Surgical Recovery in the Elderly: Systematic Review of Patient-Centered Outcomes and Prospective Study of Post-Operative Delirium

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I. PREFACE

As the baby-boomer generation continues to age, we are seeing a dramatic increase in the number of older persons. In Quebec, there are now more than 1 million people over the age of 65, with the most rapidly growing age group being those above 85 [1]. As a result, more surgical procedures are being performed on elderly patients and as the number of elderly surgical patients continues to increase at a rapid rate, studies that examine the post-operative period in this population will become increasingly valuable. The issues surrounding the care of the elderly are drastically different from the rest of the population and must be well understood in order to allow evidence-based decision making for clinicians, patients and families. This will hopefully allow health-care professionals to achieve, age independent, optimal results [2].

In the post-operative phase, recovery (or convalescence) is often prolonged in older patients. This process is influenced not only by physical factors, but also by mental and psychological status, as well as by social support, levels of independence, questions of quality of life and maintenance of functional ability [3,4].

In 1958, Francis Moore wrote that recovery was “the interlocking physical, chemical, metabolic, and psychological factors commencing with the injury, and terminating only when the individual has returned to normal physical well-being, social, and economic usefulness, and psychological habitus” [5]. As such, using outcome measurements that are sensitive to changes in all of these health domains may provide important information to patients and clinicians. If this is

true, then consequently, the assessment of the quality of care should no longer be limited to one-dimensional traditional outcomes such as morbidity, mortality and length of hospital stay. These outcomes would be considered insufficient to assess the many different health domains that are affected by surgery and affect the recovery process.

Thesis components

This thesis is comprised of three parts:

PART 1 is a systematic literature review which attempts to answer the hypothesis that few studies use patient-centered outcomes to examine the post-operative course in the elderly following gastrointestinal surgery. This study allowed us to develop a framework to categorize patient-centered outcomes in the elderly surgical population.

PART 2 is a pilot study that was carried out in order to elucidate the relationship between pre-operative cognitive impairment and post-operative delirium in the elderly. The data collected in PART 2 allowed us to power a larger prospective clinical study, PART 3.

PART 3, is currently being planned to test the hypothesis that patient-centered outcomes provide a more dynamic, accurate and multidimensional approach to assessing the post-operative period in the elderly.

INTRODUCTION

Compte tenu du vieillissement de la génération des baby-boomers, on observe une augmentation considérable du nombre de personnes âgées. Au Québec, on compte maintenant plus de un million de personnes âgées de plus de 65 ans, et celles qui ont plus de 85 ans forment le groupe d'âge qui augmente le plus rapidement (1). Par conséquent, les interventions chirurgicales pratiquées sur les personnes âgées sont plus nombreuses qu'auparavant. Étant donné que le nombre de personnes âgées qui doivent subir de telles interventions croît rapidement, les recherches qui portent sur la période postopératoire de cette population vont devenir de plus en plus pertinentes et précieuses. Les questions liées aux soins à donner aux personnes âgées sont tout à fait différentes de celles qui se posent pour les autres groupes d'âge. Aussi, il importe de bien en saisir la teneur afin que les décisions des cliniciens, des patients et de leur famille s'appuient sur des données probantes. Ce faisant, on peut espérer que les professionnels de la santé obtiennent des résultats optimaux, quel que soit l'âge de leurs patients (2).

Au cours de la période postopératoire, le rétablissement (ou la convalescence) est souvent plus long chez les personnes âgées. En fait, il s'agit d'un processus qui est non seulement influencé par des facteurs physiques, mais aussi par l'état mental et psychologique aussi bien que par le soutien social, le niveau d'indépendance, la qualité de vie et le maintien de la capacité fonctionnelle (3,4).

En 1958, Francis Moore définissait le rétablissement en ces mots :

« l'interdépendance des facteurs physiques, chimiques, métaboliques et

psychologiques qui agit dès la survenue de la blessure et se termine seulement lorsque la personne retrouve son état de bien-être physique antérieur, son utilité sociale et économique et son état psychologique habituel (5). Dans ce sens, mesurer les résultats influencés par les changements qui surviennent dans tous ces aspects de la santé peut fournir des renseignements précieux aux patients comme aux cliniciens. Si l'on admet cela, alors, l'évaluation de la qualité des soins ne doit plus se limiter aux résultats unidimensionnels et traditionnels que sont la morbidité, la mortalité et la durée du séjour hospitalier. Car ces résultats ne suffisent pas à évaluer les différents aspects de la santé touchés par l'intervention chirurgicale, lesquels influencent à leur tour le processus de rétablissement.

Objet du mémoire

Le présent mémoire se divise en trois parties.

La première partie consiste en une revue systématique de la documentation scientifique qui cherche à vérifier l'hypothèse suivante : peu d'études utilisent les résultats axés sur le patient pour examiner la période postopératoire des personnes âgées qui ont subi une opération gastro-intestinale. Cette revue permet d'élaborer un cadre qui donne la possibilité de catégoriser les résultats axés sur le patient pour une population de personnes âgées qui ont subi une intervention chirurgicale.

La deuxième partie est une étude pilote qui a été menée dans le but de clarifier la relation entre la déficience cognitive préopératoire et le delirium postopératoire chez les personnes âgées. Les données colligées dans le cadre de cette étude

pilote ont permis d'effectuer une étude clinique prospective de plus grande envergure qui fait l'objet de la troisième partie.

La troisième partie, dont la planification est en cours, cherche à vérifier l'hypothèse selon laquelle les résultats axés sur le patient donnent lieu à une approche plus dynamique, précise et multidimensionnelle pour évaluer la période postopératoire chez les personnes âgées.

PART 1- MEASURING SURGICAL RECOVERY IN THE ELDERLY USING PATIENT-CENTERED OUTCOMES: A SYSTEMATIC REVIEW

I. ABSTRACT

Objectives: As the number of elderly surgical patients continues to increase at a rapid rate, studies that examine the post-operative period in this population will become increasingly valuable. Surgical recovery, the “return to normal physical well-being, social, and economic usefulness, and psychological habitus”, is a process that may best be measured using multidimensional outcomes that are patient-centered. The primary aim of this study was to determine to what extent patient-centered outcomes are being used in scientific literature, in the elderly, following gastrointestinal surgery and to determine, using an innovative model, which domains of the post-operative period are being examined using these outcomes. Our secondary aim was to examine the subset of articles that focused on recovery and post-operative delirium and assess their quality.

Methods: The database MEDLINE was searched for articles published between 1988 and 2009, using several keywords to satisfy three general criteria: patient age (elderly), intervention (gastrointestinal surgery), and outcome type (patient-centered). All selected articles were independently reviewed by two researchers. The patient population and study characteristics, as well as all outcomes used, were recorded. A framework derived from the Wilson-Cleary Model for Health Related Quality of Life was developed to categorize patient–centered outcomes into one of three health domains: symptom status, functional status, or general health perceptions. In turn, these health domains encompass 8 patient-centered outcome categories: pain, vitality, patient satisfaction, psychological function, social function, physical function, independence, and cognitive function. A sub-

analysis, including a quality assessment, was performed on the studies that explicitly examined recovery and delirium.

Results: An initial search yielded 2980 articles. Eighty-eight studies, measuring at least one patient-centered outcome in the elderly following gastrointestinal surgery, were retained. Applying the proposed framework, 27 studies (30.7%) examined symptom status, 61 studies (69.3%) examined functional status and 32 studies (36.4%) examined general health perceptions. Independence was the most commonly measured patient-centered outcome while social function was the least commonly measured. A subset of 24 studies described recovery and a subset of 15 studies examined post-operative delirium. Studies examining recovery and delirium met a varying number of our quality assessment criteria.

Conclusions: Using an adapted framework to categorize patient-centered outcomes, this study has uncovered that, to date, few studies use patient-centered outcomes to assess the post-operative period in the elderly following gastrointestinal surgery. Future studies should attempt to determine whether using patient-centered outcomes provides additional information that is useful to clinicians and patients. An assessment of the post-operative period, using patient-centered outcomes, may provide elderly patients with a more complete, picture of what to expect following gastrointestinal surgery and may ultimately help in the decision making and recovery process.

Keywords: Systematic Review, Elderly, Patient-Centered Outcomes, Recovery, Gastrointestinal surgery

Résumé

Objectifs: Compte tenu de la croissance rapide du nombre de personnes âgées qui doivent subir des interventions chirurgicales, les recherches qui portent sur la période postopératoire au sein de cette population vont devenir de plus en plus pertinentes et précieuses. Le rétablissement après une opération, ou le « retour à l'état de bien-être physique antérieur, l'utilité sociale et économique et l'état psychologique habituel » constitue un processus qu'on peut le mieux évaluer à l'aide de résultats multidimensionnels axés sur le patient. L'objectif premier de la présente étude était double : déterminer dans quelle mesure les résultats axés sur le patient, en l'occurence les personnes âgées ayant subi une opération gastro-intestinale, sont utilisés dans les études scientifiques et établir au moyen d'un modèle innovateur les différents aspects de la période postopératoire étudiés à l'aide de ces résultats. Le deuxième objectif consistait à examiner, parmi ces études publiées, celles qui mettent l'accent sur le rétablissement et le delirium postopératoire pour en évaluer la qualité.

Méthodologie: La base de données MEDLINE a servi à la recherche des articles publiés de 1988 à 2009 à l'aide de nombreux mots-clés définis à partir de trois critères généraux : l'âge du patient (personne âgée), l'intervention (opération gastro-intestinale) et le type de résultat (axé sur le patient). Tous les articles choisis ont été revus par deux chercheurs. Les caractéristiques de la population à l'étude et des études elles-mêmes, aussi bien que les résultats utilisés, ont été consignés par écrit. Un cadre de référence inspiré du *Model for Health Related Quality of Life* de Wilson-Cleary a été élaboré pour classer les résultats axés sur le patient dans l'une des trois catégories suivantes : état des symptômes, état

fonctionnel et perception de la santé générale. Ces trois catégories ont été divisées à leur tour en huit sous-catégories, ou résultats axés sur le patient : la douleur, la vitalité, la satisfaction du patient, les fonctions psychologiques, les fonctions sociales, les fonctions physiques, l'indépendance et les fonctions cognitives. Une analyse secondaire, y compris l'évaluation de la qualité des études qui se sont penchées sur le rétablissement et le delirium, a également été effectuée.

Résultats: Une première recherche a permis de relever 2 980 articles. De ce nombre, 88 études qui mesuraient au moins un résultat axé sur le patient pour une population âgée ayant subi une opération gastro-intestinale ont été retenues. À l'aide du cadre proposé, on a pu cerner 27 études (30,7 %) qui portaient sur l'état des symptômes, 61 études (69,3 %) sur l'état fonctionnel et 32 études (36,4 %) sur la perception de la santé générale. L'indépendance était le résultat axé sur le patient le plus couramment mesuré, alors que la sous-catégorie fonctions sociales l'était le moins. Un sous-ensemble de 24 articles décrivait le rétablissement ; un autre de 15 articles portait sur le delirium postopératoire. Les études qui avaient le rétablissement et le delirium pour objet n'ont pas toutes rempli également les critères de qualité.

Conclusion: Au moyen d'un cadre de référence adapté servant à catégoriser les résultats axés sur le patient, notre étude a révélé que, à ce jour, peu d'études utilisent de tels résultats pour évaluer la période de rétablissement chez les personnes âgées ayant subi une opération gastro-intestinale. D'autres études seraient nécessaires pour tenter de déterminer si l'utilisation des résultats axés sur le patient fournit des renseignements additionnels utiles aux cliniciens et aux

patients. Évaluer la période postopératoire au moyen des résultats axés sur le patient pourrait donner aux patients âgés une idée plus précise de ce à quoi ils doivent s'attendre après une opération gastro-intestinale et, ultimement, faciliter la prise de décision et le processus de rétablissement.

Mots-clés: Revue systématique, personnes âgées, résultats axés sur le patient, rétablissement, opération gastro-intestinale.

II. INTRODUCTION

Traditional surgical goals were to cure and to maximize lifespan. These traditional goals are still reflected in the surgical literature, in which mortality, complications, and length of stay are often the only outcomes used. In a review of study outcomes following gastrointestinal surgery in the elderly, Chee *et al.* demonstrated that 80% of studies defined favorable outcomes only according to morbidity and mortality [7]. Mortality is often frequently reported because it is easy to define and measure, is objective, can be easily extracted from charts or databases and represents the most drastic failure of a surgical procedure [8]. However, over the years, our surgical procedures have been refined and in many modern operations, mortality is very rare. Simply surviving surgery is no longer sufficient and using mortality as a primary outcome has limited value when the goal of the procedure is to improve patient well-being or quality of life. Traditional measures are unable to detect improvements in quality of life or overall well-being [9].

Many traditional outcomes are heavily confounded by other factors independent of recovery. Length of stay, for example, is a commonly measured post-operative outcome, however, it has been shown to vary significantly depending on a patient's level of social support and may vary depending on a particular institutions discharge policy [3,4]. Additionally, traditional outcomes that are important to the young population may not be attributed the same value, relevance, and level of importance among the elderly. Commonly used outcomes such as return to work are no longer relevant in the elderly, of whom many are

retired. Furthermore, a study conducted by Hiller *et al.* demonstrated that only 15% of elderly post-operative patients were concerned about their length of hospital stay [10]. For the elderly, the ability to take care of oneself is extremely important and for many elderly surgical patients maintaining post-surgical independence is more important than survival [7]. A study of treatment preferences conducted by Fried *et al.* demonstrated that for a low burden treatment with an outcome of severe cognitive impairment almost 90 % of participants chose not to receive therapy, despite the understanding that doing so was inevitably fatal [8]. These findings corroborate the idea that, for elderly patients, functional and cognitive outcomes can play a greater role than mortality when considering treatment preferences.

Older patients are now confronted with a much different reality than those before them. Some have already outlived their projected life expectancy, may have outlived their spouse, friends, family, and may be more concerned with issues such as dignity, quality of life, and minimizing suffering. Using outcomes that are able to detect how surgery impacts these areas may help to address these issues. “Life is not merely to be alive, but to be well.” and health in the elderly is more than just the absence of disease; in order to truly recover, patients must be able to return to pre-morbid/operative function and levels of independence [7]. Improving functional outcomes should be the goal of modern surgical procedures in the elderly. In order to be able to provide this information to patients so that they can make informed decisions, it is necessary to measure these surgical outcomes. Our judgment of the success of our surgical operations and many of our treatment decisions are based on the results of studies that still use

traditional, confounded outcomes that may not be valued or validated in the elderly.

Recently there has been a move towards incorporating the patient's point of view into post-operative measures. What the patient experiences in the post-operative period has become central to outcomes research and these outcomes, which reflect the experience of the patient, are called patient-centered outcomes (PCO) [11]. Outcomes such as: pain, vitality, independence, patient satisfaction, and social function are increasingly being used to measure the post-operative course in the elderly. Although these outcomes may be extremely subjective and difficult to measure, they may represent a more realistic view of the burden of disease and impact of surgery as experienced by the patient. Patient-centered outcomes may be more informative and valid than solely measuring traditional outcomes. A study conducted by Bergman *et al.* found that traditional measures, such as complications, mortality, and length of stay were inadequate descriptors of recovery when compared to measures such as quality of life and functional exercise capacity [12]. The purpose of patient-centered outcomes is not to replace traditional measures but rather to add to them in order to broaden our ability to measure the impact of surgery on several domains and help to tailor surgical care to benefit this complex and heterogeneous population of older patients.

In 1994, Deming said: "you can't improve something you can't measure" [13]. If we want to improve surgical care for the growing elderly population, it is imperative we accurately measure the post-operative period. This may be best done using patient-centered outcomes that are not only valued and validated in

the elderly population but may also reflect the multidimensional nature of recovery as experienced by this population. Having a detailed description of the post-operative period in several different health domains could allow us to give patients a better idea of what to expect following surgery, may help us to improve our surgical treatments and may ultimately allow us to provide better care for our elderly patients.

The Wilson-Cleary model

The relationship between clinical interventions, such as surgery, and patient-centered outcomes is both integrated and complex. Fortunately, in 1995 a landmark paper published in the Journal of the American Medical Association by Wilson and Cleary helped to elucidate the causal relationship between clinical interventions and the resulting effect on parameters such as social function and mental health [14]. The Wilson-Cleary paper helps to advance our understanding of this relationship and is subsequently one of the most well recognized and frequently cited research papers on health related quality of life to date. More than 1300 articles have cited the 1995 Wilson-Cleary paper and the influence of their work has had far-reaching effects. Citing articles include a variety of topics, ranging from management of hot flashes in breast cancer patients to changes in quality of life after liver transplantation.

Wilson and Cleary recognized the shift in modern therapeutic goals from improving physiological impairment and survival to improving patient function and overall well-being; from traditional to patient-centered outcomes. As such, Wilson and Cleary developed a model to help researchers understand the relationship

between biological and physiological impairment and health related quality of life (Figure 1). Implicit in this relationship is the idea that health related quality of life measures are valid, reliable and sensitive to important clinical changes. Wilson and Cleary also propose that health related quality of life outcomes are useful and important supplements to traditional physiological and biological measures of health. Wilson and Cleary explain how a patient's biological and physiological variables, symptoms status, functional status, and general health perceptions, are all factors that are incorporate a patient's health-related well-being. As a result, health related quality of life measures are both multidimensional and patient-centered [14].

The Wilson-Cleary model comprises five levels: Biological and physiological variables, symptom status, functional status, general health perceptions and health related quality of life. Each of these levels are intimately related critical concepts on a causal pathway. As one moves from left to right in this model, Wilson and Cleary explain, measures become increasingly complex and integrated.

The first level in the model is biological and physiological variables, which includes measures that assess the function of cells, organs and organ systems e.g. laboratory values, esophageal function, anal manometry, and pulmonary function tests. These measures are not patient-centered because they are an assessment of organ function and do not take into account the patient's perspective.

The second level in the Wilson-Cleary model is symptom status. Unlike biological and physiological variables, symptom status measures assess the patient as an

individual rather than an organ system. Wilson and Cleary define a symptom as: “a patient’s perception of an abnormal physical, emotional, or cognitive state”. Examples of symptom status measures include: pain, and vitality. Biological and physiological variables can have a direct effect on the symptom status of a patient, for example: post-operative ileus can cause an elderly patient pain and anxiety. However, it is important to keep in mind that this relationship is not always direct; it is possible for a patient to have biological and physiological impairment without the presentation of symptoms, conversely, a patient may have poor relief of symptoms despite healing of biological and physiological impairments [14]. Outcomes that measure symptom status are patient-centered. The third level in the Wilson-Cleary model is functional status. Functional status measures assess a patient’s ability to perform tasks. These tasks need not be only physical, tests of cognitive performance are also considered functional status measures. Examples of functional status measures include: activities of daily living and the Mini-mental Status Exam. The presence of symptoms can impact a patient’s ability to perform functions, for example, if a patient is in severe pain it may limit their ability to carry out daily activities and subsequently impair independence. Wilson and Cleary suggest that a patient’s personal environment mediates this relationship. Factors such as social support, family role, and personal motivation can all vary the extent to which symptom status affects a patient’s function. Outcomes that measure functional status are patient-centered. The fourth level in the Wilson-Cleary model is general health perceptions. These are subjective assessments of how patients view their overall health and are, in their very essence, patient-centered. General health perceptions integrate a

patient's biological and physiological variables, symptom status and functional status. This integration helps to demonstrate how a patient's well-being is a multidimensional and multi-factorial state. Examples of general health perceptions include level of satisfaction.

The last level in the Wilson-Cleary model is overall quality of life, much like general health perceptions, overall quality of life represents the integration and summation of a patients "experiences and feelings" that contribute to their overall quality of life [14].

Although the main purpose of the Wilson-Cleary model was to explain the causal relationship between these 5 levels, in doing so, they have outlined the many domains and factors that contribute to a patients overall health and well being. If one were inclined to take a patient-centered approach to surgical outcomes and assess the impact of surgery as experienced by the patient, it would first be necessary to identify the many domains that contribute to a patient's health; the Wilson-Cleary model allows us to comprehensively accomplish this and is therefore an important starting point for this thesis.

III. OBJECTIVES

The primary aim of this study was to determine to what extent patient-centered outcomes are being used in scientific literature to examine the post-operative period in the elderly, following gastrointestinal surgery.

The secondary aims of this study were:

1. To investigate the use of patient-centered outcomes in the study of recovery and assess the quality of such studies
2. To investigate the use of patient-centered outcomes in the study of post-operative delirium and assess the quality of these studies.

IV. METHODS

Literature search

A systematic literature review was conducted using a MEDLINE database search for articles published between 1988 and September of 2009. The literature search was performed by one researcher using the following sets of keywords in combination. Depending on MEDLINE indexing, not all keywords were mapped to MeSH headings and were therefore searched as free-text keywords.

- Quality of life, activit* of daily living/ life, HRQOL, QOL, well being, health status, functional (outcome/ decline/ assessment/ activity/ capacity/ status recovery/ independence) SF-36, patient-centered, return to (work/normal activit*/daily activit*/physical activit*)
- **AND** aged, elder*, frail elderly, geriatric*, geriatric assessment, aged 80 and over, elderly, advanced age.
- **AND** surgery (colorectal, laparotomy, laparoscopy, gastrointestinal surgery, colon, rectum, hepatobiliary, abdominal, gastric, gallbladder, biliary, small bowel, rectal, colon, pancreatic, liver) hernia repair.

Additionally, the reference lists of all selected articles were reviewed. All reference studies that met inclusion criteria, based on titles alone, were provisionally included.

Inclusion and exclusion criteria

A study was eligible for inclusion if the participants were elderly. For the purposes of our review, this was defined as an average age above 65 or the use of the keywords elderly, geriatric, or older persons to describe the patient population, regardless of mean age. Studies that reported comparison groups of the young and elderly despite a mean age below 65 were included. Additionally, any studies reporting elderly specific sub-analyses of the patient population were included. Studies were included if participants underwent Gastrointestinal or abdominal surgery and involved an outcome within the following health domains: pain, psychological function, physical function, independence, social function, cognitive function, patient satisfaction, vitality or overall quality of life. In order to meet inclusion criteria, studies must have been published in English.

Articles were excluded if they were editorials, comments, letters to the editor, systematic reviews, case reports, study proposals, descriptions of study methods or guidelines. Additionally, studies were excluded if they were performed exclusively on animal models, involved study participants who underwent exclusively a nephrectomy, adrenalectomy, hysterectomy, or prostatectomy or exclusively involved surgery in the fields of urology, plastic surgery, oral surgery, gynecology, orthopedics, vascular surgery, or cardiac surgery. Studies were excluded if participants were pediatric, adult, young adult, or adolescent. All studies with only disease specific outcomes, including but not limited to anal manometry and esophageal function in the context of gastroesophageal reflux disease (GERD), were excluded. Studies that only measured traditional

outcomes, including but not limited to: length of stay, morbidity, mortality and complications were excluded from this review.

Study selection and review procedure

Once the MEDLINE search was performed, study selection occurred in 3 stages. First, all titles were reviewed independently by two reviewers. Both reviewers accepted or rejected these titles based on the inclusion and exclusion criteria stated above. Any disagreement between reviewers was resolved through discussion until a consensus was reached. Next, the abstracts of all accepted articles were reviewed using the same procedure. When a citation lacked an abstract, the study was provisionally included for consideration on the basis of a full text review. Lastly, the full articles of all accepted abstracts were reviewed. When more than one publication described a single study with the same data, the most recent publication was included. The reference lists of the selected articles were reviewed using the same methods and inclusion/exclusion criteria outlined above.

