$50M Wellcome Leap Program
Surgery: Assess, Validate, Expand (SAVE)

Every year 313 million operations are performed around the world – surgery is an indispensable part of healthcare.[i,ii,iii] Sixty percent of all surgery is conducted in high income countries where the infrastructure, financing, and highly skilled human resources are concentrated, but where only 15% of the population live.[i,iv] An additional 143 million operations are needed annually to meet basic health needs, most urgently in low resource settings, but also to achieve equity across communities in all countries.[v] **This lack of access to essential and emergency surgery results in at least 1.5 million deaths each year,[vi] which is equivalent to the number of deaths from HIV, malaria, multi-drug resistant TB, and complications from pregnancy *combined*.**

And this lack of access is set to get worse. Over 1/3 of the world's population lives in regions without a sufficient surgical workforce. Trauma, pregnancy-related complications, and general surgical emergencies constitute up to 80% of preventable deaths due to lack of surgical access. In parts of Asia and Africa, the surgical workforce needs to be expanded 10-100x to meet basic needs.[iv] At the same time, healthcare staffing shortages are increasing worldwide. The World Health Organization has labeled the healthcare workforce shortage in Europe a "ticking time bomb", with 40% of medical doctors (MDs) retiring within the next decade.[vii,viii] In the UK, the Royal College of Physicians noted that 52% of staff posts remained unfilled in the National Health Service.[ix] In the United States the current surgical workforce only meets 75% of demand in rural and suburban areas, with a projected shortage of over 16,000 surgical specialists in the next decade.[x,xi]

Of the 143 million "missing" operations required to save lives and prevent disability, we estimate that up to 30 million involve abdominal and pelvic conditions that could be treated using minimally invasive techniques. To date, laparoscopic surgery has improved the ability to deliver such operations while simultaneously reducing postoperative infections, length of stay, postoperative pain, and even long-term complications such as internal scarring. Moreover, it lends itself to advanced simulation, quantitative assessment, and validation that could dramatically expand the number of surgeons available.

To deliver 30 million abdominal and pelvic operations will require training an additional 100,000 surgeons. At current rates of training, this is unachievable. The number of MDs as a proportion of the population has remained essentially the same for the last 30 years; and in low- and middle-income countries, woefully inadequate.[xii] **We need a fundamental change**.

Program goals.

1. Demonstrate the capability to train non-MD practitioners to deliver routine laparoscopic surgery with equivalent outcomes to MD surgeons using a next-generation simulation, validation, and certification program of 3 years or less.

2. Shorten the timeline needed to train MD surgeons – by a full year – through the use of new tools that accelerate skills acquisition of minimally invasive techniques and enable objective quantification of competence.

3. Reduce postoperative complications and mortality by >50% through advanced sensing, monitoring, and pattern recognition strategies, especially during periods of rapid expansion of services, thus increasing the confidence of surgeons, hospitals, patients, and families.

By combining these three advances, the program aims to *double* the number of surgical providers per year to an additional 100,000 within a decade, thus increasing the provisioning of minimally invasive abdominal operations by 30 million and simultaneously reducing *global* postoperative deaths by 1 million.

Two reasons this is possible now.

First, minimally invasive surgical techniques have dramatically changed the delivery of abdominal surgery.

Since the introduction of the first laparoscopic cholecystectomy (gall bladder removal) in Germany in 1985, laparoscopy has transformed surgery. By 1992 – less than 10 years – this approach surpassed the traditional open approach for cholecystectomy in the US. Similarly, minimally invasive approaches are now more common for appendectomy, colon resection, antireflux surgery, metabolic surgery, and peptic ulcer perforation repair. Laparoscopy improves visualization while reducing postoperative infections, pain, recovery time, and length of stay.

Minimally invasive approaches also enable immersive simulation training environments, objective assessment of skills, and virtual augmentation and overlays to assist visualization and anatomic identification during surgery. In fact, the only objective assessment of surgical skill in the US is the Fundamentals of Laparoscopic Surgery program, with its strict time and performance metrics for competence. Yet the skills being evaluated are only a partial proxy for actual laparoscopic performance during surgery.

Simulation enables accelerated skills acquisition in a controlled, predictable manner, and does so using techniques that directly translate to the successful start-to-finish execution of an operation. The evidence of what is possible can be found in many high-risk/high-reliability organizations that elevated human skill and performance. In pilot training, for example, simulation is an accepted component of skills development, and use of a simulator can reduce time to pilot certification by 40%.[xiii,xiv] Surgery lacks equivalent sophisticated, full spectrum simulators that are able to quantify, validate, and safely accelerate both general and rare event exposure so as to quantitatively validate acquisition of skill. Developing these tools will create new options for scaling the workforce.

Second, new sensing and algorithmic approaches have changed our ability to predict perioperative patient trajectories earlier and with greater accuracy.

