Institution: University of Bristol

Unit of Assessment: 3

Title of case study: Widespread change in practice from nil by mouth to feeding within 24 hours after surgery aids recovery and reduces complications

1. Summary of the impact (indicative maximum 100 words)

Researchers at the University of Bristol challenged 100 years of dogma, using meta-analysis; finding that feeding people within 24 hours of gastrointestinal surgery is safe, with fewer infections and a shorter hospital stay. This evidence is enshrined in Enhanced Recovery After Surgery programmes (2009, 2012) being rolled out across the UK benefiting patients and the health service. In 2009 The Dutch Institute of Healthcare Improvements considered these data and Cochrane update to 'show unequivocally that early feeding after colonic surgery is feasible and safe'. Their project successfully introduced early feeding to over one quarter of all Dutch hospitals.

2. Underpinning research (indicative maximum 500 words)

For 100 years surgical doctrine recommended keeping people "nil by mouth" after gastrointestinal surgery until dysmotility had resolved. In 2001 Steven Thomas (Senior Lecturer Bristol University 1998 onwards), had the idea to challenge this view and led a systematic review and meta-analysis of feeding within 24 hours of surgery supported by Mathias Egger (Senior Lecturer Bristol University) (a key figure in the development of meta-analysis methodology) and Paul Sylvester (Colorectal Surgeon) at Bristol University Hospital and Stephen Lewis (Gastroenterologist Peninsula Medical School) [1]. In addition the authors explored mechanisms for their meta-analytic findings particularly changes in the body's metabolism in response to feeding and the role of sham feeding, thus providing an explanation for the empirical evidence further strengthening the evidence base and convincing people to change practice.

Trials of early feeding were being undertaken but they were individually too small to be informative. At the time, Bristol University through Dr Egger and Professor Davey Smith (University of Bristol) were world leaders in understanding the importance of meta-analysis and harnessing this was a key contribution to moving this field of surgery forwards.

Randomised controlled trials comparing any type of enteral feeding started within 24 hours after surgery with nil by mouth in elective gastrointestinal surgery were analysed. Three electronic databases (PubMed, Embase, and the Cochrane controlled trials register) were searched, reference lists checked, and letters requesting details of unpublished trials and data sent to pharmaceutical companies and authors of previous trials. The main outcome measures were: Anastomotic dehiscence (leakage of bowel contents into the abdomen), infection of any type, wound infection, pneumonia, intra-abdominal abscess, length of hospital stay, and mortality.

Eleven studies with 837 patients met the inclusion criteria. In six studies patients in the intervention group were fed directly into the small bowel and in five studies patients were fed orally. Early feeding reduced the risk of any type of infection (relative risk 0.72, 95% CI 0.54 to 0.98) and the mean length of stay in hospital (number of days reduced by 0.84, 95% CI 0.36 to 1.33). Reductions were also seen for risk of anastomotic dehiscence (0.53, 95% CI 0.26 to 1.08), wound infection, pneumonia, intra-abdominal abscess, and mortality, but these had broader confidence intervals. The risk of vomiting was increased among those fed early (1.27, 95% CI 1.01 to 1.61). No benefit was shown for keeping people "nil by mouth" after gastrointestinal surgery. Septic complications and length of hospital stay were reduced in those who received early enteral feeding.

The original meta-analysis was updated as a Cochrane review identifying more studies and outcomes (Andersen HK, Cochrane lower GI group, Lewis SJ, Peninsula Medical School UK, Thomas S, Bristol University) in 2006 [2], 2011 and 2013. In addition to a reduction in septic complications and length of hospital stay, mortality was reduced in people fed within 24 hours.

