

Institution: University of Nottingham		
Unit of Assessment: UoA1, Clinical Medicine		
Title of case study: Enhanced Recovery After Surgery (ERAS): Improving Surgical Outcomes Worldwide		
Period when the underpinning research was undertaken: 2002 - 2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Professor Dileep Lobo	Professor of Gastrointestinal Surgery	1999-March 2002 October 2002 to present
Period when the claimed impact occurred: 2013 to 2020		
Is this case study continued from a case study submitted in 2014? No		
<p>1. Summary of the impact Professor Dileep Lobo at the University of Nottingham has been fundamental to the worldwide success of the ERAS® (Enhanced Recovery After Surgery) Society. ERAS® produces protocols on perioperative care to achieve accelerated and better recovery for patients undergoing major surgery. These protocols have been implemented by healthcare providers in more than 20 countries globally, benefitting more than 70,000 patients, and have led to improved clinical and patient outcomes, healthcare savings and commercial impact. Postoperative length of stay has been reduced by an average of 2.53 days, alongside reductions in the risk of morbidity (23%), complications (29%), pulmonary complications (55%), cardiovascular complications (53%) and infection (27%). Average healthcare savings of USD639 per patient have been achieved, with one healthcare provider in Canada experiencing a net saving of CAD3,600,000 over 2 years. Commercial impact has been achieved in Encare through revenue generation of EUR7,258,000 (02-2020) since 2014 and the creation of new jobs.</p>		
<p>2. Underpinning research The problem: For patients undergoing major surgery, perioperative care usually involves multiple healthcare professionals, each delivering different components of specialised care. Each healthcare professional is focused on their area of expertise, and due to the complexity of perioperative care, it is difficult for practitioners to know how their treatment decision will affect the overall patient’s journey. Suboptimal earlier treatment choices affect the possibilities for later treatment options, which can lead to poor patient outcomes and prolonged hospital stay.</p> <p>The solution: The ERAS® (Enhanced Recovery After Surgery) Society (www.erassociety.org) was founded in 2010 to develop perioperative care (patient care from hospital admission to discharge: preoperative, intraoperative and postoperative) and achieve early recovery for patients undergoing major surgery. The ERAS® Society publishes protocols (evidence-based best practice guidelines), currently covering 19 different surgical specialities (https://erassociety.org/guidelines/list-of-guidelines/) with more planned. These cover all aspects of the patient's surgical journey, providing guidance to all healthcare professionals involved in perioperative care. The international ERAS® Society developed from the international ERAS Study Group which assembled in 2001.</p> <p>(Figure 1: Key ERAS® elements, reproduced with permission from Crit Care Clin 2010;26:527-47)</p>		
<p>The diagram illustrates the key elements of ERAS® across three phases: Preoperative, Intraoperative, and Postoperative. A central box labeled 'ERAS' is connected to these phases. Interventions are listed around the phases:</p> <ul style="list-style-type: none"> Preoperative: Preadmission counseling, Fluid and carbohydrate loading, No prolonged fasting, No/selective bowel preparation, No premedication, Short-acting anesthetic agents. Intraoperative: Mid-thoracic epidural anesthesia/analgesia, No drains, Avoidance of salt and water overload, Maintenance of normothermia (body warmer/warm intravenous fluids). Postoperative: Mid-thoracic epidural anesthesia/analgesia, No nasogastric tubes, Prevention of nausea and vomiting, Avoidance of salt and water overload, Early removal of catheter, Early oral nutrition, Non-opioid oral analgesia/NSAIDs, Early mobilization, Stimulation of gut motility, Audit of compliance and outcomes. 		
The research and contributions to the ERAS® Society		

Professor Dileep Lobo is extensively involved with the ERAS® Society and has been involved since 2001, as the first additional person to be appointed to the original ERAS Study Group. In 2010 he was appointed as Scientific Chair, a member of the Executive Committee. His research, particularly in maintaining fluid and electrolyte (salt) balance, and co-authored surgical guidelines have directly contributed to the scientific content in the ERAS® guidelines covering 18 of the 19 different surgical specialities. His research has also contributed to the growth in adoption of ERAS® guidelines worldwide.