Data extraction

Once full articles were selected, study characteristics were extracted. These included: author, publication date, publishing journal, country of origin, type of study (cross sectional, retrospective cohort, case-control, prospective cohort, clinical trial or randomized controlled trial), and follow-up. Short-term follow-up was defined as any follow-up less than one month; mid-term follow-up was defined as between one month and 1 year and long term follow-up was defined

as any postoperative assessment greater than one year. In addition, the following data were also extracted: mean participant age (in studies where a younger cohort was compared to an older cohort, the mean age of the older cohort was used), gender, number of participants, whether it was a multicenter or single center study, inclusion and exclusion criteria, surgical procedure, and surgical indication. Finally, all assessed outcomes (e.g. pain or fatigue) and their measurement tools (e.g. visual analog scale or McGill pain Questionnaire) were noted.

Outcome classification

In order to accomplish our study objectives we required a framework or model that would allow us to comprehensively classify, into specific categories, the patient-centered outcomes that we found in our review. However, at the time of this review, no such classification scheme existed.

Overall quality of life comprehensively describes all of the factors that may contribute to a patient's overall health and well being, therefore, all patient-centered outcomes fit into one of these domains. The Wilson-Cleary model outlines the broad domains that contribute to a patient's overall quality of life; therefore, we used the Wilson-Cleary model as the starting point and direct inspiration to create our framework.

In their model, Wilson and Cleary were primarily concerned with establishing causal relationships between health domains rather than classifying outcomes [14]. Their model reflects this goal and therefore lacks the depth and detail

necessary for comprehensive categorization of outcomes. It was therefore necessary for us to adapt the Wilson-Cleary model to fit our objectives.

The first modification we performed was to eliminate biological and physiological variables. This level is not patient-centered and therefore, with respect to the objectives of our review, served no purpose for our classification scheme. Next, we eliminated the overall quality of life domain. This was done because quality of life assessments are broader categories that incorporate the multiple patient-centered outcomes which we already included in our model. These include outcomes such as: pain, independence and satisfaction. What remained were symptom status, functional status, and general health perceptions, we decided to label these three remaining levels our 3 “health domains”.

In order to be able to categorize each patient-centered outcome more specifically, it was necessary to subdivide each of the three health domains into what we labeled “patient-centered outcome categories”. Based on Wilson-Cleary’s analysis of the 5 levels and a consultation with several experts in surgical outcomes research, we identified the 8 patient centered outcome categories as: pain, vitality, patient, satisfaction, psychological function, social function, physical function, cognitive function, and independence. Outcomes that assess pain or vitality belong to the symptom status health domain, measures of patient satisfaction, psychological function, or social function belong to the general health perceptions domain and measures of physical function, independence or cognitive function belong to the functional status domain (Figure 2).

Any outcome that sought to measure a patient’s level of discomfort was classified under the patient-centered outcome category of pain. Examples of pain outcomes

include: overall pain and discomfort. Studies using outcomes which assessed a patient's level of wakefulness or energy were classified into the patient-centered outcome category of vitality. Examples of outcomes that assess vitality include: level of energy and drowsiness.

Any outcome that measured the ability of a patient to perform a particular physical task was classified into the patient-centered outcome category of physical function. Examples of physical function outcomes include: hand-strength and functional reach. Studies which included outcomes that evaluated a patient's cognitive ability were classified into the patient-centered outcome category of cognitive function. Examples of cognitive function outcomes include: delirium and attention. Outcomes which evaluated the ability of a patient to perform functions independently were classified into the patient-centered outcome category of Independence. Examples of independence outcomes include: activities of daily living, and discharge destination.

Studies which used outcomes that assessed a patient's mental behaviour were classified into the patient-centered outcome category of psychological function. Examples of psychological function outcomes include: mood, anxiety, and depression. Outcomes that evaluated a patient's overall satisfaction were classified into the patient-centered outcome category of patient satisfaction. Examples of patient satisfaction outcomes include: willingness to undergo the surgery again and satisfaction with the surgical outcome. Finally, any outcome that evaluated social status changes, the ability to interact with others or level of social support were classified into the patient-centered outcome category of social function.

The authors of this review recognize that patient-centered outcome categories and health domains are not mutually exclusive and some assessments can be classified into several categories. Impairment in one domain or category may affect performance in another, however, describing these relationships was outside the scope of this review.

Health domains were either recorded as assessed or not assessed based on whether a measurement was used from a patient-centered outcome category. Extra weighting was not given to studies that used multiple patient-centered outcomes within the same domain or category. For example, if a study assessed both pain and vitality, this would only count as one assessment of the symptom status health domain, additionally, if a study assessed vitality in more than one way, this would still only count as a single pain assessment.

Quality assessment

A quality assessment analysis was performed on the subset of the selected articles that explicitly examined recovery or explicitly examined delirium in the elderly following gastrointestinal surgery. Articles were included in the recovery subset if they mentioned: convalescence, recovery, or return to preoperative function or baseline. Articles were included in the delirium subset if they mentioned: delirium, confusion, or cognitive dysfunction. The methodological quality of these articles was assessed by one researcher using 15 criteria developed by Vedel et al. [15]. This quality assessment is a combination of the MAStARI-SUMARI, STROBE and MOOSE quality assessments tools (Appendix I).

V. RESULTS

Literature search

The initial search yielded 2 980 articles (Figure 3). According to the inclusion and exclusion criteria, 1 400 were excluded based on title alone. Of these articles 220 were excluded because the study participants were not elderly, 441 studies did not involve GI or abdominal surgery, and 463 studies did not use any patient-centered outcomes. An additional 287 studies were excluded for a variety of other reasons (Figure 4). After examining the abstracts of all provisionally included titles, a further 1 484 articles were excluded. Finally, 25 studies were excluded after examining full texts. Seventy-one articles were initially included in this review. After examining the reference lists of all accepted studies, 1 685 references were identified, 245 (14.5%) of these titles met our inclusion criteria. The abstracts of these reference titles were subsequently examined and seventeen full articles (6.9%) that met inclusion criteria were identified and included; the final result was 88 full articles that used patient-centered outcomes in the elderly following gastrointestinal surgery.

A. All patient-centered outcome studies

Characteristics of all patient-centered outcome studies

This review examined studies published in English from all countries. Seventy-seven percent were of European origin (27.7%) and 28 of the accepted studies (31.2%) were published in North America (4 Canadian). Thirteen articles (14.8%) were published in Asia and four articles (4.5%) were published in Australia. The remaining 24 studies (27.3%) involved more than one publishing country. Accepted studies varied in the number of participants; a minimum of eight participants and a maximum of 89 405 participants were reported. Twenty-six studies (29.5%) examined less than 50 study participants, and 3 studies (4.5%) examined more than one thousand elderly surgical patients (Figure 5). The overall mean age for participants was 74.4 years. One study had a mean age of patients in their fifties, thirteen studies (14.7%) examined a patient population with a mean age in their sixties, 40 studies (45.4%) had a mean age in the seventies and 16 studies (18%) had a mean age in the eighties, (Figure 6).

This review included publications using a variety of study types. The majority of studies (63.3%) were prospective. Thirty-six studies (40.9%) used a prospective cohort design, 12 (13.6%) were clinical trials and 8 studies (9.1%) were randomized controlled trials. Twenty-four studies (29.5%) used a retrospective cohort design, 3 studies (3.4%) were case-control, and five articles (5.7%) were cross-sectional (Figure 7).

Studies examined the postoperative course of patients who underwent a variety of surgical operations for a variety of reasons (Figure 8). Cancer was the most

common disease process examined. Thirty percent of all studies involved patients undergoing cancer surgery (26 studies). Thirty-six studies (40.9%) examined the post-operative course in elderly patients for multiple surgical indications. All surgical indications are listed in Figure 8.

A variety of different post-operative follow-up lengths were used, these ranged from one post-operative day to 14 years following surgery (Figure 9). Twenty-two articles (25%) had a short term follow-up period (0-1 month), 26 articles (29.5%) had a mid-term follow-up period (>1month-1year), and 38 articles (43.2%) had a long term follow-up period (>1 year). The remaining two articles (2.2%) did not report follow-up length.

This review examined studies published between 1988 and September 2009. Most studies (77.3%) examining patient-centered outcomes in the elderly were published after 1999. A breakdown of the number of studies published per year can be see in Figure 10.

Patient-centered outcomes of all studies

The outcomes of all 88 studies included in this review were recorded and classified into one of the three health domains: symptom status, functional status and general health perceptions (Table 2, Figure 17). Of the studies included in this review, the most common health domain assessed was functional status, 61 studies (69.3%) measured at least one patient-centered outcome in this domain (Table 3). The least common health domain assessed was symptom status. Twenty-seven studies (30.7%) examined at least one patient-centered outcome

in this domain. The final health domain, general health perceptions, was examined in 32 of the 88 studies included in this review (36.4%).

Nineteen studies (21.6%) used outcomes in both the symptom status and functional status health domains. Seventeen studies (19.3%) used outcomes in both the general health perceptions and functional status health domains, and 15 studies (17%) used outcomes in both the general health perceptions and symptom status health domain. Nine studies (10.3%) used outcomes in all three health domains (Figure 18). A list of each study and which health domains were assessed are included in Table 2.

Each of the three health domains incorporated 2 or 3 patient-centered outcome categories (Figure 2). All outcomes used by studies were classified into one of the 8 patient-centered outcome categories; pain, vitality, physical function, cognitive function, independence, psychological function, social function, and patient satisfaction (Figure 19, Table 4). A list of which studies used outcomes from which patient-centered outcome categories, some examples of common outcomes and tools, and a breakdown by study of which outcomes were used, can be seen in Tables 4, 5, and 6 respectively.

The most commonly examined patient-centered outcome category was independence which was examined in 35 studies (39.8%). The least commonly measured patient-centered outcome category was social function, 6 studies (6.8%) measured a patient-centered outcome from the social function category. Twenty-four studies, (27.3%) measured pain, 11(12.5%) measured vitality, 24 studies (27.3%) measured physical function, 22 studies (25%) measured cognitive function, 9 studies (10.2%) measured psychological function, and 26

studies (29.5%) measured patient satisfaction (Figure 19, Table 3). In addition to the 8 identified patient-centered outcome categories, 29 of the 88 studies included in this review (33%) measured quality of life. The studies which examined quality of life, as well as the individual quality of life tools are listed in table 1 and 7 respectively.

B. Recovery study subset

Characteristics of recovery study subset

From the 88 studies included in this review, an additional analysis was conducted involving a subset of 24 studies (27.3%) which explicitly aimed to describe the recovery process (Table 1). In this subset, the majority of studies (83%) were published after 1998, 83% were prospective, one third had a short-term length follow-up period (<1 month), one third had a mid-term follow-up (1 month to 1 year), and one third had a long-term follow-up (>1 year) (Figure 11). The mean age of study participants was 76 years. Seven studies (29%) examining recovery had less than 50 participants, 9 studies(37.5%) had between 100 and 1000 participants, and none of the studies examining recovery using patient-centered outcomes had more than 1000 participants (Figure 12).

Patients in these studies underwent the following procedures: cancer surgery (9 studies, 37.5%), hernia repair (1 study, 4.2%) GERD (1 study, 4.2%), and diverticulitis (1 study, 4.2%). Twelve studies (50%) involved operations for more than one disease process (Figure 13).

Patient-centered outcomes of recovery study subset

Applying the proposed framework in the recovery study subset (n=24), functional status was the most commonly assessed health domain (Table 8). Twenty-two recovery studies (92%) used a patient-centered outcome in this domain. General health perceptions was the least commonly evaluated health domain, 10 studies (42%) used outcomes from this domain. Finally, eleven studies (46%) used

outcomes from the symptom status health domain (Figure 20). Ten of the 24 recovery studies (41.7%), used outcomes in both the symptom status and functional status health domains, eight studies (33.3%) used outcomes in both the general health perceptions and functional status health domains, and seven studies (29.2%) used outcomes in both the general health perceptions and symptom status health domain. Twelve studies (50%) used an outcome from at least two domains, while 6 (25%) studies described recovery using outcomes from all three domains (Figure 21). A list of the studies examining recovery and the health domains assessed is included in Table 8. Among the recovery studies, the most commonly examined patient-centered outcome category was physical function, 13 studies (54.2%) measured patient-centered outcomes from this category (Figure 22, Table 9). Social function was the least commonly examined patient-centered outcome category, 2 studies (8.3%) used patient-centered outcomes from this PCO category. 10 studies measured pain (41.7%), 6 measured vitality (25%), 9 measured cognitive function (37.5%), 11 measured Independence (45.8%), 6 measured psychological function (25%), and 6 measured patient satisfaction (25%). In addition to the 8 identified patient-centered outcome categories, 4 of the 24 recovery studies included in this review (16.7%) examined quality of life. An analysis of all outcomes and tools used in studies examining recovery can be found in Table 10.

Quality of recovery study subset

The quality of each of the 24 studies examining recovery was assessed based on 15 criteria proposed by Vedel *et al*. (Table 16) [15]. Studies met between 2 and 11 quality assessment criteria. All studies had a clearly formulated research question. Seventy-five percent of studies were not based on a random/ pseudo-random sample and 42% of studies included a sample of adequate size (n≥100). The source and method of selection of participants was described in 83% of studies. All but one study clearly defined the criteria for inclusion and exclusion of participants and outcomes were clearly defined in all but one study (96%). Thirty-four percent of studies made no mention of the source of data, confounding factors were not reported in 92% of studies and when applicable, sufficient group comparisons were conducted in 54% of studies. The outcomes of people who withdrew were not described or included in the analysis in 67% of studies. Seventy-one percent of studies maintained at least 75% of patients throughout follow-up, while 92% of studies made no mention of how missing data was handled. An appropriate statistical analysis was used in 71% of the studies and a sensitivity analysis was not performed in any of the studies examining recovery [15].

C. Delirium study subset

Characteristics of delirium study subset

Fifteen studies in this review explicitly examined post-operative delirium in the elderly following gastrointestinal surgery (Figure 1). Delirium studies had a range of follow-up lengths; 8 studies (53%) were short-term (<1 month), 33% were mid-term (1 month to 1 year), and 13% were long-term (>1 year) (Figure 14). The mean age of study participants was 68 years. Five of the fifteen studies (33%) examining recovery had less than fifty participants, and two studies (13%) had over one thousand participants (Figure 15). Post-operative delirium was examined in patients undergoing surgery for: cancer (4 studies, 26.7%), biliary disease (one study, 6%), and IBD (one study, 6%). Nine studies (60%) examining post-operative delirium involved surgical operations for multiple disease processes (Figure 16).

Patient-centered outcomes of delirium study subset

Among the delirium study subset (n=15), the most commonly examined health domain was functional status, which was examined in 11 of 15 delirium studies (73%) (Table 11). The least commonly examined health domain was general health perceptions, 4 delirium studies (24%) used a PCO in this health domain. Lastly, nine studies (60%) used outcomes from the symptom status health domain (Figure 23). Five delirium studies (33.3%) used outcomes in both the symptom status and functional status health domain, 4 studies (26.7%) used outcomes in both the general health perceptions and functional status health

domains, and 3 studies (20%) used outcomes in both the general health perceptions and symptom status health domain. Three of the fifteen studies (20%) examining post-operative delirium used outcomes from all three health domains (Figure 24). A list of the studies examining post-operative delirium and which health domains were assessed is included in Table 11. The most commonly examined patient- centered outcome category was cognitive function, which was examined in all 15 studies (Figure 25, Table 12). Social function was the least commonly measured patient-centered outcome category, none of the delirium studies used an outcome in the social function category. Three studies measured pain (20%), two studies measured vitality (13.3%), two studies measured physical function (13.3%), three studies measured independence (20%), one study measured psychological function (6%), and three studies measured patient satisfaction (20%). An analysis of all outcomes and tools used by studies examining post-operative delirium can be found in Table 13.
In addition to the 8 identified patient-centered outcome categories, quality of life was a common outcome examined by many studies included in our review, however, none of the of the delirium studies measured quality of life.

Quality of delirium study subset

The quality of each of the 15 delirium studies was assessed using the same criteria as the recovery quality analysis (Table 17) [15]. Studies met between 5 and 9 quality assessment criteria. All studies had a clearly formulated research question. Seventy-three percent of studies were not based on a random/ pseudo-sample and only 20% of studies included a sample of adequate size (n≥

100). The source and method of selection of participants was stated in 81% of studies. All but one study clearly defined the criteria for inclusion and exclusion of participants and outcomes were clearly defined in all but two studies (87%). All studies described the source of their data, however, none of the studies reported confounding factors. When applicable, sufficient group comparisons were conducted in 67% of studies. None of the studies reported outcomes of people who withdrew. Thirty-three percent of studies maintained at least 75% patients throughout follow-up, and none of the studies on delirium reported how missing data was handled. An appropriate statistical analysis was used in 73% of studies and a sensitivity analysis was performed in only 13% of studies examining delirium [15].

VI. DISCUSSION

To our knowledge this is the first systematic review to investigate the use of patient-centered outcomes in the elderly following gastrointestinal surgery. We performed an exhaustive literature search over a period of 20 years evaluating and categorizing the use of patient-centered outcomes in the elderly following surgery.

A. All patient-centered outcome studies

Characteristics of all patient-centered outcome studies

After the 88 articles in our review were examined, it was observed that the majority of studies were published in Europe. As the advantages of using patient-centered outcomes continue to be illuminated and the trend towards using more patient-centered outcomes continues (Figure 10), it may become increasingly important for Canadian researchers to include patient-centered outcomes in their future studies.

A large variation in the number of study participants was seen among studies included in this review. A small sample size limits the conclusion one can draw from any publication. Furthermore, the larger the sample size, the greater the chance that this sample will accurately reflect the population from which the sample was drawn and as a generalization, if feasible, a larger sample size is preferable. Among the studies included in our review, a large number (34%) had between 100 and 999 participants (Figure 5), and 4.5% of studies included more

than 1000 patients. This number likely reflects the difficulty in collecting patient-centered outcome information, which can often be more detailed, labour intensive and much more costly. Studies with more than 1000 participants are often carried out using a retrospective database, which makes the acquisition of multiple data points easier. Most of the studies in this review, however, were prospective (63.3%, Figure 7). Patient-centered outcomes are often collected prospectively because few databases exist that these outcomes, thus limiting the number of patients that can be included. The use of patient-centered outcomes to measure the post-operative course is a relatively new phenomenon, as seen in the peak of publications after 1999 (Figure 10), it is likely that in the coming years we will begin to see more studies using patient-centered outcomes. As the use of these outcomes becomes more ubiquitous, more databases will likely begin to include patient-centered outcomes resulting in studies with larger sample sizes.

Although many of the studies included in this review were prospective, very few were clinical trials (13.6%) or randomized controlled trials (9.1%) (Figure 7). Randomized controlled trials provide the best evidence and causality for clinical practice. If patient-centered outcomes are shown to be a more accurate way of describing the post-operative period, it would be imperative that high quality studies i.e. clinical trials, include patient-centered outcomes in order to ensure accuracy in their results and to provide proper guidance for treatment.

The mean age of study participants in this review was 74.4 years. Although this number, by current convention is considered elderly, it is likely that in the coming years, as the average age of our patients continues to increase, we will need to re-define our notion of what we consider elderly. The elderly are known to have

more co-morbidities and often present symptoms differently, therefore, it is important to ensure that studies which set out to examine the elderly population include elderly patients of more advanced age in order to have results that reflect an aged population and to be generalizable to a wide range of elderly patients [3,4].

Patient-centered outcomes of all studies

The post-operative course often involves the impairment and subsequent recovery in several health domains [12]. Using multiple patient-centered outcomes from several different health domains may provide the most complete picture of the convalescent period in the elderly and may allow clinicians to understand how surgical procedures affect several aspects of a patients overall well-being. In our review, 10.3% of studies used outcomes from all three health domains (Figure 18). If using outcomes from multiple health domains provides the most complete picture of recovery in the elderly, then currently, far too few studies are providing a complete description of the post-operative period in the elderly.

Although independence was the most common patient-centered outcome category assessed, less than 40% of studies used an outcome from the independence category (Figure19). In the elderly, independence is an outcome that often incorporates several other factors including social function and physical function, for this reason, it may be an extremely important patient-centered outcome to assess because it reflects impairment in several other areas. Measuring independence may also be extremely important to measure in the

elderly because they attribute a high level of importance to their independence [3,4].

It is understood that social function, including discharge disposition or requirement for social support (Table 5), is an outcome of major significance to many elderly patients, however, social function was the least commonly examined patient-centered outcome category [6]. Less than 7% of studies measured a patient centered outcome from this category. In order to determine how surgical interventions impact social function in the elderly and make this information available to patients, it is necessary that future studies include a measure of social function as an outcome; this information could be extremely valuable to clinicians and elderly patients of varying levels of social support.

Quality of life assessments often incorporate multiple health domains and patient-centered outcome categories. A breakdown of one of the most common quality of life assessments, the Short Form-36 (SF-36), a questionnaire involving 36 questions regarding symptoms, function, and satisfaction, reveals that questions regarding all three health domains and all 8 patient-centered outcome categories are included. Therefore, if we assume that using PCO from several health domains provides the most complete picture of recovery then it follows that measures of quality of life may also provide a multidimensional description of the post-operative period. This is promising considering one third of studies in this review assessed quality of life. Quality of life assessments are quick, easily administered, and may be the most efficient way to incorporate multiple patient-centered outcomes into a study involving elderly surgical patients.

B. Recovery Study subset

Characteristics of recovery study subset

A subset of 24 studies explicitly examined post-operative recovery in the elderly following gastrointestinal surgery. When compared to all studies, the recovery subset had fewer studies with a follow-up length greater than one year (Figure 11). Forty-three percent of all studies used long-term follow-up lengths compared to 33.3% of studies in the recovery subset. This difference is likely because recovery articles may be more concerned with an immediate return to pre-morbid function, which often occurs in less than one post-operative year [16].

None of the recovery studies had more than 1000 participants (Figure 12) in contrast to 4.5% of all studies (Figure 5). This is likely due to a more detailed analysis in recovery studies, seen by the larger variety of patient-centered outcome categories assessed (Table 10). Using a larger number of outcomes to assess the post-operative period is more labour intensive and costly, and often limits the number of patients that can be included.

Patient-centered outcomes of recovery study subset

Similar to all studies, in the recovery subset, functional status was the most common health domain assessed (Figure 20). However, compared to all studies, of which 69.3% examined functional status (Figure 17), 92% of the recovery subset examined functional status. This difference is likely because most assessments of post-operative recovery examine a return to pre-operative or pre-morbid physical function, a concept included in the functional status health

domain. Unlike all studies, the subset of studies examining recovery had a larger percentage of articles using two or more health domains. Forty-one percent of recovery studies used outcomes from the symptom status and functional status domains (Figure 21) in contrast to 21.6% in all studies (Figure 18). Additionally, 33.3% of recovery studies examined outcomes from the general health perceptions and functional status health domains while 19.3% of all studies did so. Furthermore, 25% of recovery studies (Figure 21) looked at all three health domains in contrast to 10.3% of all studies (Figure 18). One could interpret this difference as demonstrating how recovery studies often describe the post-operative course in multi-dimensional terms. Doing so may offer researchers a broader picture of how surgical interventions negatively or positively impact several domains that would not be captured using traditional outcomes such as length of stay or complications.

Not surprisingly, more than half of all recovery studies (54.2%) examined physical function as a patient-centered outcome (Figure 22). Physical function, including metrics of strength and mobility are very often used among studies examining post-operative recovery. These physical outcomes are often of great importance to elderly patients and are measured as an indication of return to baseline function [2,16]. Compared with all studies, fewer recovery studies examined quality of life (33.3% vs. 16% respectively). The reason for this discrepancy among all studies and recovery studies is unclear.