Researchers at the University of Bristol (Steven Thomas Professor at Bristol University) and Peninsula Medical School have investigated possible mechanisms for these findings. Surgery induces a catabolic response, resulting in a loss of insulin sensitivity. Postoperative insulin resistance has been related to postoperative complications and length of hospital stay. Researchers at the University of Bristol and Peninsula Medical School completed a trial of peri-operative feeding among 120 people having a resection of colorectal cancer and anastomosis. [3] Oral nutritional supplements, even in small volumes of feed, given both pre and post operation improved post-operative insulin resistance, handgrip strength and pulmonary function and resulted in fewer complications. Reduced postoperative stay could be due to improved speed of recovery of the bowel function. Researchers at the University of Bristol and Peninsula Medical School undertook A systematic review and meta-analysis of sham feeding using chewing gum [4] In the sham feeding group there was a reduction in time to flatus by 14 h (95% CI: -20 to -8h,), time to bowel movement by 23 h (95% CI: -32 to -15 h,) and a reduction in length of hospital stay by 1.1 days (95% CI: -1.9 to -0.2 days). This evidence supports the concept that early oral feeding is important in stimulating gut function. These mechanistic studies have contributed to understanding of evidence for early postoperative feeding and thus strengthened the evidence base.

3. References to the research (indicative maximum of six references)

[1] Lewis SJ, Egger M, Sylvester P, Thomas S. Early enteral feeding versus "nil by mouth" after gastrointestinal surgery: systematic review and meta-analysis of controlled trials. BMJ. 2001 October 6; 323(7316): 773.. DOI: 10.1136/bmj.323.7316.773

[2] Andersen HK, Lewis SJ, Thomas S. Early enteral nutrition within 24h of colorectal surgery versus later commencement of feeding for postoperative complications. Cochrane Database Syst Rev. 2006 Oct 18;(4):CD004080. DOI: 10.1002/14651858.CD004080.pub2

[3] Lidder P, Thomas S, Fleming S, Hosie K, Shaw S, Lewis S. A randomised placebo controlled trial of preoperative carbohydrate drinks and early postoperative nutritional supplement drinks in colorectal surgery.Colorectal Dis. 2013 Feb 13. doi: 10.1111/codi.12130

[4] Noble EJ, Harris R, Hosie KB, Thomas S, Lewis SJ. Gum Chewing Reduces Postoperative Ileus? A Systematic Review and meta-analysis. Int J Surg. 2009;2:100-5. DOI: 10.1016/j.ijsu.2009.01.006

4. Details of the impact (indicative maximum 750 words)

Our meta-analysis of early feeding in 2001 was the first level 1a evidence to show there is no benefit in keeping people "nil by mouth" after gastrointestinal surgery. The British Medical Journal commissioned a lead editorial in the same issue, by two internationally renowned nutrition experts, who commented: '*What impact could the findings of this systematic review have on daily surgical practice? The review shows that there is no clinical benefit to starving patients in the early postoperative period after gastrointestinal resection. Further, the finding that postoperative infections can be reduced and hospital stay shortened by starting early postoperative enteral nutrition should challenge clinicians to consider this treatment*.' [a] Guidelines followed and the original meta-analysis and Cochrane review are widely cited in Nutrition Policy documents [b, c].

Guidelines in Europe and the UK - Enhanced Recovery of patients After Surgery (''ERAS'') is now the focus of perioperative management and key aspects of perioperative care include re-establishing oral feeding as soon as possible after surgery. In the UK in 2009, The Association of Surgeons of Great Britain and Ireland, issued guidelines for implementation of enhanced recovery protocols [d]. *'Patients should be allowed oral fluids as tolerated on the day of the surgery and built up to an oral diet over the next 24 hours. Patients who are not meeting their nutritional requirements by 72 hours after surgery should be assessed by a dietician'.* This recommendation is based on our meta-analysis of early enteral feeding [1,2]. In 2009 [e] and 2012 [f] the ERAS group cited the meta-analyses [1, 2] as evidence for post-operative nutritional care in an 'evidence-based protocols for optimal perioperative care'. Early post-operative nutrition is now embedded, as a key element of ERAS programmes in the UK and the meta-analysis [1, 2] was a key motivator for the adoption of early feeding. Researchers at the University of Bristol and Peninsula Medical

School had highlighted the benefits of post-operative nutrition prior to the implementation of ERAS programmes. The multimodal nature of ERAS now makes it impractical to assess the role of nutrition alone, so our evidence describes the key role of early feeding. A recent study of an ERAS programme showed 57% of patients now take feed within 24 hours of their surgery (Gustafsson U. et al *Arch Surg*. 2011; **146**: 571-7 DOI: 10.1001/archsurg.2010.309)