Research into maintaining fluid and salt balance:

Professor Lobo published a landmark paper in *Lancet* **2002 (1)** reporting on a randomised controlled trial (RCT) in which 20 patients were randomly assigned to receive either postoperative intravenous fluids (water and sodium) in accordance with standard hospital practice or with restricted intake. The paper established that patients kept in a state of near zero fluid and salt balance experienced better outcomes than those overloaded with salt and water, including reduced hospital length of stay of 3 days, reduced likelihood of complications and faster return of gastrointestinal function. Maintaining fluid and salt balance was a paradigm shift from the existing perioperative approach of 'starve, stress, drown', which involved starving patients before operations, stressing patients during operations and overloading patients with fluids (drowning) after operations.

In **2010**, Professor Lobo conducted a meta-analysis **(2)**, reporting on 9 RCTs involving 801 patients, which confirmed that patients managed in a state of fluid balance fared better than those managed in a state of fluid imbalance, including reduced hospital length of stay of 1.77 days and 51% reduction in the risk of developing postoperative complications. Subsequent research in **2012 (3)**, part funded by **G2**, reported on a RCT with 12 healthy subjects receiving either 0.9% saline or Plasma-Lyte 148. This confirmed that excess saline caused increased interstitial fluid overload and hyperchloraemic acidosis compared with balanced crystalloids and demonstrated for the first time in humans that this resulted in impaired renal haemodynamics. This further reinforced the importance of maintenance of salt and fluid balance and that 0.9% saline should not be the default solution that's used during surgery as it causes hyperchloraemic metabolic acidosis and results in other adverse clinical outcomes. Professor Lobo's research **(1, 2, 3)** made a substantial contribution to the principle of avoidance of salt and water overload, which features in both the Intraoperative and Postoperative elements of ERAS® care pathways (figure 1).

Research contributing to the success of the ERAS® Society:

ERAS® was originally viewed as a way to reduce patient hospital length of stay. In **2010** Professor Lobo published a meta-analysis **(4)** reporting on 6 RCTs and 452 patients, demonstrating that following ERAS® guidelines resulted in improved outcomes for patients, including reduced hospital length of stay of 2.55 days and 47% reduction in the risk of developing postoperative complications. This was found to be experienced in Switzerland, Czech Republic, USA and multiple centres in the UK. The Chairman of the ERAS® Society views **(4)** as one of few key papers establishing ERAS® in patient care.

In his role as Scientific Chair, Professor Lobo carries out research to ensure the ERAS® guidelines remain up to date as new scientific evidence emerges, ensuring the continued success of ERAS® in improving patient outcomes. His **2016 (5)** meta-analysis on Goal-directed Fluid Therapy (GDFT), reporting on 23 studies and 2,099 patients, found that GDFT may not benefit all patients undergoing major abdominal surgery, particularly patients managed in an ERAS® setting. Previously, the ERAS® recommendation was to use GDFT for every patient where possible, which was resource intensive for healthcare providers as they needed to buy equipment, now GDFT is recommended for high risk patients or patients having high risk procedures. This led to the publication of updated guidelines in colorectal surgery in **2018**.

Research contributing to the success of Encare

Encare, an independent commercial entity operating from Sweden, was set up in 2009 based on the needs from the ERAS® Society to be able to register, monitor, audit and follow up data from the ERAS published guidelines. Professor Lobo's **2018 (6)** paper on ERAS® training, an international Delphi study spanning 11 countries, has influenced international

ERAS® training through Encare. The key emphasis on requirements for success were around team working and communication.