Quality of recovery study subset

After performing a quality assessment using criteria developed my Vedel et al (Appendix I), it was discovered that studies examining recovery varied in the number of quality assessment criteria that they met [15]. The majority of studies were not based on random samples and, according to the criteria, few studies had adequate numbers of participants. The data source and confounding factors were also sparsely mentioned. Furthermore, when applicable, group comparisons were often inadequately described. Overall, recovery studies did a poor job of describing the outcomes of people who withdrew and the handling of missing data was rarely reported. In addition to the small number of studies that use patient-centered outcomes to evaluate recovery in the elderly, this quality assessment has drawn our attention to the lack of high quality studies that examine recovery using patient-centered outcomes.

C. Delirium study subset

Characteristics of delirium study subset

Considering the high incidence of post-operative delirium among elderly non-cardiac patients, reported to be as high as 40%, it is surprising that so few studies examine delirium using patient-centered outcomes [6]. A subset of 15 studies (17%) among all 88 included in this review, examined post-operative delirium in the elderly following gastrointestinal surgery. The etiology of delirium still remains unclear and studies that examine delirium in the elderly may help to identify pre-operative risk factors for this common post-operative complication.

The mean age of delirium study participants was 68. This value is much lower than the mean age reported among all studies and in the recovery subset (76 and 74.4 years, respectively). Increasing age has been shown to be a significant risk factor in the development of post-operative delirium and it is therefore important that studies examining delirium include patients of more advanced age in order to ensure the accuracy and generalizability of their results [17-24]. In order to have accurate predictions of relative risks and incidences of delirium, studies should strive to include elderly patients from a variety of age groups.

Fifty-three percent of studies examining delirium had a short-term follow up length (<1 month) (Figure 14). This is in stark contrast to studies examining recovery which had an even split of short, medium and long-term studies (Figure 9) and all studies, which had 43.2 % long-term studies (Figure 11). This difference is likely because delirium is a transient and acute condition that often develops and resolves within the first post-operative week. Most studies are primarily

concerned with the initial onset and resolution of delirium and may therefore not perform long-term follow-ups.

Patient-centered outcomes of delirium study subset

Similarly to all studies and the subset of studies examining recovery, the subset of studies examining post-operative delirium used outcomes in the functional status health domain most commonly (73%) (Figure 23). Several studies have reported that delirium is associated with impaired functional status outcomes like independence and cognitive function [17-24]. However, contrary to all of the studies, which examined outcomes in the symptom status health domain least frequently, delirium studies assessed general health perceptions least frequently (24%). This difference was likely because patients with delirium are confused, have altered mental status and are often cognitively compromised, rendering them unable to provide information regarding patient satisfaction and psychological function [17]. In contrast with all studies and the recovery subset, which used outcomes in the symptom status domain in 30.7% and 33.3% of studies respectively (Figure17 and 20), 60% of delirium studies examined outcomes in the symptom status health domain (Figure 23). This may be because studies have shown that pain increases one's likelihood of developing post-operative delirium and therefore many studies examine post-operative pain. Similar to the recovery subset, of which 25% of studies examined all three health domains, 20% of delirium studies used an outcome from all three health domains (Figure 24) nearly twice the proportion of publications from all studies. The reason for this is not entirely clear, however, understanding how delirium impacts

all three health domains could potentially be important information for clinicians and patients and may help the decision making and recovery process.

Not surprisingly, cognitive function was the most common patient-centered outcome category assessed among articles examining post-operative delirium (Figure 25). Studies examining delirium often include a cognitive analysis that involves a pre and post-operative cognitive assessment in order to demonstrate cognitive decline at the onset of delirium. It has been demonstrated that reduced cognitive function is a risk factor for the development of post-operative delirium, a topic that will be discussed in depth in PART 2 and 3 of this thesis [17-24]. It was therefore unsurprising that all delirium studies in this review measured cognitive function, this is likely a reason that functional status was the most commonly assessed health domain among this subset.

In a similar trend with the other analyses (figures 19 and 22) social function was sparsely examined. None of the studies that examined post-operative delirium measured social function. Studies have shown that patients who develop delirium have a significantly higher risk of requiring specialized post-discharge care [17-24]. This decision is often influenced by levels of social support, therefore, understanding how delirium impacts social function and vice versa may help clarify the relationship between delirium and discharge disposition. Additionally, none of the delirium studies examined quality of life, compared to 33% of all studies. This difference likely reflects the singularity and specificity of delirium articles. Understanding how delirium impacts overall quality of life may influence a patient's decision making and in order for patients to have this information available and be better informed, it would be necessary for researchers to include

measures of quality of life in studies that examine post-operative delirium. Furthermore, as Wilson and Cleary suggest, measures of overall quality of life integrate multiple factors that contribute to a patient's post-operative experience [14]. If this is true, then measuring quality of life would provide the most integrated approach to understanding how delirium impacts elderly patients and could be used to optimize recovery and reduce the impact of delirium.

Quality of delirium study subset

Studies examining post-operative delirium met a varying number of the requirements of our quality assessment (appendix I) [15]. The majority of studies did not use a random or pseudo-random sample, and most studies were of inadequate size. None of the studies reported confounding factors, despite the fact that the exact etiology of delirium remains unclear [17]. Only a small number of studies maintained a large percentage of patients-throughout follow-up and no studies mentioned how missing data was handled. Although many of the studies examining delirium were of high quality, several of these studies did not include multiple criteria of our quality analysis. More high quality studies using patient-centered outcomes to examine delirium may be needed in order to provide the most clear, accurate and unbiased information for patients and clinicians regarding the risk factors and potential treatments for delirium.

VII. CONCLUSION

Surgical recovery, the “return to normal physical well-being, social, and economic usefulness, and psychological habitus”, is a process that may be best measured using multidimensional patient-centered outcomes. In this review we have demonstrated that very few studies use patient-centered outcomes to assess the post-operative period in the elderly following gastrointestinal surgery. We have also uncovered that few studies examine recovery and delirium in the elderly and that these studies met a varying number of our quality assessment criteria. Based on an adaptation of the Wilson Clearly model for health related quality of life, we have created a framework to classify patient-centered outcomes. This framework was used to determine which dimensions of the post-operative period were being assessed using patient-centered outcomes. To our knowledge, this is the first systematic review of patient-centered outcomes in the elderly following surgery.

Future work should aim to determine whether using this framework in clinical studies as a design guide will enhance our ability to describe the post-operative period in the elderly. The authors of this review hypothesize that using patient-centered outcomes from several health domains may provide a more complete picture of the post-operative period when compared to traditional outcomes such as complications and length of stay. Additionally, given the variability among the elderly in preference to particular deficits following surgery, having information on the impact of surgery in several domains may prove to be extremely useful information for patients. A more detailed description of the post-operative period

could result in more adequately informed patients and caregivers who have a more realistic idea of what to expect following surgery.

As the geriatric population continues to grow, we will begin to see more and more elderly patients in our operating rooms. Surgical outcomes are used to judge the successes and benefits of our surgical treatments and to enhance the care of our patients; if we expect to reduce the impact of surgery in multiple domains we need to ensure that we use outcomes that are sensitive to changes in these domains. It is our hope that this review encourages researchers to use a greater variety of outcomes that are patient-centered. Ultimately we cannot improve what we do not measure and using patient-centered outcomes from multiple health domains may help us to actually improve these outcomes and allow us to provide elderly surgical patients with the highest quality care possible.

PART 2- PRE-OPERATIVE COGNITIVE IMPAIRMENT AND ITS IMPACT ON POST-OPERATIVE DELIURIM: A PILOT STUDY

I. ABSTRACT

Objectives: Delirium is an acute confusional state and a common post-operative complication among the elderly. Delirium is associated with higher mortality rates, longer lengths of hospital stay and poor functional recovery. The primary objective of this prospective pilot study was to determine the incidences of pre-operative mild cognitive impairment and post-operative delirium among elderly surgical patients at our institution. The secondary objectives were to establish the relationship between pre-operative mild cognitive impairment and post-operative delirium and to measure the impact of delirium on complications and length of stay.

Methods: Between May and August 2010, 35 patients over the age of 70 underwent elective general, colorectal, vascular or ENT surgery. They were pre-operatively assessed for the presence of a mild cognitive impairment using the Montreal Cognitive Assessment (MoCA). Patient characteristics including: Age, gender, level of education, co-morbidities, diagnosis, and procedure were also assessed. Post-operative delirium was diagnosed by the Confusion Assessment Method (CAM). Finally, complications and lengths of stay were recorded.

Results: The mean age of participants was 78 years. Sixty-three percent of patients underwent general surgery, 31% had vascular surgery and 6% had ENT surgery. Twenty-nine of 35 patients (83%) had a mild cognitive impairment. Post-operative delirium occurred in 6 of 35 patients (17%). There was no significant difference in complications among patients with and without delirium; however, patients who developed delirium had a significantly longer length of stay. Patients

with a mild cognitive impairment were not more likely to develop post-operative delirium.

Conclusion: In the patient population at our institution there was a surprisingly high incidence of mild cognitive impairment. MCI did not seem to be associated with delirium in the small sample. Seventeen percent of elderly patients in this study developed delirium.

Résumé

Objectifs: Le delirium est un état confusionnel aigu qui constitue une complication postopératoire courante chez les personnes âgées. Il est associé à des taux élevés de mortalité, des séjours hospitaliers d'une durée plus longue que pour les autres patients et un rétablissement fonctionnel prolongé. Le premier objectif de l'étude pilote prospective était le suivant : déterminer l'incidence de la déficience cognitive légère préopératoire et l'incidence du delirium postopératoire chez les personnes âgées qui ont subi une intervention chirurgicale dans notre établissement. Le deuxième objectif consistait, d'une part, à établir la relation entre la déficience cognitive légère préopératoire et le delirium postopératoire ; d'autre part, à mesurer l'impact du delirium sur les complications et la durée du séjour hospitalier.

Méthodologie: Du mois de mai au mois d'août 2010, 35 patients âgés de plus de 70 ans ont subi une opération ajournable, soit en chirurgie générale, en chirurgie colorectale, en chirurgie vasculaire ou en ORL. Avant l'opération, tous les patients se sont soumis à une évaluation visant à détecter une déficience cognitive légère à l'aide du *Montreal Cognitive Assessment (MoCA)*. Leurs caractéristiques, dont l'âge, le sexe, le niveau de scolarité, les comorbidités, le diagnostic et le type d'opération, ont également été prises en compte. La *Confusion Assessment Method (CAM)* a servi à diagnostiquer le delirium postopératoire. Les complications et la durée de séjour ont été consignées par écrit.

Résultats: La moyenne d'âge des participants de l'étude étaient de 78 ans. Soixante-trois pour cent (63 %) des patients ont subi une intervention en chirurgie générale, 31 % en chirurgie vasculaire, et 6 % une intervention en ORL. Vingt-neuf (29) patients sur 35 (83 %) souffraient d'une déficience cognitive légère. Le delirium postopératoire a été observé chez 6 patients sur 35 (17 %). En ce qui concerne les complications, aucune différence significative n'a été notée entre les patients qui ont souffert de delirium et les autres. Cependant, la durée de séjour des patients qui ont souffert de delirium a été plus longue que la durée de séjour des autres patients. Les patients atteints d'une déficience cognitive légère n'étaient pas plus susceptibles que les autres de développer un delirium postopératoire.

Conclusion: On a noté chez les patients de notre établissement un taux étonnamment élevé de déficience cognitive légère. Cette déficience ne semblait pas associée au delirium, dans notre petit échantillon à tout le moins. Les résultats indiquent que 17 % des patients âgés ayant participé à l'étude ont souffert de delirium.

II. INTRODUCTION

In the systematic review presented in PART 1, we developed a model to categorize patient-centered outcomes into one of three domains: symptom status, functional status, and general health perceptions. We suggest that the picture of recovery may vary depending on the number of health domains that are assessed and that measuring patient-centered outcomes from each of the three health domains in our model may provide the most complete picture of recovery in the elderly following surgery. In order to evaluate this hypothesis, and test the validity and utility of our model, we plan to conduct a prospective study that uses patient-centered outcomes to measure recovery in the elderly. Furthermore, in our review's sub-analysis, we demonstrated that post-operative delirium using patient-centered outcomes has been sparsely studied, despite a high incidence and significant impact in elderly surgical patients. Consequently, we decided to explore the relationship between cognitive function and post-operative delirium to evaluate our patient-centered model of recovery. A general summary of the protocol, which we plan to further develop, is presented in PART 3. Beforehand, in order to power this study, as well as to plan and budget for it, it was therefore necessary to determine the incidences of cognitive impairment and postoperative delirium in our particular patient population. The pilot study that was conducted to provide this information is discussed here, in PART 2.

Background

As the elderly population continues to grow in size, so too will the number of elderly surgical patients. As a result, surgical teams must be prepared to deal with post-operative complications which are common among the elderly [1]. Delirium is an acute confusional state and a common postoperative complication, particularly among elderly surgical patients. Post-operative delirium can occur in as many as 50% of elderly patients following non-cardiac surgery and should be considered a medical emergency [6]. Unfortunately, delirium is often misdiagnosed as depression or goes unrecognized all-together [25]. Delirium is characterized by impaired cognitive function, fluctuating levels of consciousness, reduced focus, and in many cases, perceptual disturbances [17,18]. Delirium is associated with many adverse outcomes including: higher mortality rates, increased risk of postoperative complications, poor functional recovery, longer lengths of hospital stay and a greater likelihood of requiring specialized post discharge care [19]. These adverse outcomes may result in a greater use of resources and a more difficult recovery for the patient. There is a need for a clinically relevant and easy to administer screening tool that can predict post-operative delirium in the elderly. The ability to pre-operatively identify patients who are at risk for delirium would be an invaluable tool that could help direct preventative treatments known to reduce the incidence of delirium and may aid patient decision making.

The etiology of delirium remains unclear, although several risk factors, at every level of surgical care, pre-op, intra-op, and post-op have been identified, including: increasing age, previous alcohol or drug abuse, electrolyte imbalances,

medication use, nutritional state, sensory impairment, functional status, type of surgery, and length of surgery [17-24].

Although several studies have shown that cognitive impairment may increase a patient's risk of developing post-operative delirium, few studies have evaluated the utility of pre-operative cognitive assessments to predict delirium. Among these studies, the Mini-Mental State Examination (MMSE), used to screen for dementia, is the most commonly used cognitive instrument for the prediction of delirium. A study conducted by Veliz-Reissmuller *et al*. in 2007 demonstrated that patients with lower MMSE scores had an increase risk of developing post-operative delirium after cardiac surgery [26]. Although pre-operative cognitive dysfunction has been shown to increase ones risk of developing post-operative delirium, few studies have examined whether patients with a mild cognitive impairment (MCI) are at a greater risk for developing post-operative delirium. Mild cognitive impairment is a transitional state between the normal cognitive decline of aging and the development of dementia and it has been hypothesized that patients with MCI may be at a greater risk of developing delirium. Since MCI is a transitional state before the development of dementia, determining whether patients with MCI are more likely to develop post-operative delirium could provide an earlier screening tool for elderly surgical patients.

Among the studies that examine MCI, the MMSE has been commonly used to identify MCI in patients, unfortunately, it has been shown that the MMSE has limited sensitivity in patients with mild cognitive impairments (MCI), who often score in the normal range on the MMSE [27]; Therefore, a more sensitive cognitive test is required that can identify patients who may score in the normal

range on the MMSE but may still be at an increased risk of developing post-operative delirium. The Montreal Cognitive Assessment (MoCA) is a brief cognitive exam that has been shown to be more sensitive than the MMSE and is able to detect MCI with 90% sensitivity [28]. Unlike the MMSE, the MoCA is specifically designed to identify MCI, however to our knowledge, the MoCA has never been used to predict delirium in elderly surgical patients.

III. OBJECTIVES

The goal of this pilot study was to establish the parameters necessary to power and conduct a larger prospective study that will examine whether the Montreal Cognitive Assessment (MoCA), can predict the incidence of delirium in elderly surgical patients and whether measuring patient-centered outcomes from each domain of our model provides a more complete description of recovery. Accordingly, this pilot study's had two main objectives:

1. The primary objective was to determine the incidence of pre-operative mild cognitive impairment and post-operative delirium in our patient population.
2. The secondary objectives were to establish the relationship between pre-operative MCI and post-operative delirium and to measure the impact of delirium on traditional outcomes such as: morbidity (complications) and length of stay.

IV. METHODS

Study Participants

We sought to enroll 40 consecutive patients, being evaluated at our institution's Pre-admission Testing Center, and meeting the following inclusion criteria:

- Aged 70 years or more
- Fluent in French or English
- Undergoing elective surgery in general, colorectal, vascular, gynecological, or urological surgery
- Expected length of stay of at least two days

Patients were excluded if they met the following criteria:

- Evidence of pre-operative delirium
- Known active and untreated psychiatric disorder
- Sensory impairment
- Known dementia or an adjusted Mini-Mental State Exam (MMSE) score below 23
- Refusal to participate in pre or post-operative assessments
- Inability to complete the MoCA or MMSE

Written informed consent was obtained from all patients. The study design was approved by the ethics review board at the Jewish General Hospital (protocol #: 10-053).

Cognitive Measures

All pre and post-operative cognitive assessments were performed by the same research assistant trained to administer the following three measurement tools: the MoCA, MMSE, and Confusion Assessment Method (CAM) (appendix II).

1. MMSE

The MMSE is a brief assessment of mental status that has been validated to be used to detect cognitive impairment. The MMSE comprises 11 questions that assess 5 areas of cognitive function including: orientation, registration, attention and calculation, recall, and language. In our study the MMSE was administered to determine whether patients had pre-operative dementia and to serve as a standard by which to compare the MoCA. Any raw score above 23 (out of a possible 30) was considered normal. Adjusted MMSE scores were calculated after adjusting cut-offs scores for age and level of education [29].

2. MoCA

The MoCA is a brief cognitive screening test that has been validated to be used to detect mild cognitive impairment. The MoCA assesses the following cognitive domains: attention and concentration, executive function, memory, language, visuo-constructional skills, conceptual thinking, calculations, and orientation. In our study the MoCA was used to identify patients with a mild cognitive impairment. The MoCA was scored after adding a point if the study participant had less than twelve years of education. Any score equal to or above 26 (out of a possible 30) was considered normal [28].

3. CAM

The confusion assessment method is a brief screening tool that has been validated to be used to diagnosis delirium. The CAM uses four characteristics including: 1. Evidence of an acute change in mental status. 2. Difficulty focusing attention. 3. Disorganized thinking. 4. Altered level of consciousness. The diagnosis of delirium requires a present/ abnormal rating of criteria 1 and 2 and either 3 or 4 [22].

Data collection

Pre-operative assessments

Pre-operative assessments included the MMSE, MoCA and CAM. Baseline assessments of patients were performed at the Pre-admission Testing Centre at least one week before the planned surgery. Demographic data were collected including: age, gender, co-morbidities index (from which the Charlson Comorbidity Index was derived), education level, diagnosis, and procedure type. The MMSE, and MoCA were administered consecutively, after which, the CAM criteria were applied [30].

Post-operative assessments

Post-operative assessments were aimed to identify the presence of post-operative delirium. Assessments began the day after surgery and were performed at the patient's bedside, daily, for one week or until discharge, whichever came first. Patients were considered to have delirium if they tested positive on the CAM. All diagnoses of delirium were confirmed by a clinician.

Charts were reviewed and any post-operative complication was recorded, as was length of hospital stay.

Quality Assessment

A self assessment of study quality was performed based on the 15 criteria used to assess study quality in PART 1. The quality assessment , developed by Vedel *et al.,* is a combination of the MAStARI-SUMARI, STROBE and MOOSE quality assessments tools (Appendix I) [15].

Statistical analysis

Overall incidence of pre-operative MCI and post-operative delirium were calculated. A descriptive analysis was performed on the demographic and pre-operative cognitive assessments, stratified by the presence or absence of delirium. Logistic regression analysis was performed with delirium (yes/no) as the dependent variable. Odds ratios and 95% confidence interval ($\alpha = 0.05$) for the following independent variables were calculated: age, gender, CCI, and MCI. Complication rates and length of stay were compared between those with and without delirium using Pearson's Chi-square and Student's t-test, respectively. A p value < 0.05 was set as the criterion for significance. The software used for analysis was IBM PASW Statistics 18 (Somers, NY).

V. RESULTS

Recruitment and enrollment

Between May and August of 2009, 162 consecutive patients were approached to take part in the study. One hundred twenty-two patients were not enrolled for the reasons listed in Figure 26. Forty patients underwent pre-operative assessments, however, 5 patients were excluded from the final analysis for the following reasons: three of these patients had a length of stay less than two days, one patient died before undergoing surgery and one patient underwent emergency surgery before their elective operation (Figure 26). There was no significant difference, with respect to baseline characteristics, between the 5 excluded patients and those patients included in the final analysis of this study. All 35 patients enrolled in the study were maintained throughout the study period, no patients withdrew, additionally, there was no missing data for patients included in the final analysis.

Demographic information

The MoCA and MMSE were administered in English in 80% of patients and in French in the remaining patients. The mean age of study participants was 78.3 ± 5.6 years. Seventeen patients were male (49%), and the average Charlson co-morbidity index was 2.3 ± 1.9. One patient (2.8%) had no formal education, 14 patients (40.0%) completed elementary school, 12 patients (34.3%) completed high school and 8 patients (22.9%) completed university. Twenty-two patients (64.7%) underwent general surgery, 11 patients (31.4%) underwent vascular

surgery and 2 patients (5.7%) underwent ENT surgery. The indication for surgery was cancer in 23 (65.7%) patients. All patients either underwent surgery for cancer or vascular disease. All general surgery/ENT patients had a diagnosis of cancer, whereas, none of the vascular patients had cancer.

Pre-operative cognitive assessment

None of the patients included in this study were diagnosed with pre-operative delirium. The mean pre-operative MoCA score was 21.8 ± 3.7. Twenty-nine of the 35 patients scored below normal on the MoCA, which corresponded to an 82.8% incidence of mild cognitive impairment. The mean pre-operative MMSE score was 27.5 ± 1.7 (Table 18).

Post-operative cognitive assessment

Post-operative delirium occurred in 6 patients (17.1%). Delirium lasted for one day in all patients. In 5 of the 6 patients (83%) who developed delirium, the first diagnosis was made on post-operative day 1. The remaining patient presented with delirium on post-operative day 2 and again on day 5. The diagnosis of delirium was made by the investigators, using the CAM in all cases. In addition, amongst those patients, two were physically and chemically restrained.

Complications and length of stay

5 patients (14.2%) developed post-operative complications including: a stroke, unplanned intubation, a urinary tract infection (UTI) and two deaths (beyond the one week follow-up period). Lengths of stay, measured from admission to

discharge, ranged from 4 (the minimum required) to 54 days. The mean length of stay was 12.7±10.8 days.

Impact of delirium

When comparing baseline characteristics between patients who developed delirium and those who did not, there was a trend towards patients with delirium being older, more often female, less educated, suffering from a greater comorbid disease burden, and more often being associated with vascular or ENT procedures (Table 18). However, neither age, gender, CCI, MCI, or procedure type were significantly associated with the development of post-operative delirium when included in the logistic regression model.

Among those who developed delirium, one patient (16.7%) developed a post-operative complication (stroke). Among those who did not develop delirium, 4 patients (13.8%) developed post-operative complications; one patient had a UTI, one had an unplanned intubation, and 2 patients died (beyond the one week follow-up). The difference in complications among patients with and without delirium was not statistically significant (p= 0.7), however, patients who developed delirium had a significantly longer length of hospital stay (22.7±17.4 vs. 10.7±7.9 days, p=0.01).

Quality assessment

This study met all but three criteria of our quality assessment in PART 1. Missing criteria included: inadequate sample size (less than 100 patients), non-random sampling, and no sensitivity analysis.