Uptake projects internationally - The reach of the work [1, 2] to other countries can be demonstrated, where it has translated into everyday practice and justification for changing national perioperative care policy. People in the Netherlands remained exposed to unnecessarily prolonged starvation after abdominal surgery and The Dutch Institute of Healthcare Improvement intervened in 2009 [g]. They made an explicit link to our work as a justification to change practice: *'The most recent scientific evidence regarding early nutrition is summarized in a Cochrane review, [2] which shows unequivocally that early feeding is feasible and safe. This is translated into useful recommendations that link up with everyday practice in the Guidelines on Enteral Nutrition of the European Society of Parenteral and Enteral Nutrition [c] and the consensus review of clinical care for patients undergoing colonic resection of the enhanced recovery after surgery group [b]'* They successfully introduced early feeding to over one quarter of all Dutch hospitals in a nationwide collaborative project – patients were eating 3 days earlier and 65% were eating a normal diet after only 2 days [g]. In 2009 they concluded: *'The present nationwide collaborative effort was successful in implementing a change towards an early start of oral nutrition after abdominal surgery'.* So, as a result of the research [1, 2] they have achieved a change in practice.

The beneficiaries of the impact are patients and the health service - '*Traditional nutritional management of patients undergoing major abdominal surgery has involved a period of "nil by mouth" with nasogastric decompression followed by a clear liquid diet that gradually progresses to regular food on the 4th to 5th day post- operatively.'* Although the evidence *'for the safety, feasibility and benefit of early postoperative nutrition, surgical patients in the Netherlands'* (had remained) *'exposed to unnecessary post-operative starvation [g, h]*.'

How have patients benefitted? - Early postoperative nutrition helps decrease the negative impact of the metabolic response to surgery. The re-establishment of oral feeding as early as possible has become one of the key aspects of modern multimodal recovery programmes [b, g]. Trials of ERAS showed (that included early feeding as a key component) show that ERAS programmes reduce length of stay and are safe [i]. Work on peri-operative feeding [3] has shown that even when small amounts of feed are consumed surgical patients have metabolic benefits, which is reflected in improved physiological measures and indicate fewer post-operative complications.

How have Health Services benefitted? - Overall the reduction in hospital stay among people fed within 24 hours corresponds to about one day, which is economically important. Reduction in complication rates may explain this observation, as might a faster return of gastrointestinal function. The reduced number of infections is also important in regard to costs of interventions. Perioperative feeding supplements reduce weight loss and complications and are cost effective [j]. In the wider context, studies of the economic impact of ERAS (including early post-operative feeding) have shown a reduction in costs associated with ERAS [k] and a Norwegian study has found that 'nursing care time per day was reduced after implementing the ERAS protocol' [l]. The economic benefits of ERAS are thus substantial.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[a] Postoperative starvation after gastrointestinal surgery. Early feeding is beneficial. Silk DBA, Menzies Gow, N. BMJ. 2001 October 6; 323(7316): 761–762. DOI: 10.1136/bmj.323.7316.761
Editorial showing how this research challenged existing surgical feeding practices

[b] Fearon KC, Ljungqvist O, Von Meyenfeldt M, Revhaug A, Dejong CH, Lassen K, et al. Enhanced recovery after surgery: a consensus review of clinical care for patients undergoing colonic resection. Clin Nutr 2005;24:466–77. DOI: 10.1016/j.clnu.2005.02.002
Policy document citing this research as primary evidence to recommend that patients should be encouraged to commence oral food intake four hours after surgery.

[c] Weimann A, Braga M, Harsanyi L, Laviano A, Ljungqvist O, Soeters P, et al. ESPEN Guidelines on enteral nutrition: surgery including organ transplantation. Clin Nutr 2006;25:224–44. DOI: 10.1016/j.clnu.2006.01.015
Policy document citing this research as primary evidence to recommend that the amount of initial oral intake should be adapted to the state of gastrointestinal function and to individual tolerance.