The amount of patient data we capture in a hospitalized patient is extensive. Information derives from simple assessments of general patient appearance and mental state coupled with regular measurement of vital signs, to laboratory values, culture results from blood and fluid samples, and imaging studies. From this information clinicians attempt to make determinations for next steps in care and treatment based on experience, knowledge, and pattern recognition. Yet this information has become increasingly complicated, nuanced, and in many ways overwhelming, especially in the intensive care unit where continuous monitoring is obligatory and includes such measures as beat-to-beat heart rate variability, pulse pressure variation due to respiratory dynamics, bedside assessments of intravascular volume and heart function using ultrasound, and brain and pupillary activity. Integrating and interpreting all these signals requires years of training and frequently includes specialists in intensive care medicine. With recent advances in data analytics and machine learning, algorithms and automation – combined with ever increasing amounts of patient data captured— have allowed the early detection of patient deterioration and alerted teams to impending decline in some of the best-in-class hospitals in the world, resulting in up to a 15% decline in mortality.[xv,xvi]

We need advances in such tools and techniques to better evaluate patient biophysiology and we need to integrate data across modalities such as vital signs, laboratory results, tissue perfusion, and bedside assessments. Reliably understanding and accurately predicting patient recovery or deterioration is still lacking, and so we need new sensors, diagnostics, and analytics for anticipating the trajectory of a surgical patient. Hospitals that perform high numbers of surgeries often develop the capacity to recognize patient deterioration quickly. Our goal is to embody these lessons in scalable, predictive caregiver-sensor-algorithmic systems that can be broadly disseminated to reduce risk post-operatively, especially during periods of rapid expansion of services.

The arc of surgery.

Abdominal surgery is complex. For it to be successful, a patient must be properly diagnosed; undergo a timely and carefully performed operation while being continuously monitored for problems; safely emerge from anesthesia; recuperate from surgery; and, should a complication occur, quickly receive appropriate interventions and support. In the words of the late Paul Farmer, the arc of surgery requires "staff, stuff, space, and systems". Human resources, consumable and durable materials, and organizational capacities are vital for managing and successfully treating patients. Failures at each step result in unnecessary delays, excess harm, additional costs, and avoidable mortality, each of which undermines confidence in the health system.

While the lack of durable and consumable goods is easy to blame for lack of service, the biggest factor is the lack of a surgical workforce. The Lancet Commission on Global Surgery recommends at least 20 surgeon/obstetrician/anesthesia providers per 100,000 population to meet basic health needs; many regions are an order of magnitude below this threshold, with little capacity to expand the workforce.[iv] Specialty surgical training typically requires completion of medical school followed by 5-7 years of graduated responsibility under the mentorship of fully qualified and credentialed surgeons. However, training is highly variable as the full breadth of operative experience is unpredictable; even common operations may be infrequently performed during the years of surgical apprenticeship.[xvii,xviii] Skills acquisition is assumed based on volume metrics, with numeric targets substituting for quantifiable, skills-based assessments. Countries with insufficient human resources are particularly challenged in expanding the workforce, since so few experienced surgeons exist to provide the necessary guidance, training, mentorship, and oversight for the next generation of clinicians.[xix] Yet even in highly resourced countries, the timeline of surgical training is failing to generate enough providers. The current paradigm of surgical skills training and development meets neither present day nor future health needs.

Beyond provider skill, the safety of surgery is paramount. Postoperative mortality is already the third leading cause of death globally, and expanding surgical capacity without simultaneously improving the monitoring and safety of surgery will save many lives but also result in 6 million postoperative deaths, most of which can be averted.[xx] Complications arise in 15-20% of patients undergoing open abdominal surgery regardless of locale, institution, or setting.[xxi,xxii] Many complications can be anticipated, and all must be identified and dealt with quickly. Early identification, rapid supportive care, early reintervention, and close monitoring and ongoing assessment – collectively called "rescue" care – can ensure patients suffering complications are safely steered back to recovery and hospital discharge. The ability to "rescue" is highly variable; in the US, the difference between hospitals with low mortality and high mortality following surgery is not a function of complication rates (which are roughly the same) but rather a function of the ability to "rescue" patients with complications and nurse them back to health.[xxiii] This disparity is seen more acutely across country income levels, with mortality rates following complications 2-3 fold higher in lower vs higher resource settings, even while complication rates are roughly equivalent.[xxiv,xxv]

The method of patient monitoring and evaluation is part of this variability in mortality. Assessment involves observing vital signs captured on a minute-by-minute basis, interpreting laboratory findings assessed over hours to days, and deciphering imaging studies, which may be rapidly available in some settings and entirely absent in others. None of these modalities are integrated, prognostic, or provide proactive decision support for clinicians caring for these complicated patients. Because the insults of surgery and the effects of perioperative medications mimic numerous conflicting physiological responses, differentiating between normal recovery and imminent complications is challenging, even for the most experienced clinician. Enhancing the discrimination of diagnostics would be invaluable for improving perioperative management and preventing perioperative mortality.

In the arc of surgery, recovery from an operation is as important as its provision.

Program objectives.