VI. DISCUSSION

Mild cognitive impairment

The most unexpected and notable finding in this pilot study is the strikingly elevated incidence of MCI, which occurred in 83% of patients. This figure is much higher than what has been previously reported in the general population. A systematic review of incidences of mild cognitive impairment conducted by Luck *et al*. in 2009 reported an incidence of mild cognitive impairment between 1.7 and 22.6% [31]. This is a significant and somewhat worrisome finding considering none of these patients had a previous diagnosis of MCI, thought by some to be a precursor to dementia.

All patients with a mild cognitive impairment and all patients who developed delirium scored in the normal range on the MMSE. This result is consistent with the finding of others demonstrating that the MMSE is not sensitive enough to detect MCI since patients with MCI often score within the normal range [28]. There are several possible reasons to explain such an unusually high incidence of MCI. Firstly, this pilot study only examined a small number of patients and it is certainly possible that our sample was not representative of the population at large. In this case, a larger sample size would better reflect the true prevalence of MCI. Secondly, the high incidence of mild cognitive impairment could be explained by the adjustment techniques for level of education used on the MoCA. Unlike the MMSE, which lowers cut-off scores based on increased age and a lower level of education, the MoCA adds a point to the score of each participant with a level of education below 12 years. Preliminary research currently being

conducted by Phillips et al., the developers of the MoCA, may suggest that a change in cut-off score, taking into education, could reduce the number of misdiagnoses of mild cognitive impairment, however, this has yet to be confirmed (Chertkow, H., personal communication). It has also been suggested, that additional points should be added for very low level of education, between 4-9 years [32]. Thirdly, the high incidence of MCI could be due to improper administration of the MoCA by non-clinical researchers; however, the MoCA is fairly objective and easy to administer and our researcher had been well trained prior to starting the study. In addition, studies by Gill *et al*. in 2008 have demonstrated excellent inter-rater and test-retest reliability on the MoCA; However, this study does not specify whether or not the MoCA was administered by non-clinicians [27].

An interesting alternative to consider is that the 83% incidence of MCI may be accurate. All of the patients in our study either underwent surgery for vascular issues or a diagnosis of cancer. It has been suggested that patients with chronic vascular problems or cancer, such as those included in our study, are at a greater risk for developing cognitive impairments [33]. These factors could, in part, explain the unusually high incidence of mild cognitive impairment in our patient population.

A study conducted by Tervo *et al*. concluded that vascular factors may play an important role in the development of MCI [34]. This study proposes that cognitive impairment among patients with vascular problems could be a result of impaired cerebral perfusion or sub-clinical, non-symptomatic (silent) strokes. Additionally, a study conducted by Beeri *et al*. in 2009 demonstrated that patients with chronic

vascular problems such as hypertension and type II diabetes were at a greater risk for developing mild cognitive impairment [33].

Cancer has also shown to be a risk factor for MCI. A study conducted by Pereira *et al.* in 1997 demonstrated that there was an increased incidence of cognitive impairment among elderly cancer patients on their ward [34].

Delirium

Seventeen percent of our patients developed post-operative delirium. This incidence was comparable to previous studies examining post-operative delirium in elderly non-cardiac patients, which have reported an incidence of between 15-40% [6].

Patients who developed delirium seemed to be slightly older, were more often female, had higher mean Charlson co-morbidity indices, had more vascular procedures and were on average less educated. However, this did not reach significance in our model. This is in contrast to several studies, which have shown age, co-morbidities, and a low level of education to be important risk factors for the development of post-operative delirium [17-24]. On average, patients who developed post-operative delirium had lower MoCA scores, however, MCI was not significantly associated with the development of post-operative delirium. These results were unsurprising considering the small sample size and high incidence of MCI in our patient population. It is nevertheless interesting to note that among the patients that developed post-operative delirium, only one did not have a mild cognitive impairment.

Post-operative delirium is known to be associated with several adverse outcomes

including higher morbidity (complications), mortality, and length of stay; however, among our patient population, delirium was not significantly associated with complications. This result is likely due to the small sample size and small number of patients who developed post-operative complications. In our population, the development of delirium was associated with significantly longer lengths of hospital stay; this result was expected based on previous scientific literature [17-24].

Quality assessment

When compared to the studies examining post-operative delirium in PART 1, our pilot study was of relatively high quality, despite missing three quality assessment criteria (appendix II) [15]. First, our sample size was less than 100 patients; however, this was a pilot study that was meant to power a future large prospective study that will include at least 100 patients. Second, patients were not randomly selected. Although patients were enrolled consecutively from the Pre-admission Testing Centre at our institution, which has some degree of randomness, it is possible that this sample was not representative of the larger population as a result of a sampling bias. Third, a sensitivity analysis was not performed. A sensitivity analysis was beyond the scope and objective of this pilot study and will be included in future studies.

Feasibility

Non-clinical interviewers were able to carry out pre-operative cognitive assessments of elderly surgical patients at our institution's Pre-admission Testing Centre. Additionally, all diagnoses of post-operative delirium by interviewers, using the CAM, were confirmed by a clinician. This demonstrates that our interviewers were able to accurately perform post-operative bedside assessments for delirium on the recovery ward. The assessment of pre-operative cognitive function and post-operative delirium by non-clinician interviewers in our hospital setting is both effective and feasible for the larger prospective study proposed in PART 3.

Limitations

This study carries important limitations that must be acknowledged. Because the objective of this small pilot study was to provide the necessary information to conduct a larger prospective study, the small sample size limited the quality of the analysis and the conclusions that could be drawn from our results. The small sample size likely affected the predictive value of our risk factors, including MCI, as well as the true magnitude of the impact of delirium. Other limitations include the fact that interviewers were not blinded to the pre-operative cognitive scores of patients. The same interviewers performed both pre and post-operative assessments in order to establish whether a change in baseline mental status had occurred. Although the CAM criteria allow researchers to objectively identify the presence of delirium, previous knowledge of cognitive scores could have biased the diagnosis of delirium. In addition this study did not collect information

on several known risk factors for delirium, including: intra-operative blood loss, operative time, pre-operative functional limitations, history of prior delirium or alcohol abuse, BUN/Cr ≥18, and use of narcotic analgesics or benzodiazepines [17-24]. All of these factors have been shown to increase one's risk of developing delirium and it is possible that there was a significant difference in some of these factors among patients who developed post-operative delirium and those who did not. If a significant difference between the two groups did exist with regard to one or more of these factors, this could have confounded our results.

VII. CONCLUSION

This pilot study has uncovered a surprisingly high incidence of mild cognitive impairment among elderly surgical patients at our institution; 83% of our patients had a mild cognitive impairment. In our patient population, the incidence of post-operative delirium was 17% and patients who developed delirium had significantly longer lengths of hospital stay. Furthermore, MCI was not predictive of delirium; however, due to the small number of patients in this study and the high incidence of MCI, this relationship still remains unclear.

This study serves to provide the information necessary to power a larger prospective study which will examine the relationship between MCI and delirium and confirm or refute our finding of a very high incidence of MCI. The future study will also attempt to test our model of patient-centered outcomes.

PART 3- FUTURE DIRECTIONS: PROSPECTIVE STUDY

I. INTRODUCTION

The ability to pre-operatively identify patients at risk for developing delirium using a simple cognitive exam, such as the MoCA, could help target patients that would benefit from particular interventions that are known to help reduce the incidence of delirium. Additionally this information could be used to help the decision making process and better inform patients of the risks of surgery.

Additionally, if we can demonstrate that using patient-centered outcomes from all three health domains provides the most complete picture of surgical recovery in the elderly, then we will be able to establish the validity of our model. A more detailed description of the post-operative could allow patients to have a more realistic idea of what to expect following surgery. Our model could also be used as a guideline for future study design and as an assessment tool to determine if the recovery is being adequately assessed.

Our larger prospective study will improve on the limitations of the pilot study in PART 2 by increasing the sample size, randomly enrolling patients, blinding researchers to pre-operative cognitive status, including more pre, intra and post-operative risk factors for delirium, and including a sensitivity analysis.

II. OBJECTIVES

The following is a protocol skeleton for a longitudinal study of the relationship between MCI and delirium and the impact of delirium on recovery using patient-centered outcomes according to our model. This protocol is still in its infancy and is subject to change.

1. The primary purpose of this study is to determine whether mild cognitive impairment, as measured by the Montreal Cognitive impairment (MoCA), can predict the incidence of post-operative delirium in elderly surgical patients.
2. The secondary purpose is to test the validity of our model by determining how the picture of recovery changes with the number of health domains that are assessed and whether measuring patient-centered outcomes (PCOs) from all three health domains provides a more complete picture of recovery in the elderly.

III. METHODS

Study population

100 patients over the age of 70, randomly selected from patients presenting to the Pre-admission Testing Centre at our institution, at least one week before surgery and meeting the following inclusion criteria:

- Aged 70 years or more
- Fluent in French or English
- Elective surgery in general, colorectal, vascular, gynecological, orthopedic or urological surgery
- Expected length of stay of at least two days

Patients will be excluded if they meet the following criteria:

- Evidence of pre-operative delirium
- Known active and untreated psychiatric disorder
- Sensory impairment
- Known dementia or an adjusted Mini-Mental State Exam (MMSE) score below 23 Refusal to participate in pre or post-operative assessments
- Inability to complete the MoCA or MMSE

Pre-operative measurements

Patients will be pre-operatively assessed in the Pre-admission Testing Centre at our institution, at least one week before surgery. Demographic data collected will include: age, gender, co-morbidity index (from which the Charlson Comorbidity Index was derived), education level, diagnosis, and procedure type.

Patients will be assessed for the presence of a mild cognitive impairment using the MoCA. Pre-operative assessments will be conducted by two interviewers, one of which will be blinded to the results of the MoCA score. Patients will also be pre-operatively assessed for the following risk factors for post-operative delirium:

- nutritional status and BUN/Cr level
- history of prior delirium or alcohol abuse
- Use of narcotic analgesics and/or benzodiazepines.

Based on our proposed model, we will pre-operatively measure all 8 patient-centered outcome categories from all three health domains.

Patient centered outcomes from the functional status health domain include:

- physical function (grip-strength)
- independence (Katz index for activities of daily living)
- cognitive function (MoCA)

Patient centered outcomes from the symptom status health domain include:

- pain (McGill pain questionnaire)
- vitality (Short-Form 36 vitality score)

Patient centered outcomes from the general health perceptions health domain include:

- patient satisfaction (patient satisfaction questionnaire)
- social function (social functioning questionnaire)
- psychological function (geriatric depression scale)

Intra-operative measurements

All intra-operative measurements will be collected from operative reports based on a review of the patient's chart. Intra-operative measurements collected are factors known to increase a patient's risk of developing post-operative delirium including:

- blood loss
- anesthesia type
- operative time

Post-operative measurements

Patients will be assessed daily for delirium for one week or until discharge (whichever comes first) using the using the Confusion Assessment Method (CAM). Post-operative assessments will be conducted by the interviewer who was present for pre-operative assessments; however, to limit bias, this interviewer will be blinded to the pre-operative MoCA scores of patients. Post-operative patient centered outcomes measured will be the same as those that were measured pre-operatively. All 8 patient-centered outcomes will be assessed on post-operative days 1, 7 and 14. As well as 1, 3, 6 and 12 months post-operatively.

Traditional outcomes measured will be determined from a review of the patients chart, these include**:**

- complications
- length of stay
- mortality

IV. ANALYSIS

Sample size

Based on the results of our pilot study in PART 2, we would require 61, 000 patients to be able to detect a significance of p=.05 with a power of 80%.

This sample size is not feasible and is a result of the very high incidence of mild cognitive impairment in our patient population.

In PART 2 it was suggested that the high incidence of MCI could be, in part, because all of our patients either had a diagnosis of cancer or were undergoing vascular procedures. In order to obtain a much more reasonable estimate of the sample size, a more varied patient population should be used, one which includes patients who do not have cancer or vascular issues and who will likely have smaller incidence of MCI.

In our pilot study we excluded orthopedic patients, however, orthopedic patients make up a large proportion of surgical procedures in the elderly. We suggest including a cohort of orthopedic patients who do not have cancer or vascular issues. This will help to reduce the incidence of MCI. Additionally, several studies have shown that there is an increased incidence of post-operative delirium among orthopedic patients, when compared to patients undergoing general surgical procedures. A review of 12 studies conducted [37] found an average incidence of delirium of 35% among hip fracture patients.

Including orthopedic patients with a reduced incidence of mild cognitive impairment and an increased incidence of post-operative delirium may help reduce the overall incidence of MCI and increase the overall incidence of post-

operative delirium, therefore reducing the sample size required.

In order to get an estimate of the effect of including orthopedic patients on our sample size requirements, we will first enroll 35 orthopedic patients following the same protocol as our pilot study. The incidences of MCI and delirium among this orthopedic population will be used together with the results of our pilot study in order to determine the sample size required to power our future study.

Based on a study conducted by Kalisvaart *et al.* who examined the relationship between pre-operative cognitive impairment (using the MMSE) and delirium in elderly orthopedic patients, we can expect an incidence of pre-operative cognitive impairment of approximately 25% and an incidence of post-operative delirium of around 12% [36]. Based on a combination of the results of this study and our pilot data, we expect that 65% of patients who develop delirium will have pre-operative cognitive impairments, while approximately 29% of patients without delirium will have pre-operative cognitive impairments. Using these incidences and the results our pilot study, it can be estimated that we would require a minimum of 39 patients total to be able to detect a significance of p=.05 with a power of 80%. In order to meet the requirements of the quality analysis from PART 1, we will attempt to include 100 patients in our larger prospective study.

Statistical analysis

A descriptive analysis will be performed on demographic and all pre-operative assessments, stratified by the presence or absence of delirium.

Logistic regression analysis will be performed with delirium (yes/no) as the dependent variable.

Complication rates, mortality and length of stay will be compared between those with and without delirium using Pearson's Chi-square and Student's t-test, respectively. A p value < 0.05 will be set as the criterion for significance. Additionally, a sensitivity analysis will be performed for all patient-centered outcome measurements.

Patient-centered outcome comparison

All patient-centered outcomes will be compared to baseline assessments in order to determine if there has been a change following surgery and recovery curves will be drawn. Recovery will be considered complete for individual outcomes when they have returned to baseline. Overall recovery will be defined as all outcomes having returned to baseline. We will compare individual outcome and health domain recovery between one other and to overall recovery. Additionally, comparisons will be made between health domains in order to determine if differences exist based on the number of health domains assessed. We will determine if health domains fluctuate in parallel post-operatively and if clinically relevant information is gained from the measurement of particular patient-centered outcomes.

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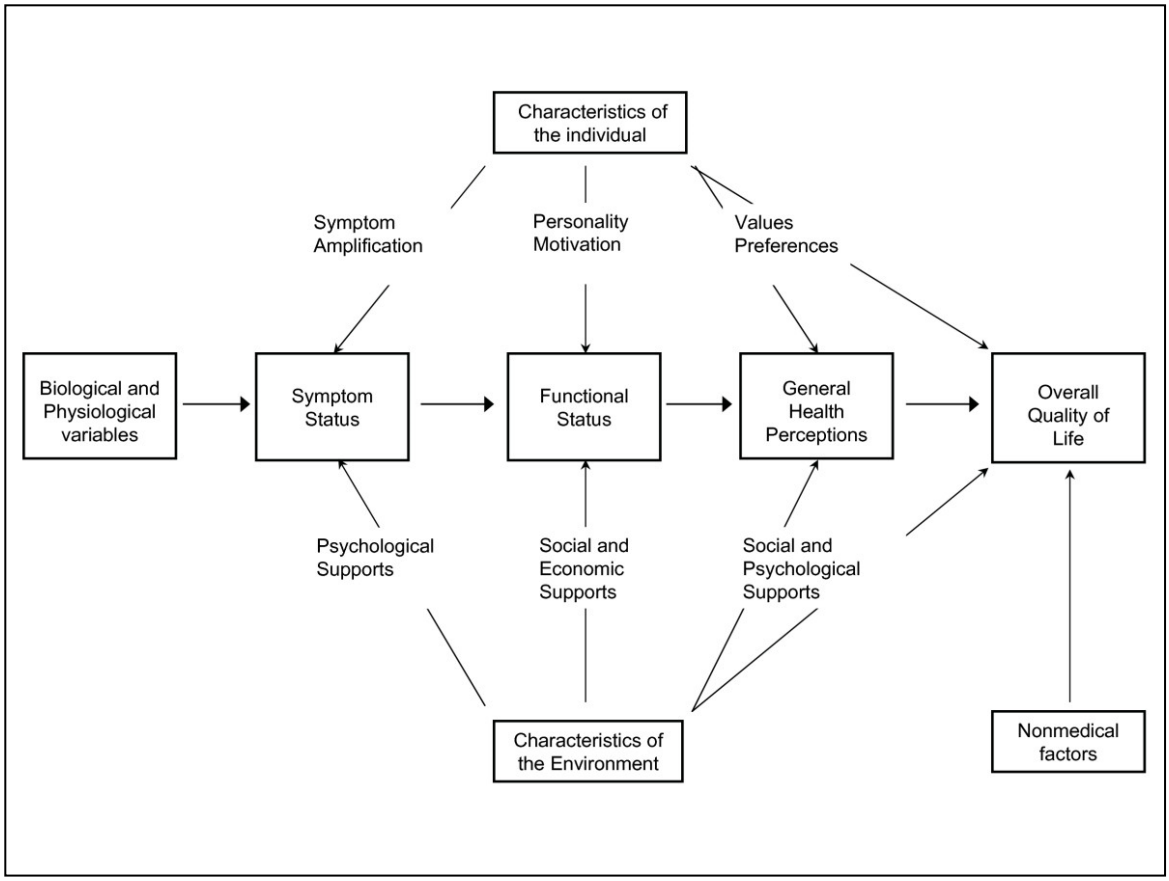
FIGURES AND TABLES

<u>Figure 1.</u> The Wilson-Cleary model for health related quality of life.



<u>Figure 2.</u> A framework to classify all patient-centered outcomes into one of three health domains. Health domains incorporate 2-3 patient-centered outcomes. Adapted from the Wilson-Cleary model of health related quality of life (Figure 1).

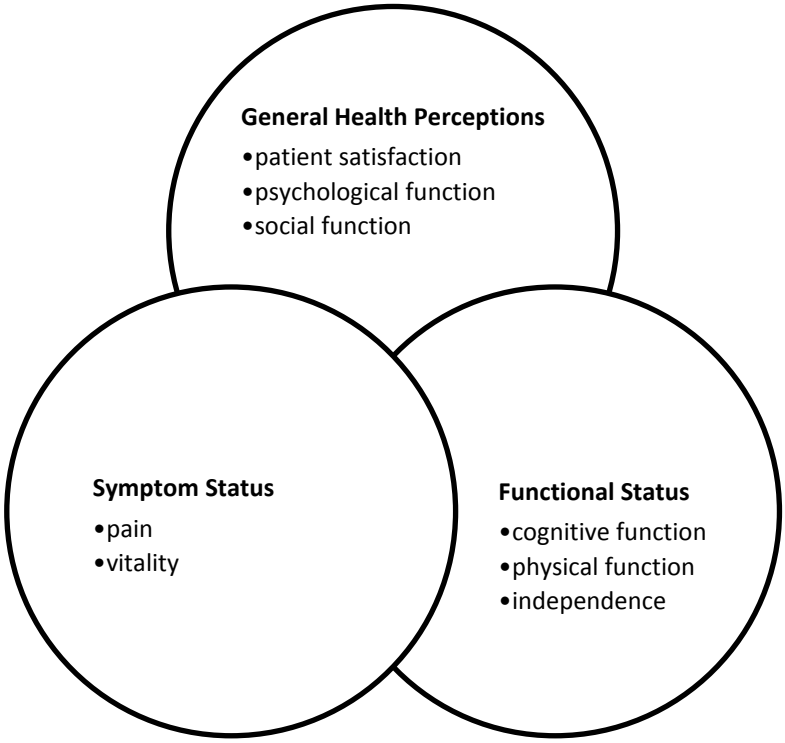


Figure 3. A flow-chart of the study inclusion and exclusion procedure.

Potentially relevant MEDLINE reference titles identified and reviewed (n=2980)

Studies excluded after reviewing the title (1400)

Reasons for exclusion:

Not elderly: 220 (16%)
Not GI surgery: 441 (31%)
Not a PCO: 463 (33%)
A review or Case study: 95 (7%)
Not human: 21 (2%)
Not English: 78 (6%)
Miscellaneous: 82 (6%)

Potentially relevant reference abstracts reviewed (n=1580)

Studies excluded after reviewing the title (1484)

Reasons for exclusion:

Not elderly
Not GI surgery
Not a PCO
Review or Case study

Potentially relevant reference abstracts reviewed (96)

Studies excluded after reviewing the title (27)

Studies excluded after reviewing the full text (52)

Reasons for exclusion:

Not elderly
Not GI surgery
Not a PCO
Review or Case study

Studies included (n=71).

Addition from References (n=17).