3. References to the research (citations to 31st December 2020)

- (1) Lobo DN, Bostock KA, Neal KR, Perkins AC, Rowlands BJ, Allison SP. 2002. Effect of salt and water balance on recovery of gastrointestinal function after elective colonic resection: a randomised controlled trial. *The Lancet* 359(9320), 1812-1818 (**683 citations**), DOI: 10.1016/S0140-6736(02)08711-1
- (2) Varadhan K, Lobo D. 2010. A meta-analysis of randomised controlled trials of intravenous fluid therapy in major elective open abdominal surgery: Getting the balance right. *Proceedings of the Nutrition Society* 69(4), 488-498 (**165 citations**), DOI: 10.1017/S0029665110001734, Erratum: 2010. *Proceedings of the Nutrition Society* 69(4), 660, DOI: 10.1017/S0029665110002028
- (3) Chowdhury AH, Cox EF, Francis ST, Lobo DN. 2012. A Randomized, Controlled, Double-Blind Crossover Study on the Effects of 2-L Infusions of 0.9% Saline and Plasma-Lyte® 148 on Renal Blood Flow Velocity and Renal Cortical Tissue Perfusion in Healthy Volunteers. *Annals of Surgery* 256(1), 18-24 (**422 citations**), DOI: 10.1097/SLA.0b013e318256be72
- (4) Varadhan KK, Neal KR, Dejong CHC, Fearon KCH, Ljungqvist O, Lobo DN. 2010. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal surgery: A meta-analysis of randomized controlled trials. *Clinical Nutrition* 29(4), 434-440 (**661 citations**), DOI: 10.1016/j.clnu.2010.01.004
- (5) Rollins KE, Lobo, DN. 2016. Intraoperative Goal-directed Fluid Therapy in Elective Major Abdominal Surgery. *Annals of Surgery* 263(3), 465-476, (102 citations), DOI: 10.1097/SLA.0000000000001366
- (6) Francis NK, Walker T, Carter F, Hübner M, Balfour A, Jakobsen DH, Burch J, Wasylak T, Demartines N, Lobo DN, Addor V, Ljungqvist O. 2018. Consensus on *Training and Implementation of Enhanced Recovery After Surgery: A Delphi Study*. *World Journal of Surgery* 42, 1919–1928 (**8 citations**), DOI: 10.1007/s00268-017-4436-2

Grants (representative)

G1 Awarded to Professor Dileep Lobo. Enhanced Recovery After Surgery Group Grant. Sponsor: Enhanced Recovery After Surgery Group. 2011 – 2012, EUR40,000
 G2 Awarded to Professor Dileep Lobo. Unrestricted grant. Sponsor: Baxter Health Care. 2009 – 2010. GBP51,398

4. Details of the impact

The ERAS® (Enhanced Recovery After Surgery) Society was established in 2010 to develop perioperative care and achieve accelerated and better recovery for patients undergoing major surgery. The global success of the ERAS® Society is only achieved through collaborative working and Professor Lobo's involvement with the ERAS® Society has made a distinct contribution to this success. These successes include improved patient outcomes, healthcare savings, revenue generation, new jobs, and influence on professional healthcare services. These represent substantial new impacts since Professor Lobo's previous impact case study which focused on changing fluid therapy guidelines to improve patient outcomes (<https://impact.ref.ac.uk/casestudies/CaseStudy.aspx?id=41004>).

Pathway to impact

Professor Lobo's publications (28 publications) and published clinical guidelines (6) have been cited in 18 of the 19 different ERAS® surgical specialities, with a total of 94 citations (**A(a, b)**). Maintaining fluid balance is a large focus of Professor Lobo's research, which has been directly cited in the fluid management elements of 12 of the 19 surgical specialities (**A(a)**). His research (**1-5**) has been indirectly cited in the fluid management elements of 4 of the remaining 7 surgical specialities (**A(a)**). As the Chairman of the ERAS® Society, based in Sweden, explains '(1,2)...have had direct impact on the guidelines and also shown to have impact on patient outcome' (**B, p. 2**). His research has been cited in protocol elements such as preoperative fasting and carbohydrate loading, postoperative nutrition and prevention of postoperative ileus (**A(a)**). As the Chairman continues '[4]... showed that ERAS® protocols reduced complications was ground breaking... In my view this is one of few key papers establishing ERAS® in patient care' (**B, p. 2**). Professor Lobo has co-authored many of the ERAS® protocols (covering 6 of the 19 surgical specialities (**A(a)**)), contributed to books on

ERAS®, been key to the annual congress, the key event for ERAS® development and carries out research to ensure ERAS® protocols remain up to date (B, p. 2), such as (5). The Chairman concludes that Professor Lobo's '*many contributions to the ERAS® Society have been particularly valuable to the success of the ERAS® Society*' (B, p. 2).