To achieve the program goals, we will:

- Create and deploy new models for minimally invasive abdominal surgery skills acquisition and objective assessment, supported by instruments tailored for this task. These new models should support the ability to both:

    - Identify and screen innate capabilities in non-MD practitioners and provide surgical training with validation of skills and certifiably comparable outcomes.
    - Decrease training time for MD surgeons.

- Produce new patient recovery or deterioration detection systems that utilize patterns from inputs as wide ranging as caregiver interactions, existing and new sensing methods, and novel biomarkers, to evaluate patient condition and predict recovery or deterioration following surgery.

- Validate the impact of these programs through a demonstration at the health system, state/province, or national level.

Call for abstracts and proposals.

We are soliciting abstracts and proposals for work over three (3) years (with a potential additional one-year option) in one or more of the following thrust areas outlined below to develop the simulation platform, develop the technologies, or demonstrate the impact of implementing these advances. Proposers should clearly relate work in these thrust areas to one or more of the program goals and objectives, but are not required to provide both platform technologies and end-to-end demonstrations. Synergies among performers will be facilitated by Wellcome Leap. The program will also assemble an expert group of professional organizations with the appropriate regulatory, certification, and oversight authority to work with performers throughout the program and enable the system demonstration(s).

Wellcome Leap accepts project proposals from any legal entity, based in any legal jurisdiction, including academic, non-profit, for-profit, and regulatory/professional organizations. Applicants are encouraged to contact Wellcome Leap about joining its Health Breakthrough Network by executing its MARFA (or CORFA for commercial entities) agreement. Full execution of the Wellcome Leap MARFA is not required for application submission but is required for any award.

Thrust Area 1: Create and deploy new models for surgical skills acquisition and quantification for MDs and non-MDs alike.

1.A) Accelerated skills acquisition is essential for expanding the surgical workforce. We seek solutions based on realistic simulation models that will enhance skill sets essential for minimally invasive abdominal surgery, including safe entry into the abdomen, recognition of anatomic structures, mobilization and manipulation of relevant anatomy, intracorporeal suturing and knot tying, and bowel division and anastomosis. Examples could include fully immersive simulation, augmented reality, improved sensing of tissue tension, and/or haptically enhanced instruments. We seek teams with expertise in computer vision and machine learning approaches that can support enhanced quantification of technical skills and comparative analyses to assess progress.

1.B) Improved instrumentation must assist the intuitive acquisition and objective quantification of skills. We seek solutions to enhance visualization (such as through 3-dimensional vision, augmented visualization, improved tissue discrimination, or other mechanisms to identify critical anatomy) and improve instrument maneuverability when operating in enclosed spaces that facilitate technical competence; however, these *must* also enable objective skills assessment.

1.C) Screening for innate skills that predict competence in the provision of laparoscopic surgery can enable early identification of MD and non-MD candidates with aptitude in technical skills, spatial awareness, and 3-dimensional perception. We seek approaches that enable discrimination and prediction of rapid technical competence amongst candidate surgical practitioners and that are verified and updated against training outcomes.

Thrust Area 2: Produce new patient recovery and/or deterioration detection systems that utilize patient-level inputs to assess patient condition and predict recovery or deterioration.

2.A) As the postoperative period is fraught and complications are common, improving the ability to identify deterioration during recovery is essential. We seek performers and teams specializing in sensor technologies, biomarker measurement (for example at the metabolome, genome, epigenome, hormone, or microbiome level), or other mechanisms (such as caregiver interactions, for example) that enable assessment of patient condition and that will provide early identification of deterioration during convalescence from surgery in humans. Physiological or interaction sensors must provide clinically relevant information within minutes of data acquisition and biomarkers must provide information within 30 minutes of collection.

2.B) We also seek team specializing in artificial intelligence, neural networks, and/or machine learning to aid in identifying and evaluating prediction models of recovery or deterioration. We seek new or enhanced algorithms that can integrate data elements and predict recovery and/or identify deterioration over the subsequent 24-36 hours with >90% sensitivity and >98% specificity.

2.C) Additionally, we are interested in discriminating between infection and inflammation within 30 minutes of assessment with >90% sensitivity and >98% specificity, along with the ability to evaluate the causative organism and its drug sensitivity profile with >90% sensitivity and specificity.

Thrust Area 3: Develop an end-to-end system demonstration of successful implementation of developments from Thrust Areas 1 and 2.

3.A) Objective measures of surgical competence are required if simulation models are to be trusted to replicate operative performance. We seek partners – including professional and governmental organizations with regulatory, credentialing, or oversight authority – interested in demonstrating and validating the simulation model as an accelerator to surgical skills acquisition and workforce expansion at a health system (regional, state, province, or national) level. This should include evidence that MD and non-MD trainees using simulation can complete a similar surgery from start to finish with equal or more competence than standard surgical trainees. For example, a proof-of-concept simulation model could replicate a minimally invasive right hemicolectomy and/or repair of a gastroduodenal perforation and predict independent completion of these operations in clinical practice.

3.B) System level demonstrations should also include objective validation of the program approach for enhanced postoperative assessment. For example, the integrated use of novel biomarkers or sensors should demonstrate a 50% reduction in mortality over historic controls.

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