Total (n=88)

Figure 4. **Values indicate the number of publications from initial search excluded based on titles alone.**

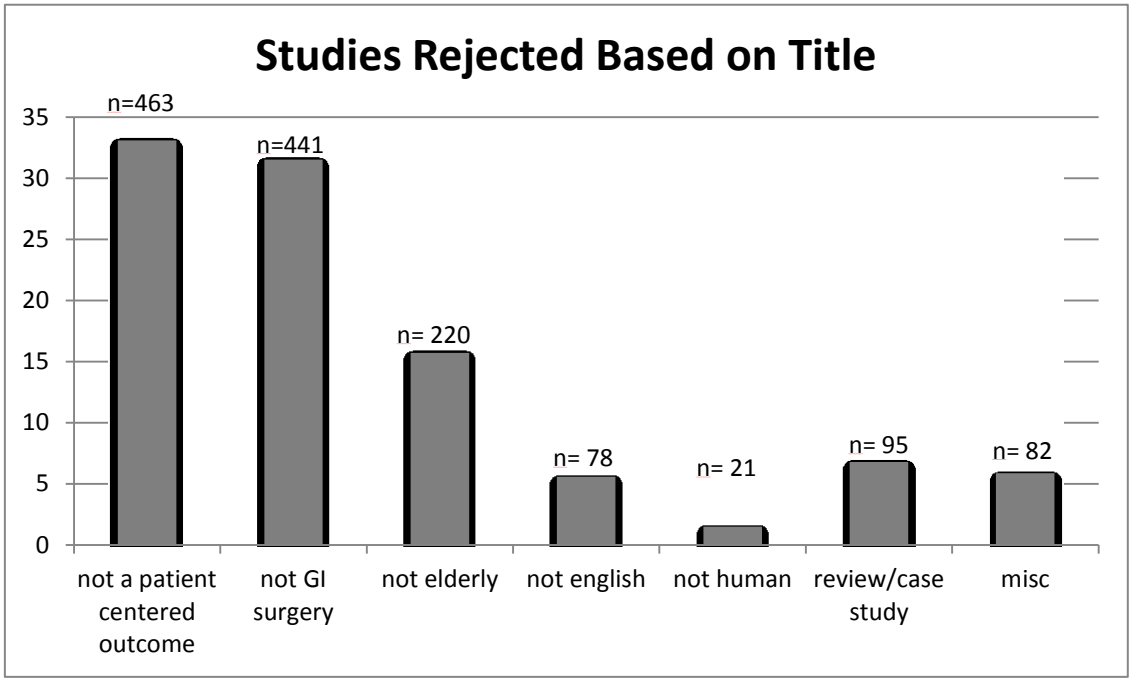


Figure 5. **Values indicate the number of accepted publications with a given number of participants.**

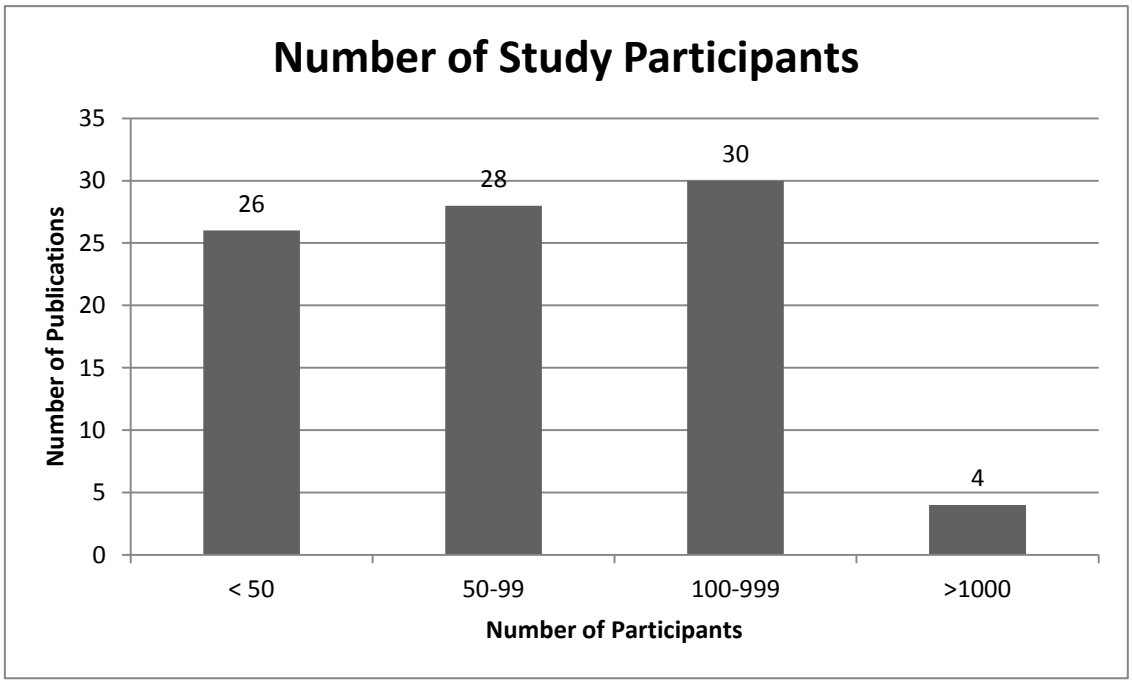


Figure 6. **Values indicate the number of publications which have a mean study population age in their fifties, sixties, seventies or eighties.**

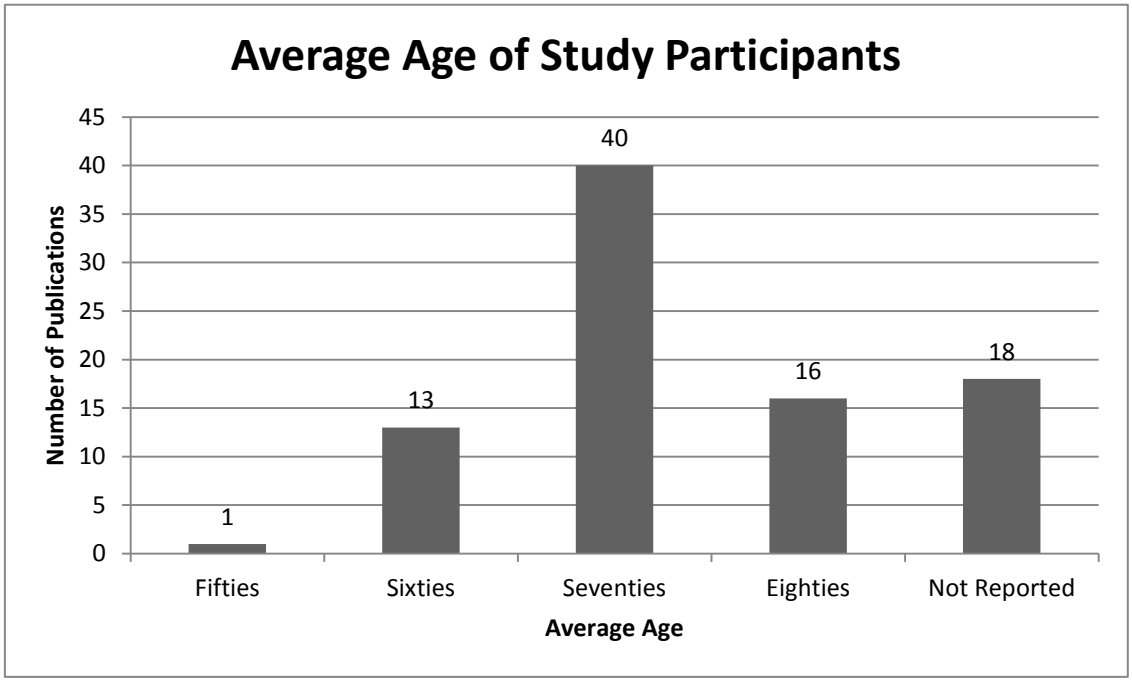


Figure 7. **Values indicate the number of publications with a given study type.**

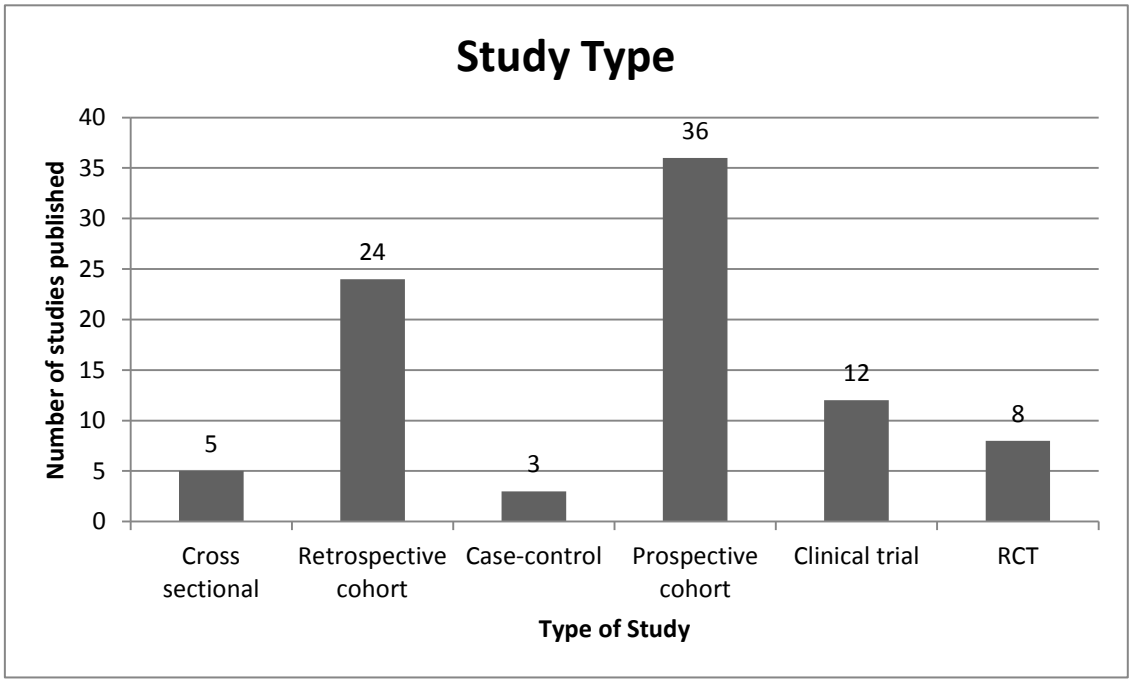


Figure 8. **Values indicate the number of publications, among accepted studies, with a given indication for surgery.**

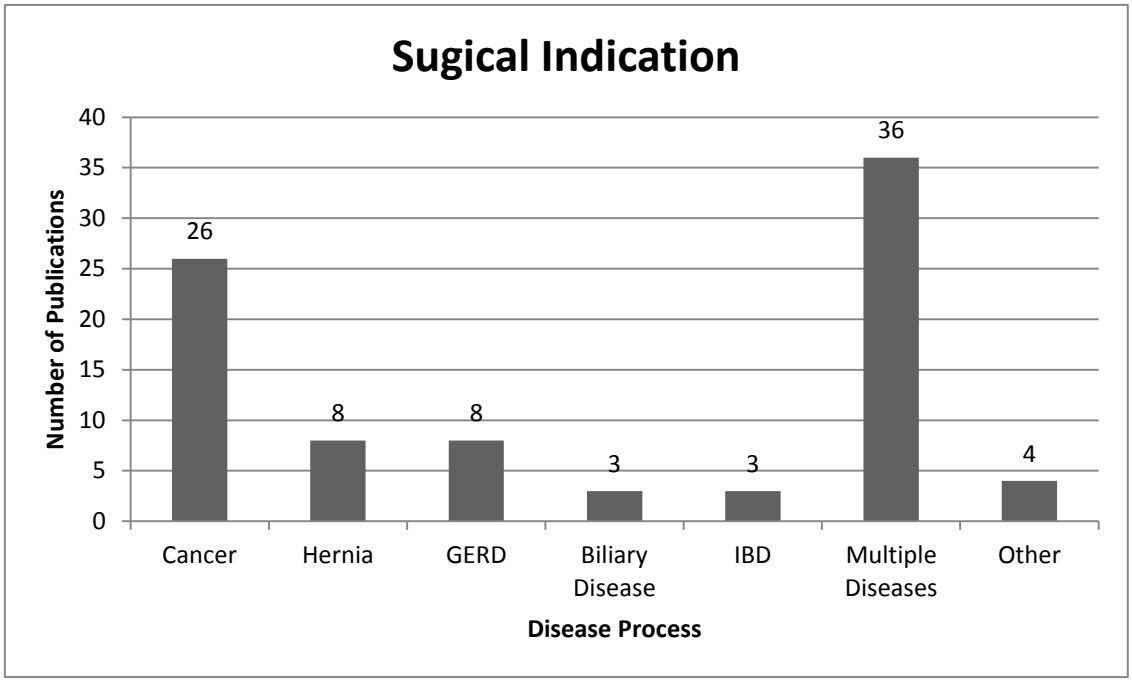


Figure 9. **Values indicate the number of publications with a short, medium or long term follow-up length. Short term, medium term, and long term follow-up lengths were : <1 month , 1 month to 1year and >1 year respectively.**

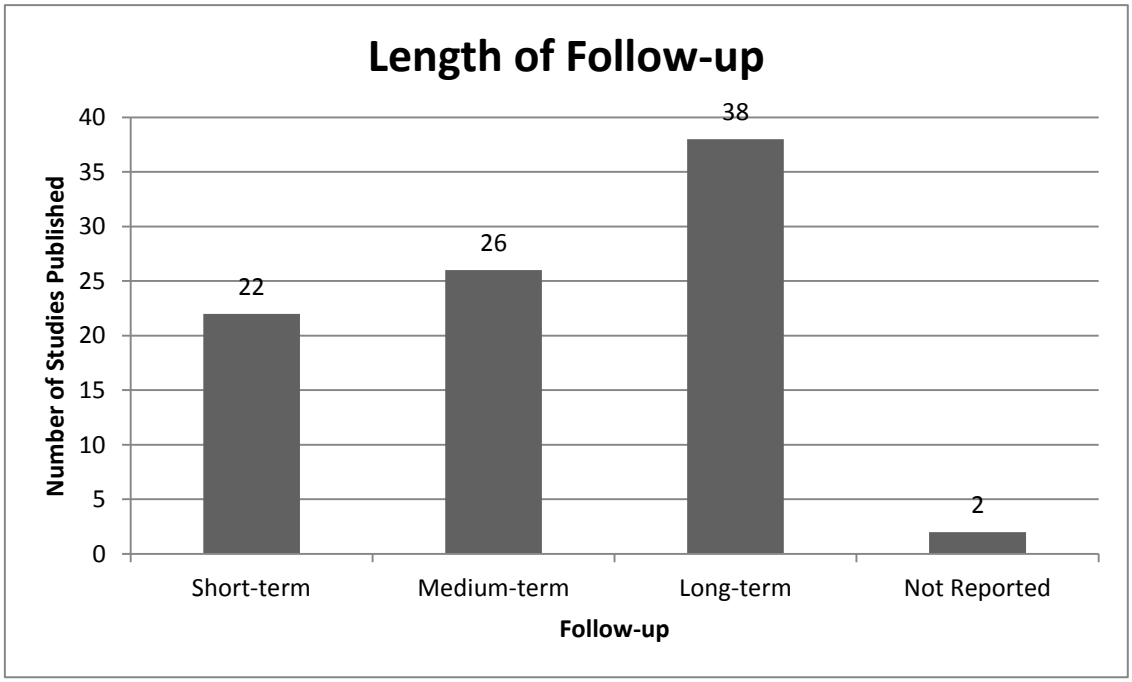


Figure 10. **Values indicate the number of studies published each year, among accepted publications.**

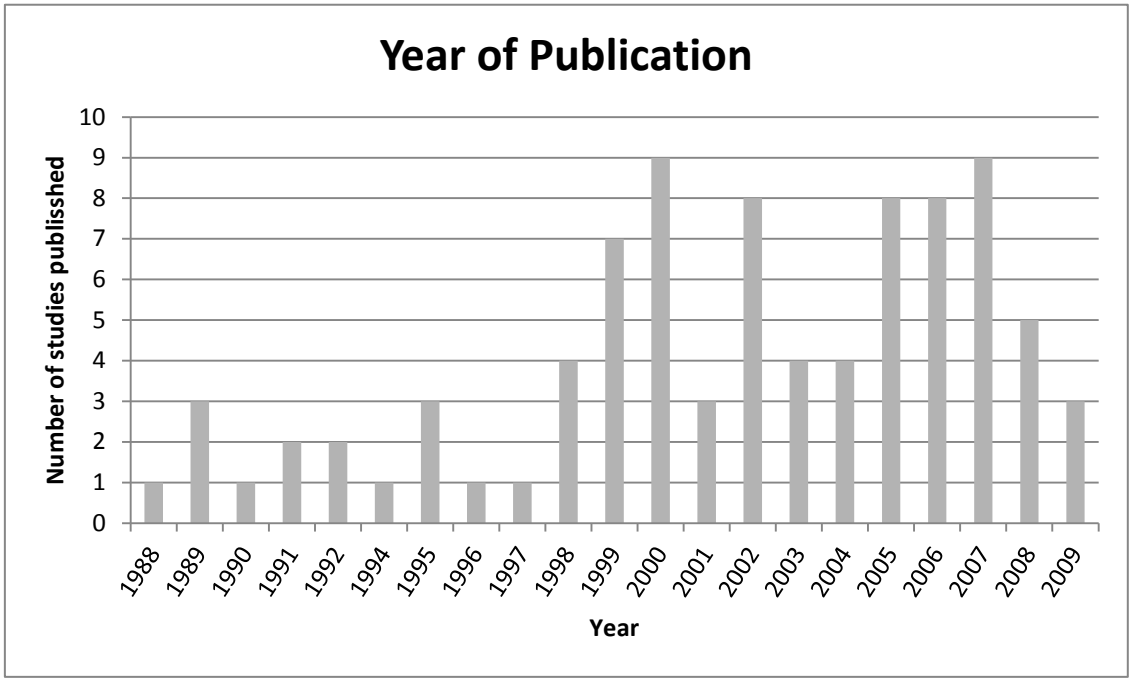


Figure 11. **Values indicate the number of publications with a short, medium, or long term follow-up length, among the subset of studies explicitly examining recovery. Short term is <1 month, medium is 1 month to 1year, and long term is >1 year.**

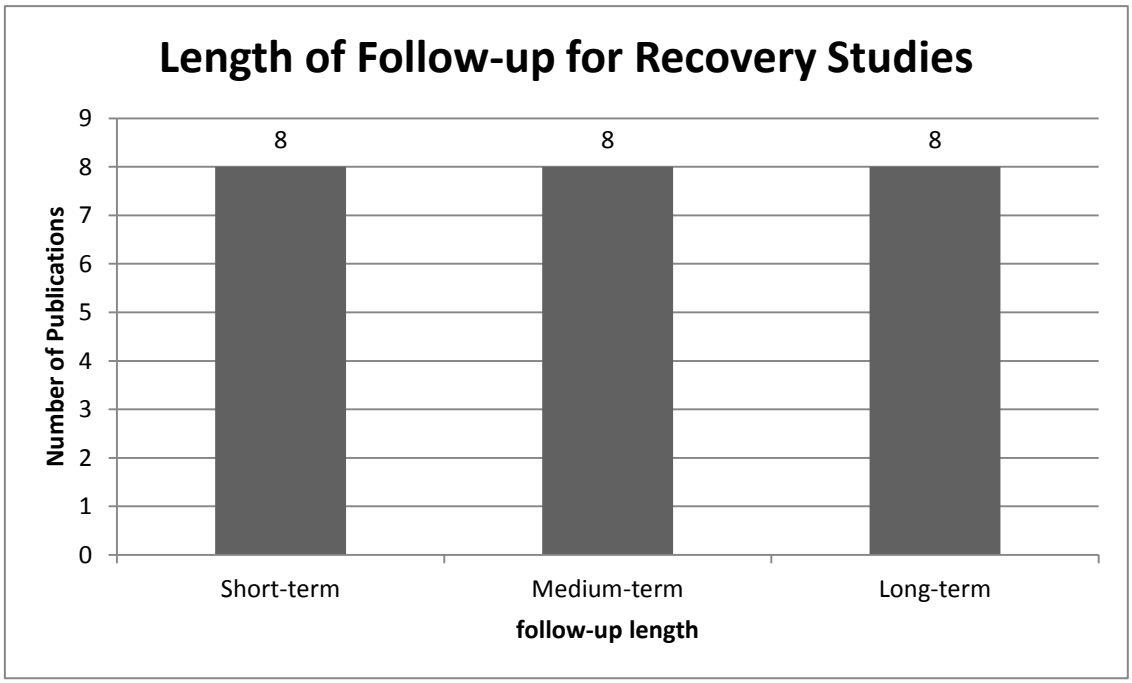


Figure 12. **Values indicate the number of publications with a given number of participants, among the subset of studies that explicitly examined recovery.**

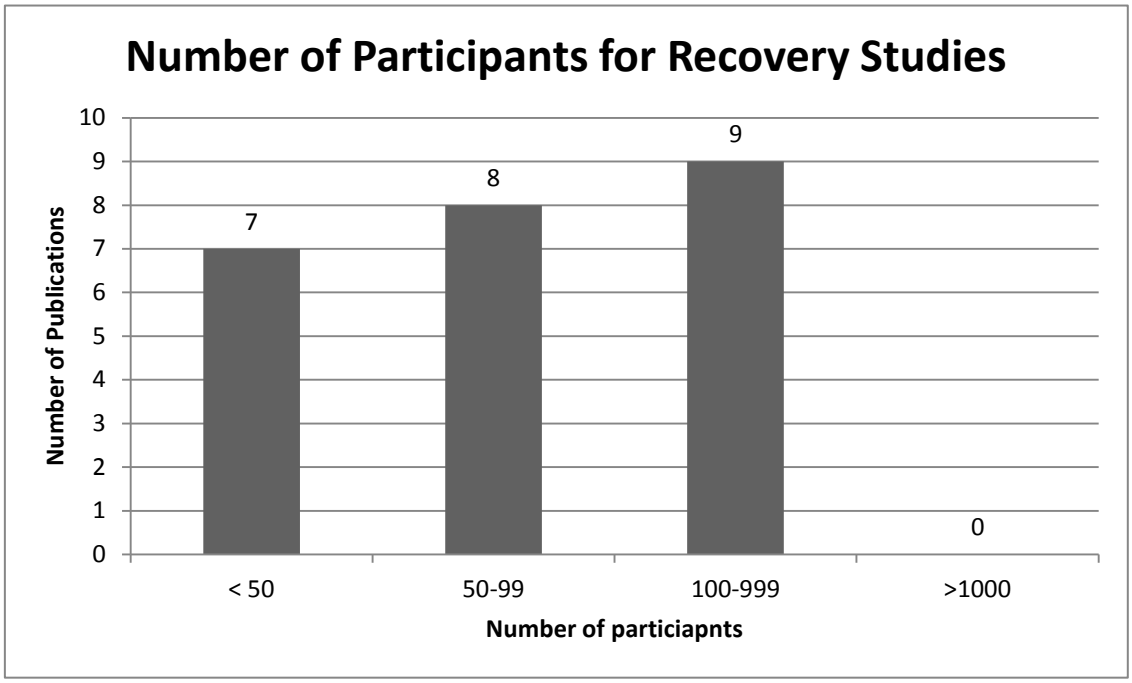


Figure 13. **Values indicate the number of publications with a particular surgical indication, among the subset of articles that explicitly examined recovery.**

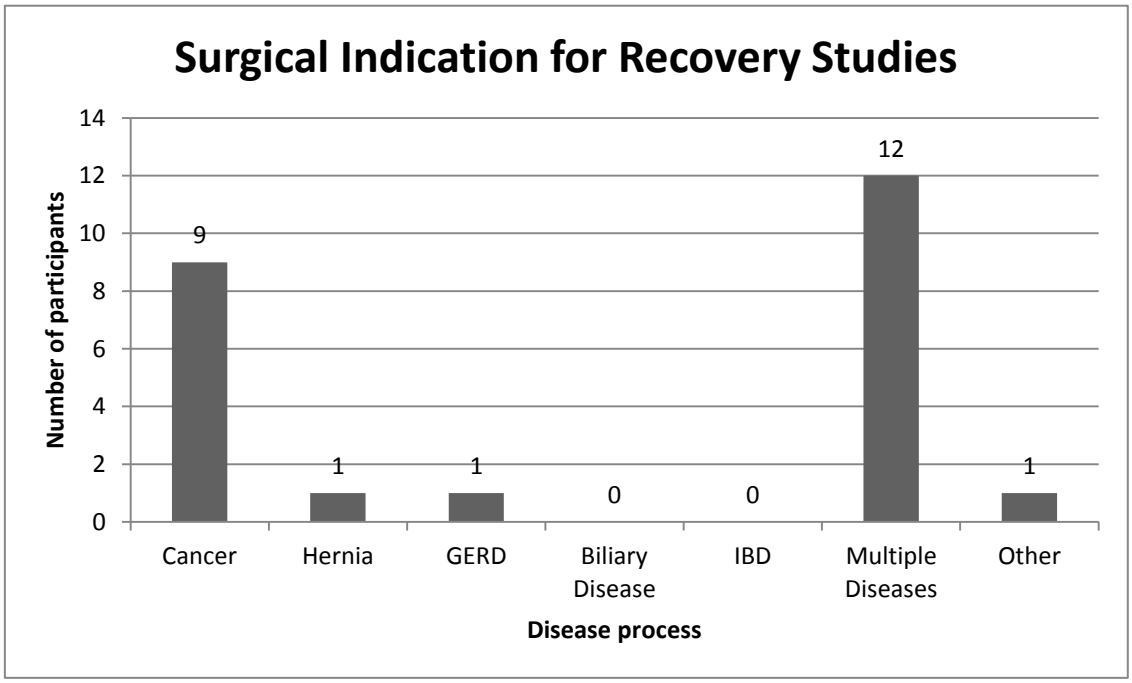


Figure 14. **Values indicate the number of publications with a short, medium, or long term follow-up length among studies examining post-operative delirium. Short term is <1 month, medium is 1 month to 1year, and long term is >1 year.**