Adoption of the ERAS® Society guidelines

ERAS® protocols are formally implemented by healthcare providers through Encare, an independent commercial company. Encare provides an information system for patient management, the ERAS Interactive Audit System (EIAS) and training to healthcare providers on the ERAS® Protocols through the ERAS Implementation Program (EIP). The CEO of Encare confirmed in April 2020 '*there are more than 120 hospitals in over 20 countries that have implemented ERAS® through the ERAS Implementation Program and the ERAS Interactive Audit System...about 70,000 patient registrations have been made in EIAS, the last years +10,000/year*' (C, p. 1). These hospitals are located in North and South America, Europe, Africa, Asia and Australasia (<https://encare.net/>). ERAS® protocols are also informally adopted by healthcare providers, some of which produce publications on their experiences following ERAS® protocols. Up to 31st December 2020 the ERAS® protocols have been cited 4,044 times, demonstrating widespread use in healthcare (A(a)).

Improved patient and clinical outcomes

Following ERAS® protocols has repeatedly been shown to **improve patient and clinical outcomes**. Increased compliance with each element of the protocols results in improved patient outcomes (B, p. 1, C, p. 2). In 4 independent high quality meta-analyses (D(a) 1,830 patients, 17 papers, 2020, D(b) 1,133 patients, 8 papers, 2020, D(c) 3,739 patients, 27 papers, 2020, D(d) 5,241 patients, 42 papers, 2017) the following improvements in clinical and patient outcomes compared to traditional care have been found:

- decrease of 2.53 days of postoperative length of stay (D(a), p. 8)
- decrease of 32% of risk of morbidity (D(b), p. 105)
- decrease of 55% of risk of pulmonary complications (D(b), p. 107)
- decrease of 1.1 days of return of bowel function (defecation) (D(a), p. 9)
- decrease of 29% of risk of complications (D(c), p. 922)
- decrease of 53% of risk of cardiac complications (D(d), p. 907)
- decrease of 40% of risk of anastomotic leak (D(b), p. 103)
- decrease of 27% of risk of infection (D(d), p. 907)

Despite healthcare provider concerns that a shorter length of hospital stay could result in worsened patient outcomes, there has been no statistically significant difference between ERAS® protocols and traditional care in the following areas:

- readmission (D(a), p. 10, D(c), p. 924, (D(b), p. 106))
- mortality (D(c), p. 924) for both in-hospital or 30-day mortality (D(b), p. 107)

Healthcare savings

Following ERAS® protocols has led to **substantial healthcare savings**. In 2013 (month not detailed), Alberta in Canada implemented ERAS® in colorectal patients at 6 hospital sites. Between 2013 and 2015, ERAS® colorectal implementation led to '*conservative realized net savings of [CAD]\$3.6 million; a gain four times greater than the implementation investment*' (E(a)). A 1 year study from March 2016 of 139 thoracic patients in Virginia, USA, found an average cost saving of USD15,861 and USD5,299 for 2 types of thoracic surgery (E(b), p. 1,602). An independent high quality meta-analysis in 2017 also reported a saving of USD639 per patient (D(d), p. 907).

Encare: economic impact

Since 2014, Encare has achieved revenue generation of EUR7,258,000 and created 15 new jobs as a result of formal implementation of the ERAS® protocols by healthcare providers. Encare was established in 2009 '*based on the needs from the ERAS® Society to be able to register, monitor, audit and follow up data from the, by the ERAS® Society, published guidelines in perioperative care*' (C, p. 1). Encare generate revenue through providing the EIAS and EIP to healthcare providers. Between 1 January 2014 and 31 December 2019, Encare generated revenue of EUR7,258,000 (02-2020) (C, p. 2). In 2016 Encare employed their first 2 staff, having previously only engaged part-time consultants. The current team includes '*about 15 people*' (C, p. 2). Professor Lobo's research into

ERAS® training and implementation (6) has been used by Encare with training new hospital teams *'in order to stress the importance of training of teams in order to be succesful in the ERAS® work'* (C, p. 2).

