overall preoperative exercise has beneficial effects on fitness and postoperative outcome. This review highlighted that there are gaps in the literature, heterogeneity in selected patient populations and the outcome measures used in the various trials as well as a lack of guidelines on specific exercise regimes.[xxxvii]

Despite the fact that the benefit of preoperative exercise is highlighted, the relatively limited evidence base and the need for adequately powered multi-centre randomised controlled trials is highlighted in the majority of the systematic reviews looking at preoperative exercise. In contrast to the above evidence, a systematic review published in 2015 looking at patients undergoing arthroplasty found no evidence that prehabilitation or preoperative exercise provided any benefit in terms of function, pain or quality of life for these patients. The only positive conclusion reached was that it may reduce acute rehabilitation admissions.[xxxviii]

Latterly there has been a focus on patients receiving neoadjuvant chemoradiotherapy (NACRT). A study in 2015 looking at colorectal cancer patient receiving preoperative NACRT found a physical fitness decrease of up to 19%. Patients were then randomly allocated to either a 6 week cycle-based HIIT programme with three 40 minute exercise sessions per week or usual care (no prescribed exercise). The patients allocated to the 'no exercise' group showed a further 34% drop in fitness levels below initial baseline levels.[xxxix] This study appears to offer persuasive evidence that the negative impact of NACRT can be offset by an appropriate training programme.

There have been questions raised about the trainability of older patients and the best exercise programme to follow to achieve the most benefit. Older people do not appear to demonstrate similar fitness improvements to younger individuals in response to aerobic exercise. The reality is that there is a large heterogeneity in the training response seen. Up to 40 to 45% of people appear to show no initial fitness benefit with training, so termed non-responders.[xl] This appears to be dependent on genetics and environmental factors and not dependent on age or sex. However, with continued training and longer duration higher intensity programmes the proportion of non-responders decrease. This would suggest that longer duration higher intensity exercise programmes are more beneficial.

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The problem is that for a large number of patients any prehabilitation or exercise programme needs to fit into their treatment pathway. This is particularly relevant for cancer patients where patients should receive treatment within 18 weeks of referral (NHS England). Studies have demonstrated that measureable improvements in fitness can be achieved within this time frame by adopting high intensity interval training (HIIT) programmes as opposed to moderate continuous training (MCT). HIIT is typically performed at >90% of maximum heart rate therefore is done in short intervals of 30 to 60 seconds incorporating recovery periods between bursts of exercise. There is accumulating evidence that HIIT is a more effective way to improve cardiorespiratory fitness over short periods of time than prolonged sessions of MCT. A meta-analysis published in 2014 found that HIIT improved cardiorespiratory fitness almost twice as much as MCT (19.4% vs 10.3%).[xli] This improvement in cardiorespiratory fitness has also been shown in high-risk cardiac failure patients where patients either undertook a 12 week HIIT or MCT training programme. Those following the HIIT improved their aerobic capacity by 42% compared to 14% in the MCT group.[xlii]

Safety of exercise training programmes

A question that is often raised regarding preoperative exercise training is one relating to safety particularly in high-risk patient populations undertaking aerobic exercise. The most robust data relating to safety of exercise in high-risk groups comes from cardiac rehabilitation programmes. A French observational study of more than 25,000 patients undergoing cardiac rehabilitation reported one cardiac event for every 50,000 hours of exercise training.[xliii] Additionally a 2014 Cochrane review found no evidence that exercise programmes cause harm in terms of an increase in the risk of all cause death in either the short or long term in patients with stable chronic heart failure (NYHA level 1-3).[xliv] A systematic review looking at 10 studies relating to preoperative aerobic exercise training in elective intra-cavity surgery found low rates of adverse events.[xlv] The only known serious adverse event was a cardiac arrest with successful resuscitation reported in a pilot study looking at aerobic exercise in patients with small abdominal aortic aneurysms.[xlvi] Despite the low but real risk of serious adverse events it would seem sensible to continue with supervised exercise training until further evidence is published and the risks are better understood.

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Exercise Programmes and Trials

There are a variety of prehabilitation and exercise programme trial running throughout the UK. It is impossible to cover every trial and programme that is running but a small selection are covered briefly below.

5 PREPARE-ABC[xlvii]

PREPARE-ABC (SupPoRtive Exercise Programmes for Accelerating Recovery after major Abdominal Cancer surgery) is a multicentre, randomised controlled trial comparing supervised hospital based exercise, home based exercise with standard care alone for pre and post hospital discharge in patients having colorectal cancer surgery.

6 The EMPOWER trial[xlviii]

The EMPOWER trial is a multicentre randomised controlled trial comparing in-hospital exercise training with usual care in patients with local advanced rectal cancer who are undergoing NACRT. The aims are to assess the effects on physical fitness, health-related quality of life, physical activity levels, as well as post-operative morbidity and cancer staging.

7 PREPARE for surgery[xlix]

The PREPARE for surgery programme run by Imperial Healthcare NHS trust is a program for patients having oesophago-gastric surgery aimed at providing coaching and tailored support in physical fitness, respiratory exercises, nutrition, psychological wellbeing, smoking and alcohol, medication and enhanced recovery after surgery. The physical fitness element consists of a personalised exercise programme based on the results of fitness tests carried out by a personal trainer in the gym at St Mary's Hospital. This exercise programme can either be completed at the gym or as a home-based fitness programme.

8 Enhanced Recovery After Surgery Pathway ERAS+[l]

ERAS+ was implemented as a pilot project in Manchester Royal Infirmary in 2014 with the aim to reduce postoperative pulmonary complications and length of stay after major elective surgical procedures. It aims to prepare and equip patients and their families in their preparation and recovery from major surgery, including advice and structure for training on exercise, nutrition, lifestyle and oral health with a focus on the

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six weeks prior and six weeks after surgery. It delivers the programme through information videos and a multi-disciplinary led 'Surgery School'.

In 2016 the UK based group POETTS (perioperative exercise testing and training society)[li] was established with the aim of promoting standards, education and research in perioperative cardiopulmonary exercise testing and training. As well as an annual meeting it has a website with a wealth of information about exercise testing, training, evidence and guidelines.

Successful implementation and adherence of patients to preoperative exercise programmes is a challenge. Local infrastructure and resources vary and an integrated approach involving patients, healthcare professionals and commissioners is required for success. Patient support by healthcare professionals is also key to achieving engagement in exercise programmes. Close collaboration between primary and secondary care is essential to maximise opportunities for patients in the short available preoperative time period, the principal of 'making every contact count'. Shared-leaning and integrated working across primary and secondary care as set out in the NHS England 5-Year Forward View will hopefully go some way to overcoming this hurdle.

The period around the time of surgery is characterised by an increased focus on personal health along with multiple interactions with healthcare professionals. This provides a unique opportunity for improving health in general, and physical fitness particularly. This time can be seen as a 'teachable moment' and an opportunity to embed meaningful and sustained lifestyle changes in behaviour at a time when patients are particularly focused on improving their health.

Those who think they have not time for bodily exercise will sooner or later have to find time for illness.

Edward Stanley
15th Earl of Derby (1826-1893)

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MCQ Answers

1 TTFTT
2 TFTTF
3 FTFFT
4 TFFTT
5 FTTTF

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