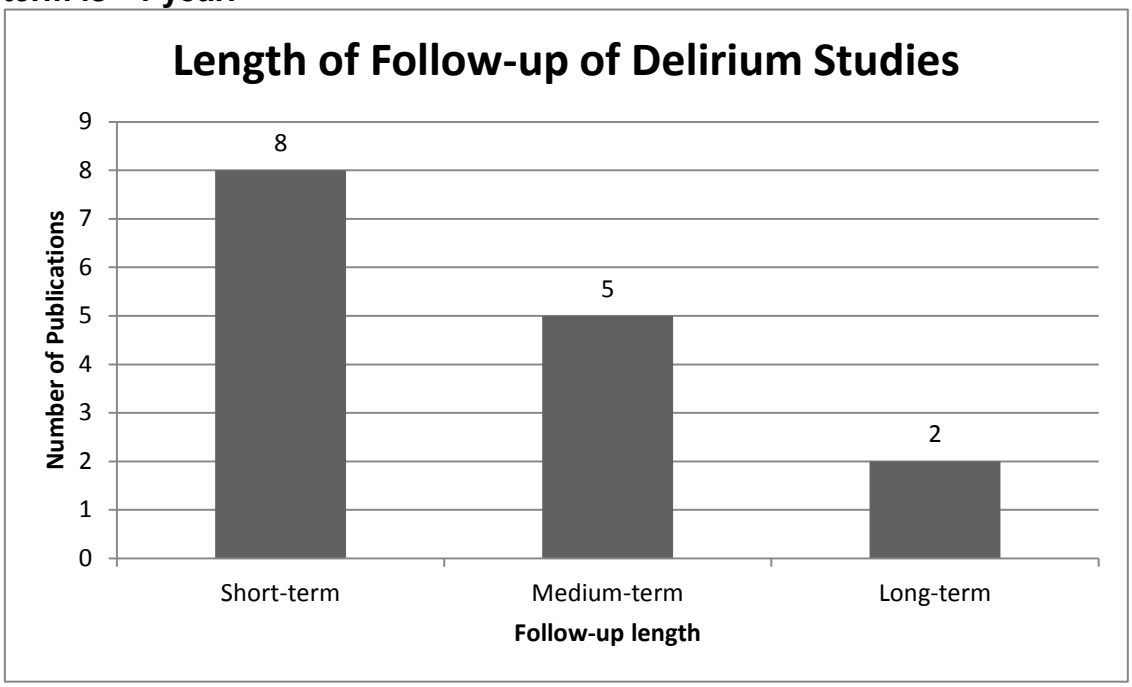


Figure 15. **Values indicate the number of publications with a given number of participants among the subset of studies that explicitly examined post-operative delirium.**

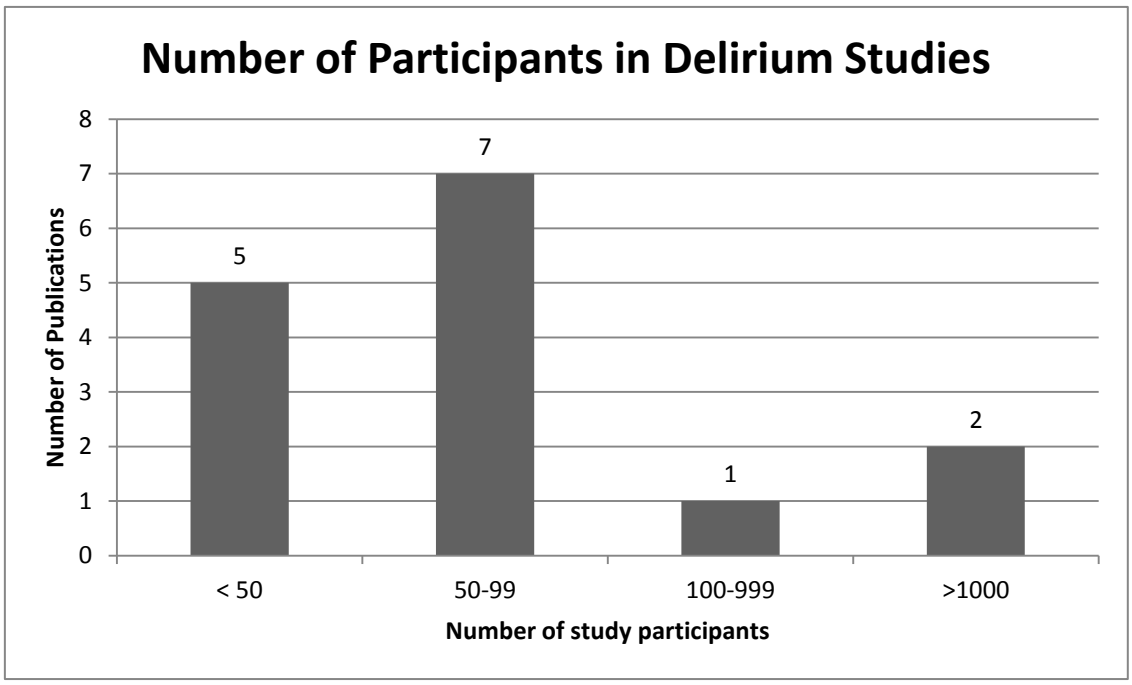


Figure 16. **Values indicate the number of publications with a particular surgical indication, among the articles that explicitly examined post-operative delirium.**

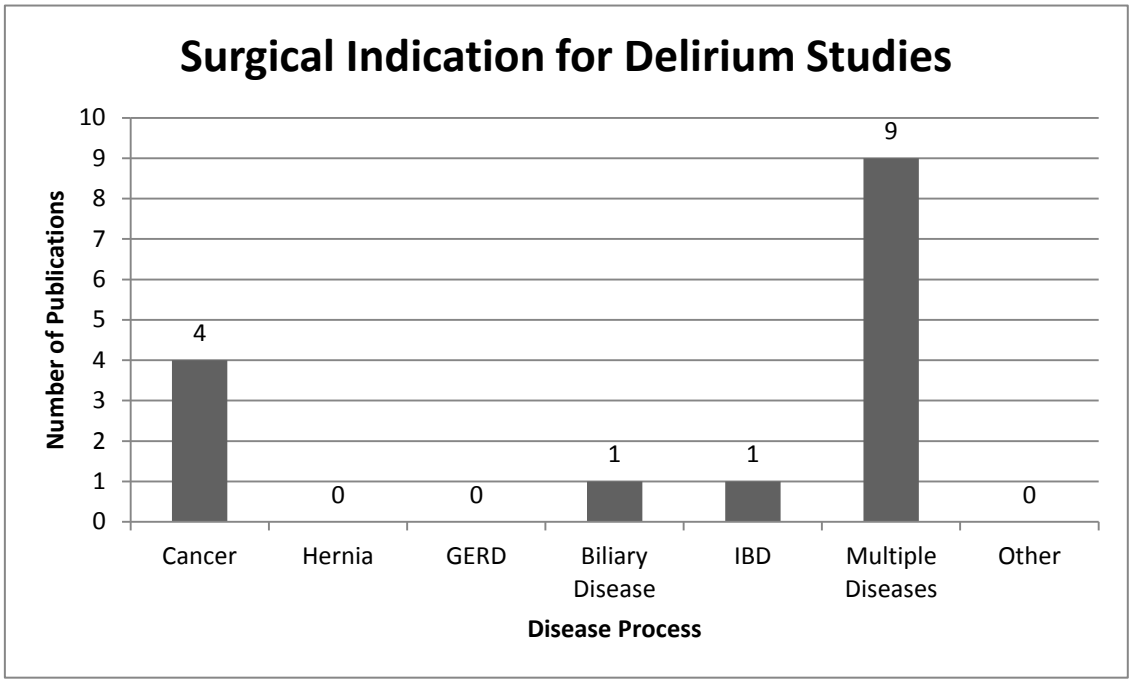


Figure 17. **All patient-centered outcomes were categorized into one of three health domains. Values indicate the number of publications with at least one patient-centered outcome in a particular domain.**

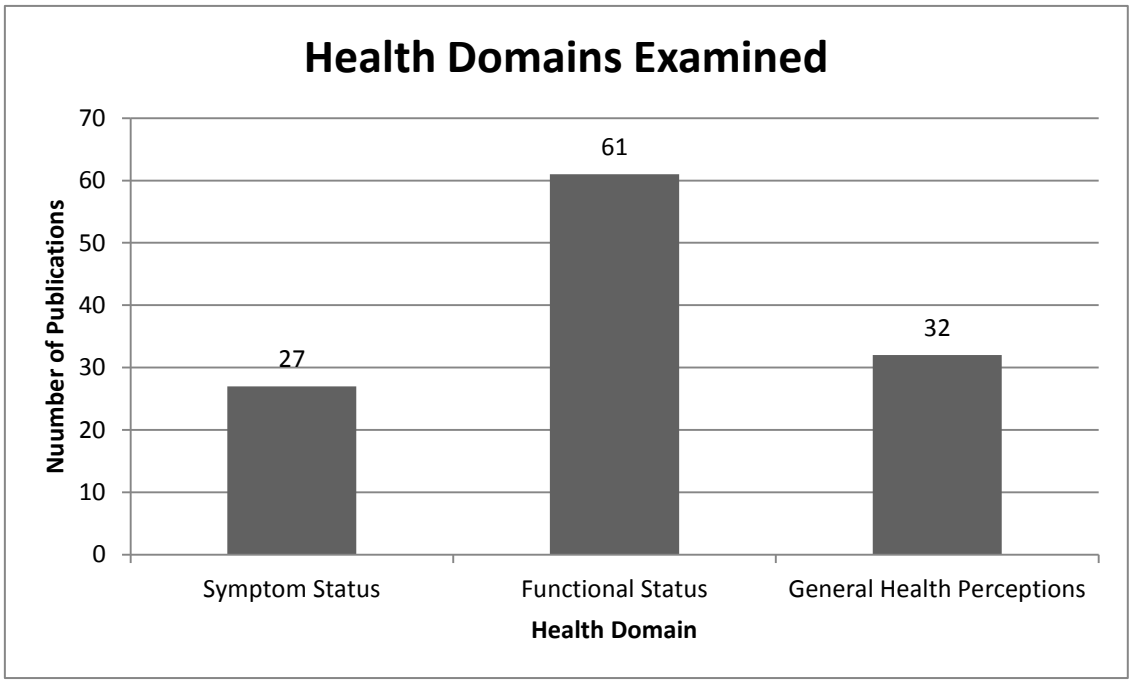


Figure 18. **Studies included in this review used outcomes that were categorized into one of three health domains. Values indicate the use of an outcome within a health domain. Multiple outcomes meant that a study could examine more than one health domain.**

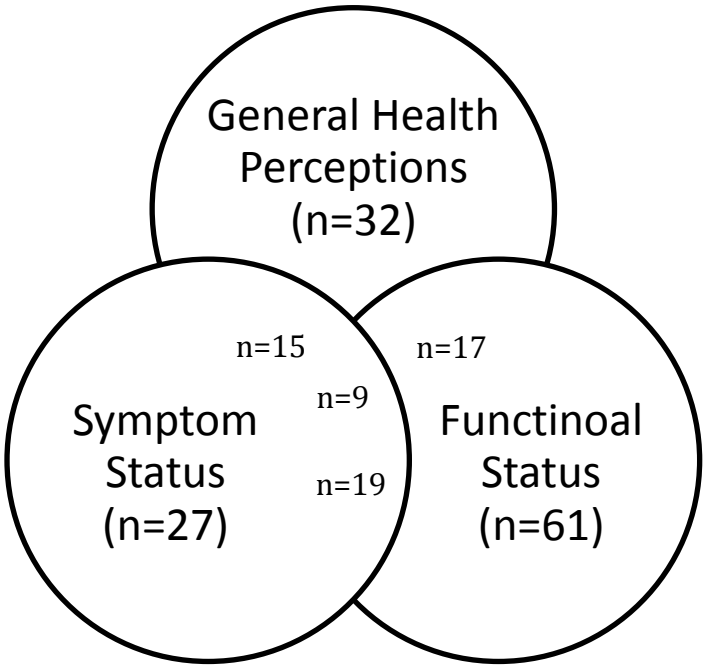


Figure 19. **Each study outcome used was categorized into one of the 8 patient-centered outcome categories. Values indicate the number of publications using each particular patient-centered outcome.**

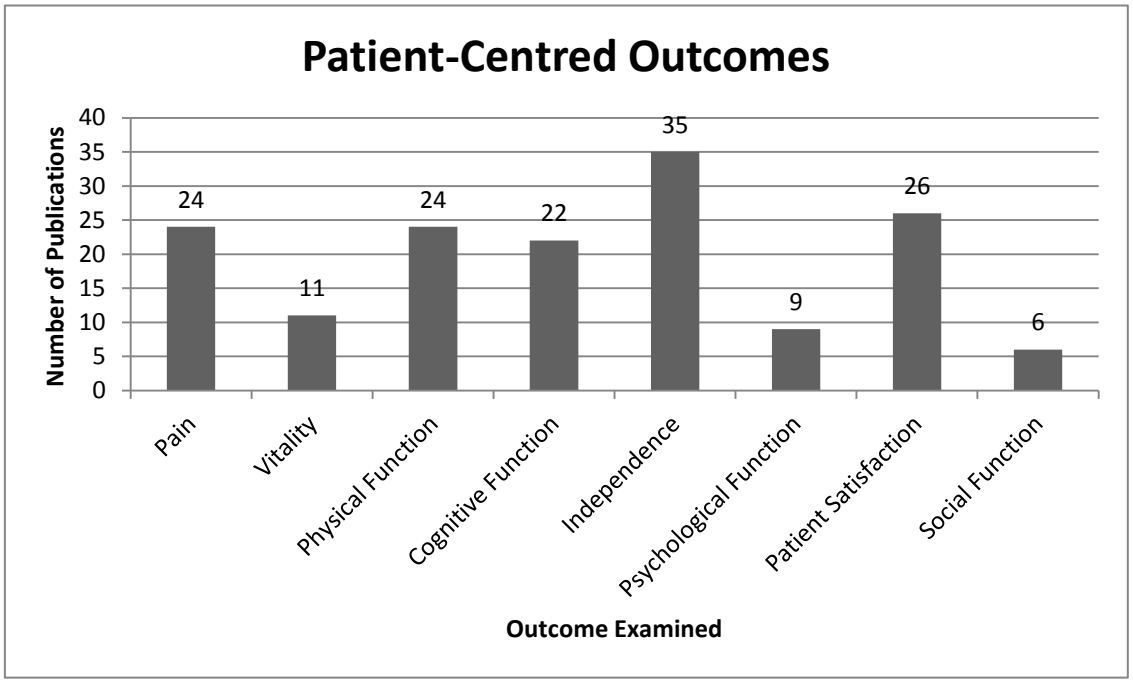


Figure 20. **Study outcomes were categorized into one of three health domains. Values indicate the number of publications, among recovery articles, with at least one patient-centered outcome in a particular domain.**

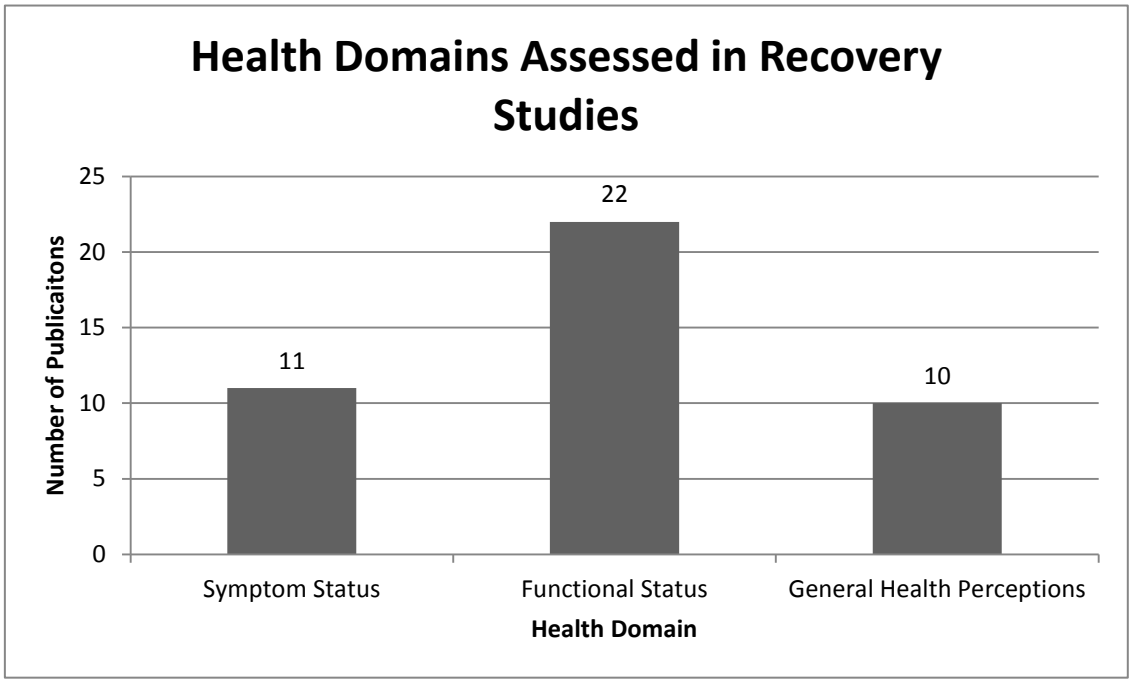


Figure 21. **Studies explicitly examining recovery used outcomes that were categorized into one of three health domains. Values indicate the use of an outcome within a health domain. Multiple outcomes meant that a study could examine more than one health domain.**

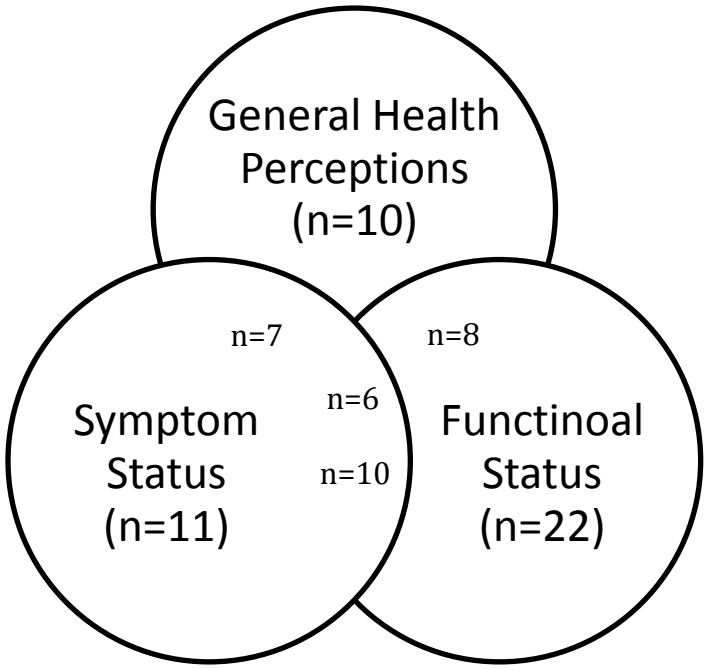


Figure 22. **Values indicate the number of publications which used a particular patient-centered outcome among the subset of 24 articles which explicitly examined recovery.**

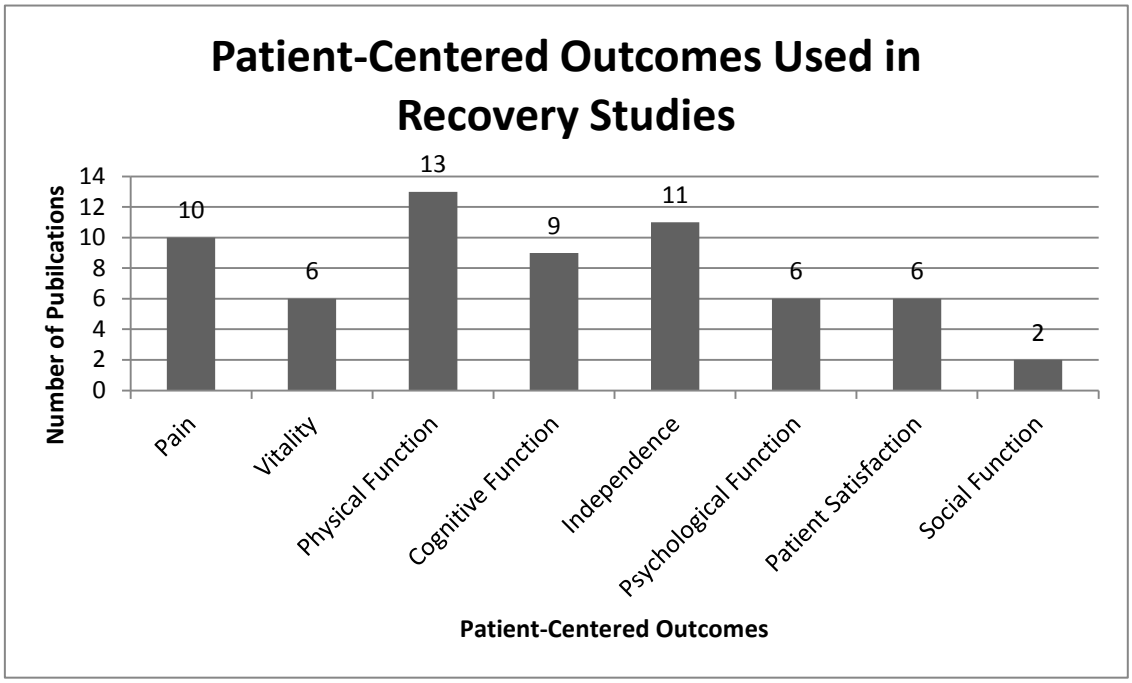


Figure 23. **Study outcomes were categorized into one of three health domains. Values indicate the number of publications, among articles examining delirium, with at least one patient-centered outcome in a particular domain.**

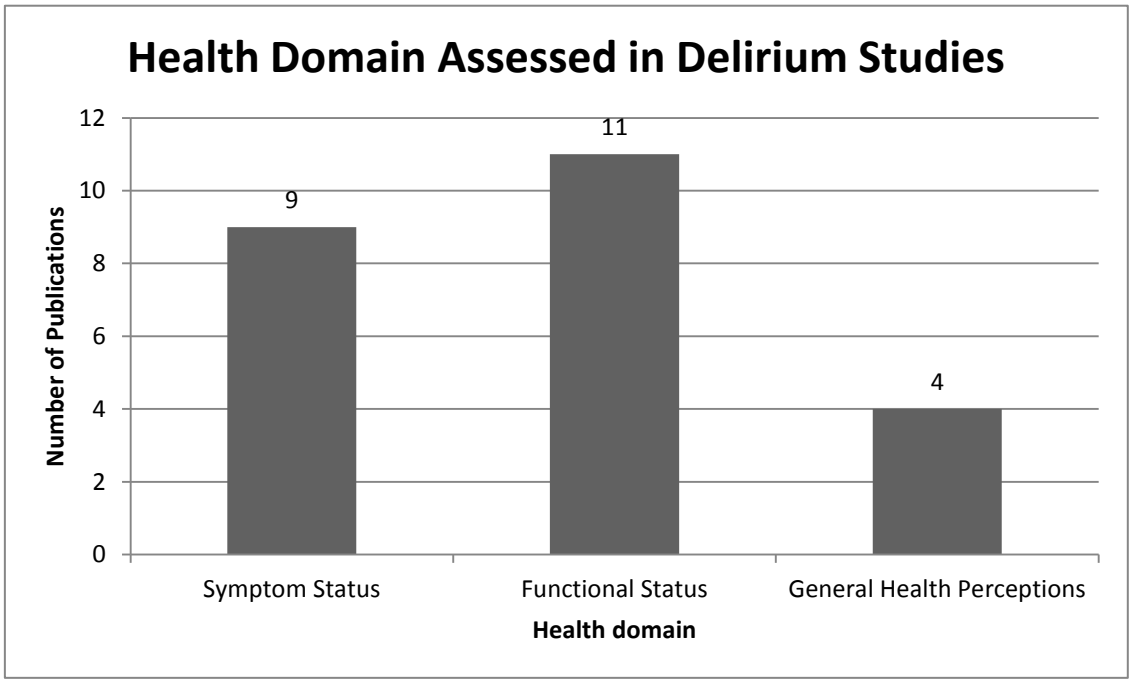


Figure 24. Studies examining delirium used outcomes that were categorized into one of three health domains. Values indicate the use of an outcome within a health domain. Multiple outcomes meant that a study could examine more than one health domain.