Developing ERAS® and improving ERAS® healthcare delivery

The ERAS® Society international annual congress is an opportunity for healthcare professionals to receive training on ERAS® and the latest scientific information. The Chairman of the ERAS® Society explains *'This is the key event for ERAS® development where the world leaders gather and where new developments are presented...and have impact on guidelines and ultimately clinical outcomes'* (B, p. 2). Between 2014 and 2019, across 6 annual congresses, there have been attendees from 65 countries, spanning all continents, in excess of 2,562 people (healthcare professionals) in total (exact figures for 2016 unavailable) (F(a), p. 3-4). Positive feedback from congresses has included *'Fantastic inspirational speakers,...Dr. Lobo...'* (F(a), p. 231) and *'learning about new evidence to improve the service and outcomes for my patients'* (F(a), p. 230). Professor Lobo has written 3 chapters and been section editor for an ERAS® book (F(b), p. xv, 23-28, 167-173, 249-257), aimed at healthcare professionals, to support understanding and implementing the process change necessary to deliver ERAS®. Between April 2020 and 15th November 2020 there were 39,479 chapter downloads (F(c)).

International influence on clinical practice

Profesor Lobo's research and expertise has continued to influence fluid management and nutrition worldwide. The European Society for Clinical Nutrition and Metabolism (ESPEN, www.espen.org) publish clinical practice guidelines. These guidelines are used 64 countries worldwide, across South America, North America, Australasia, Europe and Africa. Professor Lobo co-authored 2 ESPEN guidelines in 2017: on cancer related malnutrition (G(a)) and clinical nutrition in surgery (G(b)). His research, including (1, 2), continues to be cited in NICE Clinical Guidelines on fluid therapy in adults (G(c)).

5. Sources to corroborate the impact

A(a) List of ERAS® guidelines with list of citations of Professor Lobo's publications, **A(b)** Excel spreadsheet summarising **A(a)** including number of citations (available on request)

B Chairman of the ERAS® Society letter of support

C CEO of Encare letter of support

Improved patient and clinical outcomes, and healthcare savings:

D(a) The application of enhanced recovery after surgery for upper gastrointestinal surgery: Meta-analysis (2020), DOI: 10.1186/s12893-019-0669-3

D(b) Enhanced recovery pathways vs standard care pathways in esophageal cancer surgery: systematic review and meta-analysis (2020), DOI: 10.1007/s10388-020-00718-9

D(c) Enhanced Recovery After Surgery (ERAS) Reduces Hospital Costs and Improve Clinical Outcomes in Liver Surgery: a Systematic Review and Meta-Analysis (2020), DOI: 10.1007/s11605-019-04499-0

D(d) Enhanced Recovery After Surgery Programs Improve Patient Outcomes and Recovery: A Meta-analysis (2017), DOI: 10.1007/s00268-016-3807-4

Healthcare savings

E(a) Alberta Health Services website (weblink, last accessed 7th January 2021)

E(b) Implementing a Thoracic Enhanced Recovery Program: Lessons Learned in the First Year (2018), DOI: 10.1016/j.athoracsur.2018.01.080

Developing ERAS® and improving ERAS® healthcare delivery

F(a) 2014 – 2019 ERAS® Society Annual Congress reports (combined), with attendee numbers and countries: Spain, USA, Portugal (partial data), France, Sweden, UK,

F(b) Textbook: Enhanced Recovery After Surgery (ERAS®): A Complete Guide to Optimizing Outcomes. 2020, Springer, **F(c)** Springer email confirming downloads

International influence on clinical practice:

G(a) ESPEN expert group recommendations for action against cancer-related malnutrition (2017), DOI: 10.1016/j.clnu.2017.06.017

G(b) ESPEN guideline: Clinical nutrition in surgery (2017), DOI: 10.1016/j.clnu.2017.02.013

G(c) NICE guideline CG174: IV fluid therapy in adults (2013) (last updated 2017, weblink, last accessed 8th January 2021)