[d] Association of Surgeons of Great Britain and Ireland. ISSUES IN PROFESSIONAL PRACTICE; GUIDELINES FOR IMPLEMENTATION OF ENHANCED RECOVERY PROTOCOLS. Khan S, Gatt G, Horgan A, Anderson I, MacFie J, December 2009 published by Association of Surgeons of Great Britain and Ireland 35-43 Lincoln's Inn Fields, London, WC2A 3PE.
Guidelines document citing this research as primary evidence to recommend patients should be allowed oral fluids on the day of surgery and built up to an oral diet over the next 24 hours.

[e] Lassen K, Soop M, Nygren J, Cox PB, Hendry PO, Spies C, von Meyenfeldt MF, Fearon KC, Revhaug A, Norderval S, Ljungqvist O, Lobo DN, Dejong CH; Enhanced Recovery After Surgery (ERAS) Group. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. Arch Surg. 2009 Oct;144(10):961-9. doi: 10.1001/archsurg.2009.170. WOS:000270926400020
Consensus statement citing our research that concluded early feeding after surgery was beneficial.

[f] Nygren J, Thacker J, Carli F, Fearon KC, Norderval S, Lobo DN, Ljungqvist O, Soop M, Ramirez J; Enhanced Recovery After Surgery Society. Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations Clin Nutr. 2012 Dec;31(6):801-16. DOI: 10.1016/j.clnu.2012.08.012
Guidelines for ERAS citing our studies that recommended an oral ad-libitum diet four hours after rectal surgery.

[g] To eat or not to eat: facilitating early oral intake after elective colonic surgery in the Netherlands. Maessen JM, Hoff C, Jottard K, Kessels AG, Bremers AJ, Havenga K, Oostenbroek RJ, von Meyenfeldt MF, Dejong CH; Dutch Breakthrough Project Perioperative Care; ERAS Group. Clinical Nutrition 28 (2009) 29–33). DOI: 10.1016/j.clnu.2008.10.014
A report showing how our research led to a change in clinical practice in Holland.

[h] Lassen K, Hannemann P, Ljungqvist O, Fearon K, Dejong CH, von Meyenfeldt MF, et al. Patterns in current perioperative practice: survey of colorectal surgeons in five northern European countries. BMJ 2005;330:1420–1. DOI: 10.1136/bmj.38478.568067.AE
A survey showing variations in post-surgical feeding practices and citing our research to show it was at odds with evidence based practice.

[i] The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized controlled trials.
Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. Clin Nutr. 2010 Aug;29(4):434-40. DOI: 10.1016/j.clnu.2010.01.004
A systematic review of trials of ERAS (feeding was as a key component) showing a benefit.

[j] Randomized clinical trial of the effects of preoperative and postoperative oral nutrition supplements on clinical course and care. Smedley F, Bowling T, James M, Stokes E, Goodger C, O'Connor O, Oldale C, Jones P, Silk D. Br J Surg 2004;91: 983-990. DOI:10.1002/bjs.4578
Report of a trial showing that perioperative oral nutritional supplementation for lower gastrointestinal tract surgery reduced weight loss and incidence of minor complications, and was cost-effective.

[k] A programme of Enhanced Recovery After Surgery (ERAS) is a cost-effective intervention in elective colonic surgery. Sammour T, Zargar-Shoshtari K, Bhat A, Kahokehr A, Hill AG. N Z Med J. 2010 Jul 30;123(1319):61-70. PubMed ID: 20717178
Cost effectiveness analysis showing that ERAS is cost-effective in the medium term, with costs offset by those recovered by reduced resource utilisation in the postoperative period.

[l] Improving quality by introducing enhanced recovery after surgery in a gynaecological department: consequences for ward nursing practice. Sjetne IS, Krogstad U, Ødegård S, Engh ME. Qual Saf Health Care. 2009 Jun;18(3):236-40. DOI: 10.1136/qshc.2007.023382
Survey showing that implementation of ERAS was achieved without compromising the workload or work environment for ward nursing staff. Indeed there was a 39% reduction in total time spent on nursing activities per stay (−162 min, 95% CI −239.3 to −84.4, p<0.001).