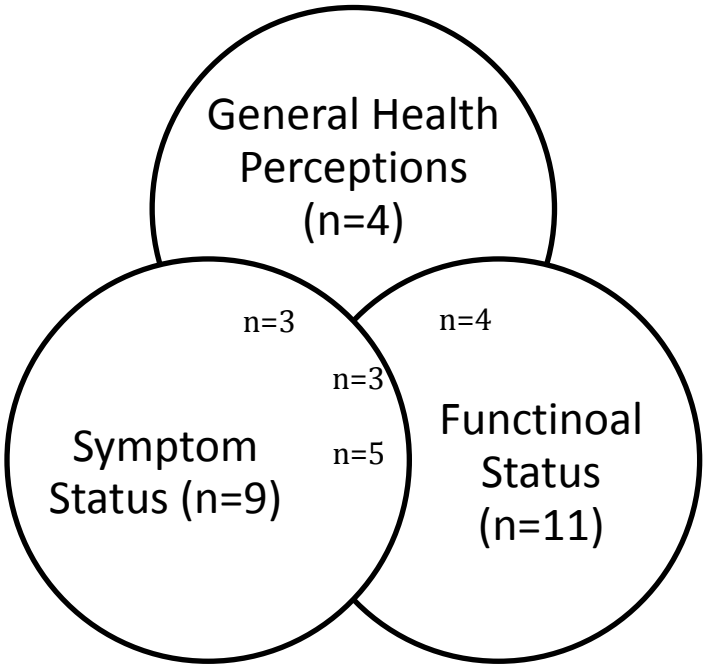
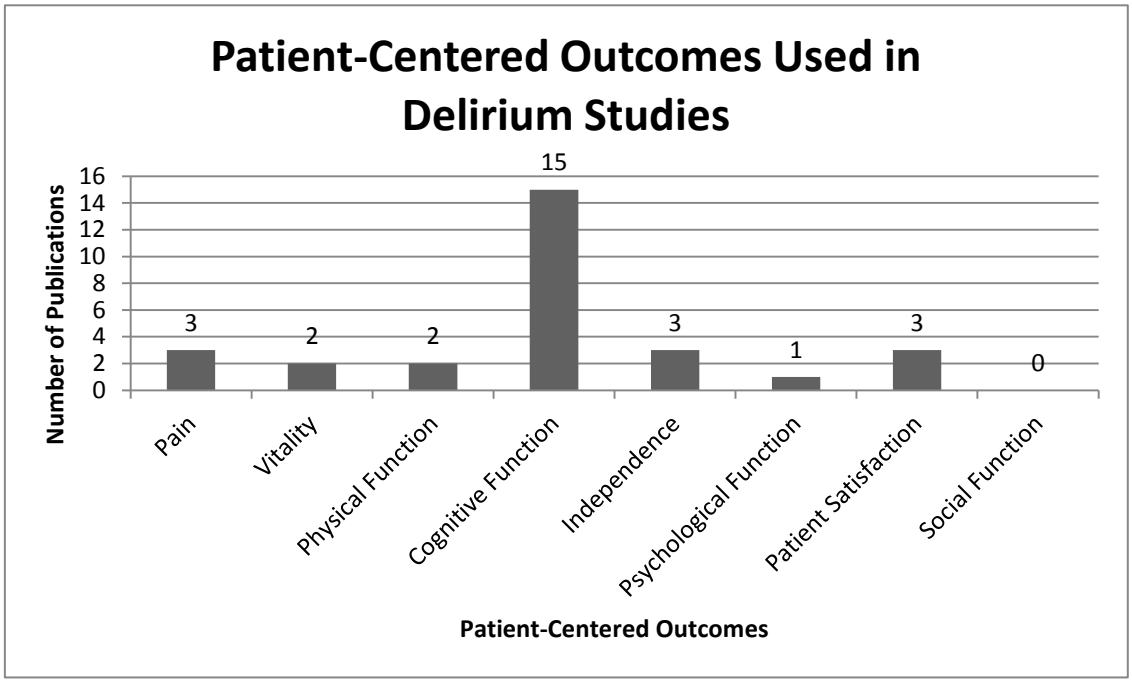


Figure 25. Values indicate the number of publications which examined a particular patient-centered outcome, among the subset of 15 articles which explicitly examined post-operative delirium.



<u>Figure 26.</u> Patient recruitment flowchart, adapted from the CONSORT recruitment flowchart recommendations.

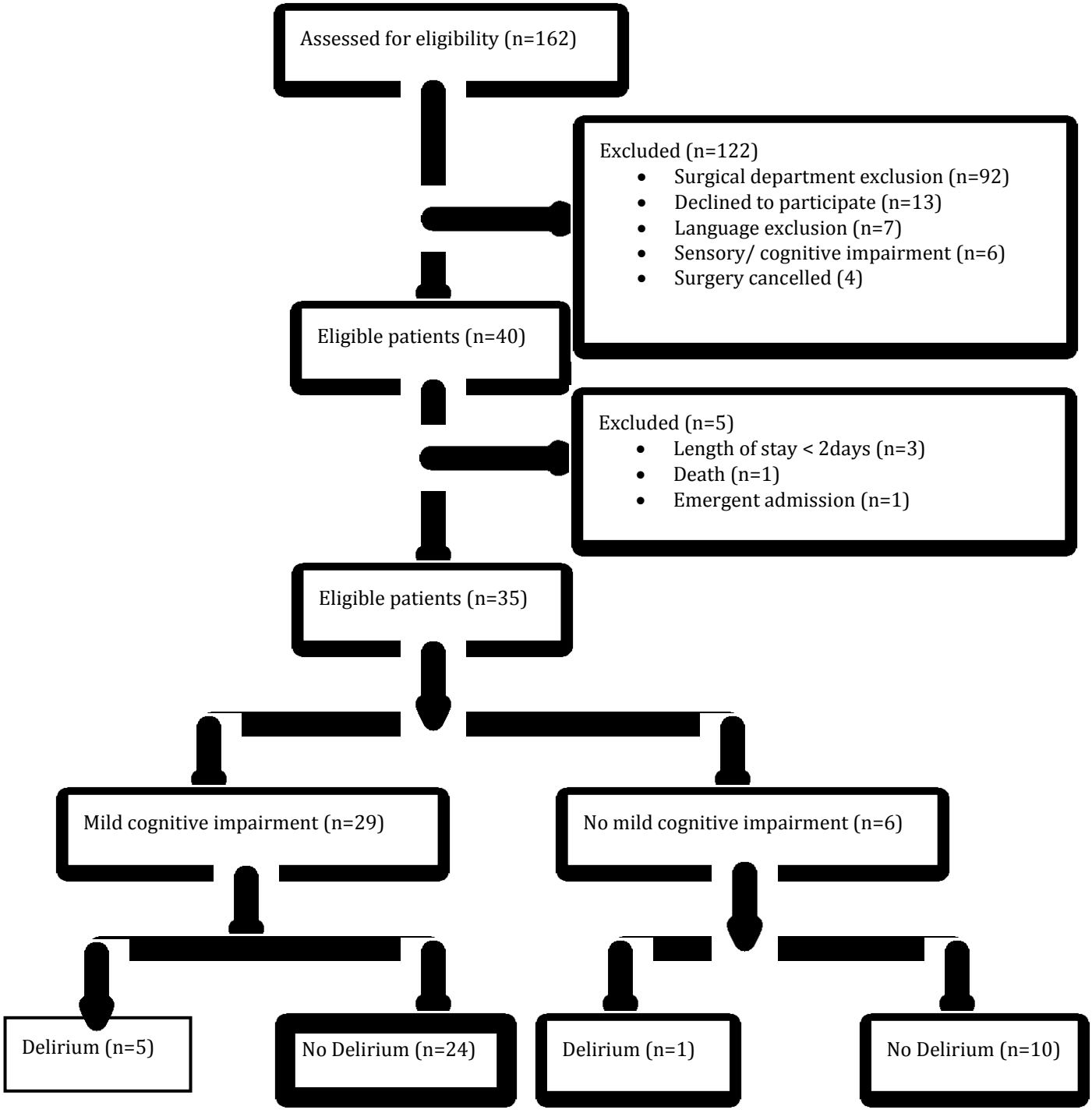


Table 1. Values indicate which studies, among all those included in this review, explicitly examined recovery, post-operative delirium, and quality of life.

Subset focus	Study number
Recovery (n=24)	1, 3, 4, 5, 18, 24, 27, 28, 31, 38, 42, 46, 49, 51, 61, 77, 79, 87, 98, 101, 111, 112, 113, 114.
Post-operative delirium (n=15)	5, 28, 40, 46, 47, 52, 57, 64, 65, 73, 97, 101, 102, 107, 118.
Quality of life (n=29)	1, 10, 12, 15, 20, 21, 22, 27, 30, 36, 37, 38, 42, 45, 48, 55, 62, 67, 68, 69, 81, 82, 83, 85, 89, 93, 91, 96, 113.

Table 2. Among all 88 studies in this review, patient-centered outcomes used were classified into one of three health domains (shaded areas).

Article Number	Publication date	Author	Symptom Status	Functional Status	General Health Perceptions
1	2007	Amemiya, T., et al.			
2	2002	Bammer, T., et al.			
3	1995	Bardram, L., et al.			
4	2005	Basse, L., et al.			
5	2006	Beaussier, M., et al.			
8	2006	Bruce, J. and Z. H.			
9	2006	Carpelan-Holmstrom,			
10	2007	Casati, A., et al.			
12	2002	Delaney, C. P., et al.			
15	2003	Diaz De Liano, A., et al.			
16	2003	DiFronzo, L. A., et al.			
17	2007	Duncan, M. A., et al.			
18	1993	Edwards, N. D., et al.			
19	2008	El Shobary, H. M., et al.			
20	2005	Fei, L., et al.			
21	2003	Fernando, H. C., et al.			
22	2007	Ferulano, G. P., et al.			
24	1999	Fredman, B., et al.			
27	2007	Gall, C. A., et al.			
28	2007	Ganai, S., et al.			
29	1999	Hall-Lord, M. L., et al.			
30	2008	Hazebroek, E. J., et al.			
31	2006	Houborg, K. B., et al.			
32	1995	Ido, K., et al.			
33	1999	Iroatulam, A. J., et al.			
34	2007	Ishiyama, T., et al.			
36	1989	Jayawardhana, B. N., et			
37	2001	Kamolz, T., et al.			
38	2002	Khajanchee, Y. S., et al.			
40	2009	Koebrugge, B., et al.			
41	2009	Kurzer, M., et al.			
42	2004	Lawrence, V. A., et al.			
43	2009	Legner, V. J., et al.			
44	2004	Lightner, A. M., et al.			
45	2002	Low, D. E. and E. J.			
46	2000	Mann, C., et al.			
47	1994	Marcantonio, E. R., et al.			
48	2006	Mastracci, T. M., et al.			
49	2002	Matsushita, I., et al.			

51	2003	Miyakura, Y., et al.			
52	1998	Moller, J. T., et al.			
53	2008	Morse, B. C., et al.			
55	2005	Nienhuijs, S. W., et al.			
56	1992	Nink, M., et al.			
57	2005	Olin, K., et al.			
61	1989	Palmer, C. A., et al.			
62	2007	Pisanu, A., et al.			
64	2000	Rasmussen, L. S., et al.			
65	1999	Rasmussen, L. S., et al.			
66	2000	Rigberg, D., et al.			
67	2008	Saeki, H., et al.			
68	2004	Scarpa, M., et al.			
69	2005	Schmidt, C. E., et al.			
72	2002	Shea, R. A., et al.			
73	2001	Shigeta, H., et al.			
75	2000	Stocchi, L., et al.			
76	1998	Takao, Y., et al.			
77	2006	Tan, K.-Y., et al.			
79	1998	Velasco, J. M., et al.			
80	2005	Vignali, A., et al.			
81	1996	Walsh, T. H.			
82	2008	Wang, W., et al.			
83	2006	Wilson, T. R., et al.			
84	1991	Wise, W. E., Jr., et al.			
85	2000	Wu, C. W., et al.			
87	2004	Zalon, M. L.			
88	2005	Zerbib, P., et al.			
89	2006	Evans, C., et al.			
91	2005	Quebbemann, B., et al.			
93	2002	Kamolz, T., et al.			
96	2000	Cavina, E., et al.			
97	2002	Aizawa, K.-i., et al.			
98	2000	Bardram, L., et al.			
101	1999	Dijkstra, J. B., et al.			
102	1990	Egbert, A. M., et al.			
104	2000	Gagliese, L., et al.			
105	1999	Gunnarsson, U., et al.			
106	1989	Morel, P., et al.			
107	1995	Ni Chonchubhair, A., et			
109	1992	Rorbaek-Madsen, M., et			
110	2007	Sinha, S., et al.			
111	1999	Stewart, B. T., et al.			
112	2000	Tuech, J. J., et al.			
113	2001	Udekwu, P., et al.			

114	1993	Watters, J. M., et al.			
115	1988	Williams, J. H. and J.			
118	1997	Kaneko, T., et al.			
120	1998	Maxwell, J. G., et al.			

Table 3. Among all studies included in the review, values indicate the number of studies examining outcomes from each health domain and patient-centered outcomes category.

Health Domain	Patient-Centered Outcomes Examined	All Studies (n=88)
Symptom Status (n=27)	Pain	24
	Vitality	11
Functional Status (n=61)	Physical Function	24
	Cognitive Function	22
	Independence	35
General Health Perceptions (n=32)	Psychological Function	9
	Patient Satisfaction	26
	Social Function	6

<u>Table 4.</u> Values indicate which studies used a particular patient-centered outcome within a given health domain.

Health Domain	Patient-Centered Outcome	Study Number
Symptom Status	Pain	3, 4, 5, 10, 17, 18, 19, 20, 22, 29, 34, 38, 41, 46, 55, 56, 72, 75, 87, 98, 102, 104, 112, 114.
	Vitality	3, 4, 24, 29, 31, 34, 56, 73, 87, 98, 118.
Functional Status	Physical Function	1, 3, 4, 5, 16, 20, 21, 31, 32, 33, 38, 41, 42, 46, 48, 49, 72, 79, 81, 96, 98, 106, 111, 114.
	Independence	3,5, 10,16, 20, 29, 33, 42, 43, 44, 47, 48, 51, 52, 53, 61, 66, 68, 75, 77, 80, 81, 84, 87, 88, 105, 106, 109, 110, 111, 112, 113, 115, 120.
	Cognitive function	1, 4, 5, 8, 24, 28, 29, 40, 42, 46, 47, 49, 52, 57, 64, 65, 73, 97, 101, 102, 107, 118.
General Health Perceptions	Patient satisfaction	2, 3, 4, 5, 9, 12, 20, 21, 27, 29, 30, 34, 37, 41, 46, 48, 55, 76, 81, 87, 89, 93, 102, 104, 105, 110
	Social function	9, 29, 33, 42, 48, 87.
	Psychological Function	18, 19, 24, 27, 29, 42, 87, 101, 104.

Table 5. Commonly used sub-outcomes and tools within the 8 patient-centered outcome categories and 3 health domains.

Health Domain	Outcome	Common Sub-outcomes	Common Tools
Symptom Status	Pain	Perception of Pain	VAS (0-100) Use of narcotics Brief Pain Inventory
	Vitality	Fatigue Vigilance Drowsiness	VAS (0-10) Glasgow coma scale Mood fatigue symptom checklist
Functional Status	Physical Function	Physical Performance Mobilization	Functional Reach Timed up and go 6 minute walk test Hand-grip strength Return to Physical Activity Step test Chair stands Hours of Mobilization
	Independence	ADL IADL Dependence Discharge Destination	Katz Index Return to Independent ADL Lawton and Brody scale
	Cognitive function	Cognitive dysfunction Mental function Delirium	Mini-Mental State Exam Roth Hopkins test (Hodkinson mod.) Visual Verbal Learning Test Concept Shifting Test Stroop Colour Word Interference Letter digit coding Digit Substitution test Shape Sorter Test Confusion Assessment Method
General Health Perceptions	Patient satisfaction	Overall satisfaction	Would repeat surgery/ recommend Likert scale Krantz health opinion survey
	Social function	Level of social support	SF-36 social support survey Likert scale Return to baseline social activity
	Psychological Function	Depression Mood Anxiety	Zung's depression scale Geriatric Depression scale Hospital anxiety depression scale VAS (0-100)

Table 6. Among all 88 studies included in this review, outcomes were classified into one of 8 patient-centered categories. "Yes" indicates that an outcome was used from that category.

Publication date	Author	Vitality	Pain	Psycho-logical Function	Social Function	Patient Satisfaction	Independence	Physical Function	Cognitive Function
2007	Amemiya, T., et						Yes	Yes	Yes
2002	Bammer, T., et al.					Yes			
1995	Bardram, L., et al.	Yes	Yes			Yes	Yes	Yes	
2005	Basse, L., et al.	Yes	Yes			Yes		Yes	Yes
2006	Beaussier, M., et		Yes			Yes	Yes	Yes	Yes
2006	Bruce, J. and Z.								Yes
2006	Carpelan-				Yes	Yes			
2007	Casati, A., et al.		Yes				Yes		
2002	Delaney, C. P., et					Yes			
2003	Diaz De Liano,								
2003	DiFronzo, L. A.,						Yes	Yes	
2007	Duncan, M. A., et		Yes						
1993	Edwards, N. D.,		Yes	Yes					
2008	El Shobary, H.		Yes	Yes					
2005	Fei, L., et al.		Yes			Yes	Yes	Yes	
2003	Fernando, H. C.,					Yes		Yes	
2007	Ferulano, G. P.,		Yes						
1999	Fredman, B., et	Yes		Yes					Yes
2007	Gall, C. A., et al.			Yes		Yes			
2007	Ganai, S., et al.								Yes
1999	Hall-Lord, M. L.,	Yes	Yes	Yes	Yes	Yes	Yes		Yes
2008	Hazebroek, E. J.,					Yes			
2006	Houborg, K. B., et	Yes						Yes	
1995	Ido, K., et al.							Yes	

1999	Iroatulam, A. J.,				Yes		Yes	Yes	
2007	Ishiyama, T., et	Yes	Yes			Yes			
1989	Jayawardhana,								
2001	Kamolz, T., et al.					Yes			
2002	Khajanchee, Y.		Yes					Yes	
2009	Koebrugge, B., et								Yes
2009	Kurzer, M., et al.		Yes			Yes		Yes	
2004	Lawrence, V. A.,			Yes	Yes		Yes	Yes	Yes
2009	Legner, V. J., et						Yes		
2004	Lightner, A. M., et						Yes		
2002	Low, D. E. and E.								
2000	Mann, C., et al.		Yes			Yes		Yes	Yes
1994	Marcantonio, E.						Yes		Yes
2006	Mastracci, T. M.,				Yes	Yes	Yes	Yes	
2002	Matsushita, I., et							Yes	Yes
2003	Miyakura, Y., et						Yes		
1998	Moller, J. T., et al.						Yes		Yes
2008	Morse, B. C., et						Yes		
2005	Nienhuijs, S. W.,		Yes			Yes			
1992	Nink, M., et al.	Yes	Yes						
2005	Olin, K., et al.								Yes
1989	Palmer, C. A., et						Yes		
2007	Pisanu, A., et al.								
2000	Rasmussen, L.								Yes
1999	Rasmussen, L.								Yes
2000	Rigberg, D., et al.						Yes		
2008	Saeki, H., et al.								
2004	Scarpa, M., et al.						Yes		
2005	Schmidt, C. E., et								
2002	Shea, R. A., et al.		Yes					Yes	

2001	Shigeta, H., et al.	Yes							Yes
2000	Stocchi, L., et al.		Yes				Yes		
1998	Takao, Y., et al.					Yes			
2006	Tan, K.-Y., et al.						Yes		
1998	Velasco, J. M., et							Yes	
2005	Vignali, A., et al.						Yes		
1996	Walsh, T. H.					Yes	Yes	Yes	
2008	Wang, W., et al.								
2006	Wilson, T. R., et								
1991	Wise, W. E., Jr.,						Yes		
2000	Wu, C. W., et al.								
2004	Zalon, M. L.	Yes	Yes	Yes	Yes	Yes	Yes		
2005	Zerbib, P., et al.						Yes		
2006	Evans, C., et al.					Yes			
2005	Quebbemann, B.,								
2002	Kamolz, T., et al.					Yes			
2000	Cavina, E., et al.							Yes	
2002	Aizawa, K.-i., et								Yes
2000	Bardram, L., et al.	Yes	Yes					Yes	
1999	Dijkstra, J. B., et			Yes					Yes
1990	Egbert, A. M., et		Yes			Yes			Yes
2000	Gagliese, L., et		Yes	Yes		Yes			
1999	Gunnarsson, U.,					Yes	Yes		
1989	Morel, P., et al.						Yes	Yes	
1995	Ni Chonchubhair,								Yes
1992	Rorbaek-Madsen,						Yes		
2007	Sinha, S., et al.					Yes	Yes		
1999	Stewart, B. T., et						Yes	Yes	
2000	Tuech, J. J., et al.		Yes				Yes		
2001	Udekwu, P., et al.						Yes		

1993	Watters, J. M., et		Yes					Yes	
1988	Williams, J. H.						Yes		
1997	Kaneko, T., et al.	Yes							Yes
1998	Maxwell, J. G., et						Yes		

Table 7. The quality of life tools used among the subset of studies that measured quality of life (n=29).

Author	QOL tool
Amemiya, T., et al.	SF-12, EuroQOL-5D
Casati, A., et al.	EORTC-QLQ-C30
Delaney, C. P., et al.	CGQL scale, SF-36
Diaz De Liano, A., et al.	EORTC-QLQ-C30
Fei, L., et al.	SF-36
Fernando, H. C., et al.	SF-36, GERD-HRQL
Ferulano, G. P., et al.	GIQLI
Gall, C. A., et al.	SF-12
Hazebroek, E. J., et al.	QOLRAD
Jayawardhana, B. N., et al.	Fansel and Bush
Kamolz, T., et al.	GIQLI (German GIQLI)
Khajanchee, Y. S., et al.	SF-36
Lawrence, V. A., et al.	MOS SF-36
Low, D. E. and E. J. Simchuk	0-10
Mastracci, T. M., et al.	SF-36, EORTC-C30, EORTC-CR38
Nienhuijs, S. W., et al.	SF-36
Pisanu, A., et al.	Karnofski, Visick
Saeki, H., et al.	Not reported
Scarpa, M., et al.	one-seven
Schmidt, C. E., et al.	EORTC-QLQ-C30
Walsh, T. H.	questionnaire
Wang, W., et al.	GIQLI
Wilson, T. R., et al.	QLQ-C30, FACT-C, SF-12, EQ-5D
Wu, C. W., et al.	Spitzer index
Evans, C., et al.	Interview (0-20)
Quebbemann, B., et al.	Impact of weight on QoL questionnaire (lite scale), bariatric surgery impact scale (modified becks depression inventory)
Kamolz, T., et al.	GIQLI
Cavina, E., et al.	Nottingham health profile sickness impact profile, VAS, NS Williams scale, fecal incontinence QoL
Udekwu, P., et al.	PQOL

Table 8. Among the subset of studies explicitly examining recovery (n=24), shaded areas indicate the use of at least one patient-centered outcome within one of three health domains.

Author	Symptom status	Functional status	General health perceptions
Amemiya, T., et al.			
Bardram, L., et al.			
Basse, L., et al.			
Beaussier, M., et al.			
Edwards, N. D., et al.			
Fredman, B., et al.			
Gall, C. A., et al.			
Ganai, S., et al.			
Houborg, K. B., et al.			
Khajanchee, Y. S., et al.			
Lawrence, V. A., et al.			
Mann, C., et al.			
Matsushita, I., et al.			
Miyakura, Y., et al.			
Palmer, C. A., et al.			
Tan, K.-Y., et al.			
Velasco, J. M., et al.			
Zalon, M. L.			
Bardram, L., et al.			
Dijkstra, J. B., et al.			
Stewart, B. T., et al.			
Tuech, J. J., et al.			
Udekwu, P., et al.			
Watters, J. M., et al.			

Table 9. Among the subset of studies that examined recovery, values indicate the number of studies examining outcomes from each health domain and patient-centered outcome category.

Health Domain	Patient-Centered Outcome Examined	Recovery Studies (n=24)
Symptom Status (n=11)	Pain	25
	Vitality	6
Functional Status (n=22)	Physical Function	13
	Cognitive Function	9
	Independence	11
General Health Perceptions (n=10)	Psychological Function	6
	Patient Satisfaction	6
	Social Function	2

<u>Table 10.</u> The sub-outcomes and assessment tools used in the subset of studies (n=24) that explicitly examined recovery.

Author and year	*Sub-Outcome*	*Assessment tool*
Amemiya, 2007		POSSUM
		E-PASS
		APACHE-II
		NCI-CTC
		Katz index
		Maintain sitting in bed
		Sitting down from standing
		maintaining standing posture
		walking on a level surface
		SF-12
		EQ-5D
		MMSE
Bardram, 1995	Pain	(0,1,2) additional analgesia required
	Nausea	vomiting
		Oral intake (mL)
	defecation	(onset day)
		hours of mobilization
	fatigue	(0,1,2)
Basse, 2005	Pain at rest	(0-3)
	Pain at activity	(0-3)
	Fatigue	(0-3)
	Mental Function	Roth Hopkins (Hodkinson
	Quality of sleep	VAS (0-10)
	Mobilization	OOB hours/day
	physical motor activity	MMLA
	Nausea/vomiting	incidence
	satisfaction/convalescence	opinion
Beaussier, 2006	Pain	VRS/ morphine consumption
	Delirium	CAM
	Nausea	(0-3)
	Vomiting	(0-3)
	Pruritis	(0-3)
	First flatus	
	Mental Function	MMSE Digit Symbol substitution test Ambulate without assistance
	global satisfaction with pain	(0-3)

Edwards, 1993	Pain	(0-5) PCA morphine consumption
	Sedation	(0-3)
	Dreams and hallucinations	(0-4)
Fredman, 1999	Nausea	(0-4)
	Vomiting	(0-4)
	Cough	(0-4)
	Dizzy	(0-4)
	Drowsy	(0-4)
	Pain	VAS (0-100)
		DSST
		shape sorter test
	Anxiety	(0-100)
	sleepiness	(0-100)
	coordination	(0-100)
		orientation and time to follow
Gall, 2007	HRQL	SF-12
	anxiety and depression	HADS
	satisfaction	SVQ
Ganai, 2007	Delirium	MD/nurse notification
Houborg, 2006	physical performance test	Isometric knee extension handgrip strength write a sentence simulate eating lift a book put on and take off coat pick up a pen turn 360 degrees 24m walk 5 chair stands step test fastest walk speed
	Quality of Life	SF-36
	Fatigue	VAS (1-10)
Khajanchee, 2001	QOL	SF-36
Lawrence, 2004		handgrip strength
		timed up and go
		functional reach
	Functional Dependence in	modified Katz scale

	IADL	Lawton Brody Scale
		MMSE
		GDS
		SF-36
		social support survey (from
Mann, 2000	Pain	VAS (0-10)
	Satisfaction of analgesia	(0-3)
	delirium	AMT
	Sedation scale	(0-3)
	Pruritis and Nausea	(0-3)
	motor function	knee and ankle flex (0-3)
Matsushita, 2002	performance status	(0-4)
	mental status	slight, mod, severe (>2/10 on
Miyakura, 2003	ADL (eat, defecate/urinate,	(1-4) all on own=1/ none on
Palmer, 1989	ADL	independent, semi-
Tan, 2006	return to pre-morbid condition	physician assessment
Velasco, 1998	return to normal activity	days
Zalon, 2004	Pain and interference	BPI and (0-10)
	depression	GDS-SF
	fatigue	modified fatigue symptom
	functional status	inferred social dependency
	self perception of recovery	(0-100)
	cognitive status	MMSE
Bardram, 2000	Pain	(0-3)
	nausea	
	fatigue	
	Pain	need for pain meds duration of mobilization content with pain management (too early?)
Stewart, 1999		discharge destination
	functional activity level	
Dijksra, 1999	cognitive function	visual verbal learning test Stroop colour word test concept shifting test

		letter digit substitution test changes in cognitive function (phone interview)
	depression	Zung self rating scale for
Tuech, 2000		discharge location
	Pain	post-op analgesic requirement
Udekwu, 2001	Perceived QoL (Patrick 1988)	
	ADL	
Watters, 1993		handgrip strength
	Pain	VA pain scale

Table 11. Among the subset of studies explicitly examining post-operative delirium (n=15), shaded areas indicate the use of at least one patient-centered outcome within one of three health domains.

Author	Symptom status	Functional status	General health perceptions
Beaussier, M., et al.			
Ganai, S., et al.			
Koebrugge, B., et al.			
Mann, C., et al.			
Marcantonio, E. R., et al.			
Moller, J. T., et al.			
Olin, K., et al.			
Rasmussen, L. S., et al.			
Rasmussen, L. S., et al.			
Shigeta, H., et al.			
Aizawa, K.-i., et al.			
Dijkstra, J. B., et al.			
Egbert, A. M., et al.			
Ni Chonchubhair, A., et			
Kaneko, T., et al.			

Table 12. Among the subset of studies that examined post-operative delirium, values indicate the number of studies examining outcomes from each health domain and patient-centered outcome category.

Health Domain	Patient-Centered Outcomes Examined	Delirium Studies (n=15)
Symptom Status (n=9)	Pain	3
	Vitality	2
Functional Status (n=11)	Physical Function	2
	Cognitive Function	15
	Independence	3
General Health Perceptions (n=4)	Psychological Function	1
	Patient Satisfaction	3
	Social Function	0

Table 13. The sub-outcomes and assessment tools used in the subset of studies (n=15) that explicitly examined post-operative delirium.

Author and year	*Outcome*	*Assessment tool*
Beaussier, 2006	Pain	VRS/ morphine consumption
	Delirium	CAM
	Nausea	(0-3)
	Vomiting	(0-3)
	Pruritis	(0-3)
	First flatus	
	Mental Function	MMSE Digit Symbol substitution test
		Ambulate without assistance
	global satisfaction with pain	(0-3)
Ganai, 2007	Delirium	MD/nurse notification
Koebrugge, 2009	Delirium	Delirium observation scale
Mann, 2000	Pain	VAS (0-10)
	Satisfaction of analgesia	(0-3)
	delirium	AMT
	Sedation scale	(0-3)
	Pruritis and Nausea	(0-3)
	motor function	knee and ankle flex (0-3)
Marcantonio,1994	Delirium	CAM
	Cognitive Status	Telephone interview for
Moller,1998	cognitive dysfunction	visual verbal learning test concept shifting test Stroop colour word interference test paper and pencil memory scanning test letter digit coding
	Mood	Zung depression scale
	confusion/ delirium	orientation part of MMSE
	intelligence	part 3 of Cattell culture fair IQ
	ADL	questions about shopping
Olin,2005	delirium	CAM
	cognitive function	MMSE
Rasmussen,2000	Delirium	DSM3 MMSE orientation part

Rasmussen,1999	cognitive function	visual verbal learning test concept shifting test Stroop colour word interference test paper and pencil memory scanning test letter digit coding four boxes test
Shigeta,2001	Delirium	DSM and CAM
Aizawa,2002	Delirium	psychiatric assessment DSM 4
Dijksra, 1999	cognitive function	visual verbal learning test Stroop colour word test concept shifting test letter digit substitution test changes in cognitive function (phone interview)
	depression	Zung self rating scale for
Egbert,1990	Pain	LAS
	sedation	05-Jan
	pain	morphine use
	mental status	Short portable mental status
Ni Chonchubhair,1995	delirium	abbreviated mental test
Kaneko,1997	delirium	DSM-3
	sleep	
	wakefulness response	

Table 14. Among the subset of studies measuring quality of life (n=29), shaded areas indicate the use of at least one patient-centered outcome within one of three health domains.

Author	Symptom Status	Functional Status	General Health
Amemiya, T., et al.			
Casati, A., et al.			
Delaney, C. P., et al.			
Diaz De Liano, A., et al.			
Fei, L., et al.			
Fernando, H. C., et al.			
Ferulano, G. P., et al.			
Gall, C. A., et al.			
Hazebroek, E. J., et al.			
Jayawardhana, B. N., et al.			
Kamolz, T., et al.			
Khajanchee, Y. S., et al.			
Lawrence, V. A., et al.			
Low, D. E. and E. J. Simchuk			
Mastracci, T. M., et al.			
Nienhuijs, S. W., et al.			
Pisanu, A., et al.			
Saeki, H., et al.			
Scarpa, M., et al.			
Schmidt, C. E., et al.			
Walsh, T. H.			
Wang, W., et al.			
Wilson, T. R., et al.			
Evans, C., et al.			
Quebbemann, B., et al.			
Kamolz, T., et al.			
Cavina, E., et al.			
Wu, C. W., et al.			
Udekwu, P., et al.			

Table 15. **Values indicate the percentages of studies using patient-centered outcomes for all studies, the subset that examines recovery, post-operative delirium and quality of life, respectively.**

Health Domain	Patient-Centered Outcomes Examined	All studies (%)	Recovery Studies (%)	Delirium Studies (%)	QoL Studies (%)
Symptom Status	Pain	12.5	25	13.3	0
	Vitality	27.3	41.7	20	17.2
Functional Status	Physical Function	27.3	54.2	13.3	27.6
	Cognitive Function	25	37.5	100	6.9
	Independence	39.8	45.8	20	27.6
General Health Perceptions	Psychological Function	10.2	25	6.7	6.9
	Patient Satisfaction	29.5	25	20	37.9
	Social Function	6.8	8.3	0	6.9

Table 16. Quality assessment of the subset of studies that explicitly examined recovery (Vedel)

Article (author, year)	*Research question*	*Random sample*	*Sample of adequate size*	*Selection of participants*	*Criteria for inclusion/exclusion*	*Definition of the outcomes*	*Source of data*	*Reliability*	*Confounding factors*	*Description of the groups (comparison)*	*Outcomes of people who withdrew*	*Maintained though the follow-up*	*Handing missing data*	*Appropriate statistical analysis*	*Sensitivity analysis*
Amemiya, 2007	Yes	No	Yes	Yes	Yes	Yes	Yes	-	Not Reported	Not applicable	Not Reported	Yes	Not Reported	Yes	Not Reported
Bardram, 1995	Yes	No	No	Not Reported	Yes	Yes	Yes	-	Not Reported	No	Not Reported	Yes	Not Reported	Not applicable	Not Reported
Basse, 2005	Yes	No	No	Yes	Yes	Yes	Not Reported	-	Not Reported	Yes	Yes	Yes	Not Reported	Yes	Not Reported
Beaussier, 2006	Yes	Yes	No	Not Reported	Yes	Yes	Yes	-	Not Reported	Yes	No	Yes	Not Reported	Yes	Not Reported
Edwards, 1993	Yes	Yes	No	Not Reported	Yes	Yes	Yes	-	Not Reported	Yes	Not Reported	Yes	Not Reported	Yes	Not Reported
Fredman, 1999	Yes	Yes	No	Yes	Yes	Yes	Yes	-	Not Reported	Yes	Not Reported	Not Reported	Not Reported	Yes	Not Reported
Gall, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-	Yes	Yes	No	Yes	Not Reported	Yes	Not Reported
Ganai, 2007	Yes	No	No	Yes	Yes	Yes	Yes	-	Not Reported	Not applicable	Not applicable	Not applicable	Not Reported	Yes	Not Reported
Houborg, 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-	Not Reported	Yes	Yes	No	Yes	Yes	Not Reported
Khajanchee, 2001	Yes	No	Yes	Yes	Yes	Yes	Yes	-	Not Reported	Yes	Not applicable	Not applicable	Not Reported	Yes	Not Reported
Lawrence, 2004	Yes	No	Yes	Yes	Yes	Yes	Yes	-	Not Reported	Not applicable	Yes	Yes	Yes	Yes	Not Reported
Mann, 2000	Yes	Yes	No	Yes	Yes	Yes	Yes	-	Not Reported	Yes	No	Yes	Not Reported	Yes	Not Reported
Matsushita, 2002	Yes	No	No	Yes	Yes	Yes	Yes	-	Yes	Yes	Not Reported	Yes	Not Reported	Yes	Not Reported
Miyakura, 2003	Yes	No	Yes	Yes	Yes	Yes	Yes	-	Not Reported	Yes	Not applicable	Not applicable	Not Reported	Yes	Not Reported
Palmer, 1989	Yes	No	No	Not Reported	Not Reported	Not Reported	No	-	Not Reported	No	Not applicable	Yes	Not Reported	Unclear	Not Reported
Tan, 2006	Yes	No	Yes	Yes	Yes	Yes	No	-	Not Reported	Not applicable	Not Reported	Not applicable	Not Reported	Yes	Not Reported
Velasco, 1998	Yes	No	Yes	Yes	Yes	Yes	No	-	Not Reported	Not applicable	Not applicable	Yes	Not Reported	Not Reported	Not Reported
Zalon, 2004	Yes	No	Yes	Yes	Yes	Yes	Yes	-	Not Reported	Not applicable	Not Reported	Yes	Not Reported	Yes	Not Reported
Bardram, 2000	Yes	No	No	Yes	Yes	Yes	Yes	-	Not Reported	Not applicable	Not Reported	Yes	Not Reported	Not Reported	Not Reported

Stewart, 1999	Yes	No	No	Yes	Yes	Yes	No	-	Not Reported	No	Not Reported	Yes	Not Reported	Unclear	Not Reported
Dijksra, 1999	Yes	No	No	Yes	Yes	Yes	Yes	-	Not Reported	Yes	Not Reported	Yes	Not Reported	Yes	Not Reported
Tuech, 2000	Yes	No	No	Yes	Yes	Yes	No	-	Not Reported	Yes	Not Reported	Yes	Not Reported	Unclear	Not Reported
Udekwu, 2001	Yes	No	Yes	Yes	Yes	Yes	No	-	Not Reported	Not applicable	Not Reported	No	Not Reported	Yes	Not Reported
Watters, 1993	Yes	No	No	Yes	Yes	Yes	No	-	Not Reported	Yes	Not Reported	Yes	Not Reported	Unclear	Not Reported

Table 17. Quality assessment of the subset of studies that examined post-operative delirium (Vedel)

Article (author, year)	Research question	Random sample	Sample of adequate size	Selection of participants	Criteria for inclusion/ exclusion	Definition of the outcomes	Source of data	Reliability	Confounding factors	Description of the groups (comparison)	Outcomes of people who withdrew	Maintained though the follow-up	Handing missing data	Appropriate statistical analysis	Sensitivity analysis
Beaussier, 2006	Yes	Yes	No	Not reported	Yes	Yes	Yes	-	Not reported	Yes	No	Yes	Not reported	Yes	Not reported
Ganai, 2007	Yes	No	No	Yes	Yes	Yes	Yes	-	Not reported	Not applicable	Not applicable	Not applicab	Not reported	Yes	Not reported
Koebrugge, 2009	Yes	No	No	Yes	Yes	Yes	Yes	-	Not reported	Yes	Not reported	Not reported	Not reported	Yes	Not reported
Mann, 2000	Yes	Yes	No	Yes	Yes	Yes	Yes	-	Not reported	Yes	No	Yes	Not reported	Yes	Not reported
Marcantonio,1994	Yes	No	Yes	Yes	Yes	Yes	Yes	-	Not reported	Yes	No	Not reported	Not reported	Not reported	Not reported
Moller,1998	Yes	No	Yes	Yes	Yes	Yes	Yes	-	Not reported	Yes	No	Yes	Not reported	Not reported	Not reported
Olin,2005	Yes	No	No	Yes	Yes	Yes	Yes	-	Not reported	Yes	Not reported	Yes	Not reported	Yes	Not reported
Rasmussen,2000	Yes	No	No	Yes	Yes	No	Yes	-	Not reported	No	No	No	Not reported	Yes	Not reported
Rasmussen,1999	Yes	No	No	Yes	Yes	No	Yes	-	Not reported	Not applicable	Not reported	Not reported	Not reported	Yes	Not reported
Shigeta,2001	Yes	No	No	Yes	No	Yes	Yes	-	Not reported	Yes	Not reported	Not reported	Not reported	Yes	Not reported
Aizawa,2002	Yes	Yes	No	Yes	Yes	Yes	Yes	-	Not reported	Yes	Not reported	Not reported	Not reported	Yes	Not reported
Dijksra, 1999	Yes	No	No	Yes	Yes	Yes	Yes	-	Not reported	Yes	Not reported	Yes	Not reported	Yes	Not reported
Egbert,1990	Yes	Yes	No	Yes	Yes	Yes	Yes	-	Not reported	Yes	Not reported	Not reported	Not reported	Yes	Not reported
Ni Chonchubhair,199	Yes	No	Yes	No	Yes	Yes	Yes	-	Not reported	No	Not reported	Not reported	Not reported	Not reported	Yes
Kaneko,1997	Yes	No	No	Yes	Yes	Yes	Yes	-	Not reported	No	Not reported	Not reported	Not reported	Not reported	Not reported

Table 18. Baseline data stratified by the presence or absence of post-operative delirium.

	Total (n=35)	Delirium (n=6)	No Delirium (n=29)
Age (years)	78.3 ± 5.6	81 ± 5.8	77.8 ± 5.5
Gender			
• **Male**	17 (49)	1 (16.7)	16 (55.2)
• **Female**	18 (51)	5 (83.3)	13 (44.8)
CCI	2.3 ± 1.9	3.7 ± 2.9	2.0 ± 1.5
Procedure Type			
• **General Surgery**	22 (62.9)	2 (33.3)	20 (69.0)
• **Vascular Surgery**	11 (31.4)	2 (33.3)	9 (31.0)
• **ENT Surgery**	2 (5.7)	2 (33.3)	0 (0)
Cancer diagnosis	23 (65.7)	4 (66.7)	19 (65.5)
Education Level			
• **None**	1 (2.8)	0 (0)	1 (3.5)
• **Elementary**	14 (40)	4 (66.7)	9 (34.5)
• **High School**	12 (34.3)	1(16.7)	11 (37.9)
• **University**	7 (20)	1(16.7)	6 (20.7)
• **Postgraduate**	1 (2.8)	0 (0)	1 (3.4)
MoCA score	21.8 ± 3.7	20.8 ± 4.4	22.1 ± 3.6
MCI present	29 (85.3)	5 (83.3)	24 (85.7)
MMSE score	27.5 ± 1.7	27.5 ± 2.4	27.6 ± 1.6

Data is presented as absolute number (%) or mean ± standard deviation
CCI: Charlson Comorbidity Index, ENT: ear, nose and throat, MoCA: Montreal Cognitive Assessment, MCI: mild cognitive impairment, MMSE: mini-mental status exam.

Table 20. Logistic regression with delirium as the dependent variable

Variable	Odds Ratio	95% confidence interval
Age	1.08	0.89 – 1.31
Gender	0.12	0.01 – 1.49
CCI	1.69	0.92 – 3.12
MCI	0.19	0.01 – 3.87

CCI: Charlson Comorbidity Index, MCI: mild cognitive impairment

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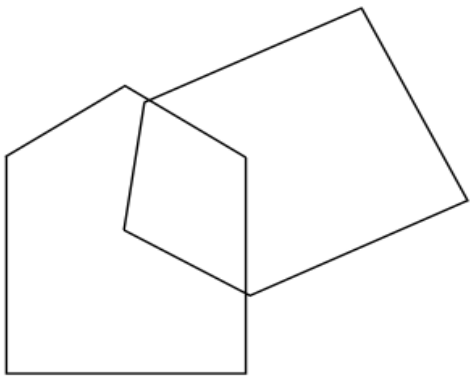
APPENDIX I - Quality analysis appraisal form (Vedel)

	Assessment	Yes	No	Unclear	Not Reported	Not Applicable
Objectives	1. Was the research question/hypothesis/theoretical framework clearly formulated?					
Participants	2. Was the study based on a random of pseudo-random sample?					
	3. Was the sample of adequate size (n≥100)?					
	4. Were the source and methods of selection of participants described?					
	5. Were the criteria for inclusion and exclusion in the sample clearly defined?					
Variables	6. Were there clear definitions of the outcomes? Were the outcomes assessed using objective criteria?					
Measurement	7. Was the source of data described?					
	8. Did the measure outcomes have an acceptable reliability/use a previously validated instrument /were they tested?					
Statistical analysis	9. Were confounding factors indentified and strategies to deal with them stated?					
	10. If comparisons were made, were there sufficient descriptions of the group?					
	11. Were the outcomes of people who withdrew described and included in the analysis?					
	12. Was a reasonable portion of sample maintained through the follow-up?					
	13. Was an appropriate technique used to handle missing data?					
	14. Was an appropriate statistical analysis used?					
	15. Were any sensitivity analyses conducted?					

APPENDIX II- COGNITIVE ASSESSMENTS

	Maxium Correct Score	Client's Score	
			ORIENTATION
1)	5	( )	What is the – date _____, day of week _____, month _____, season _____, year _____ ?
2)	5	( )	Where are we – name of country _____, province _____, city _____, place _____ (Street), floor _____ (House # / Apt #) ?
			REGISTRATION
3)	3	( )	Name 3 objects (HOUSE, TREE, CAR). Take 1 second to say each. Then ask the client all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he learns all 3. Count trials and record. **TRIALS** _____
			ATTENTION AND CALCULATION
4)	5	( )	Serial 7's 100 – 7 = ( ), 93 = ( ), 86 = ( ), 79 = ( ), 72 = ( ), 65. One point for each correct answer. (Alternatively spell "WORLD" backwards).
			RECALL
5)	3	( )	Ask for 3 objects – HOUSE ( ), TREE ( ), CAR ( )
			LANGUAGE
6)	9	( )	Name a pencil, and watch ( ) 2 points Repeat the following – "NO IFS, ANDS OR BUTS" ( ) 1 point Follow a 3 – stage command: "Take the paper in your right hand, fold it in half, and put it on the floor." ( ) 3 points Read and obey the following: CLOSE YOUR EYES ( ) 1 point Write a sentence (1 point)

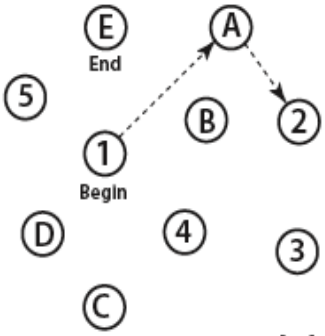
Copy design (1 point)

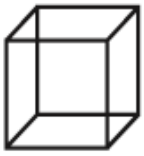


MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE





Copy cube [ ] [ ]

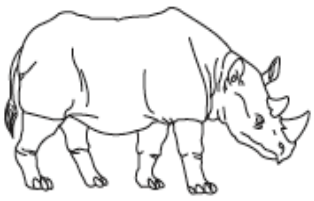
Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

POINTS __/5

NAMING

[ ]



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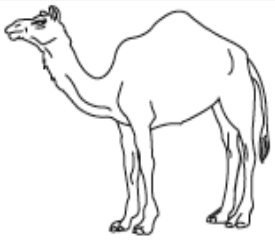

[ ]

__/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

 Version 7.1 **www.mocatest.org** Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

CONFUSION ASSESSMENT METHOD (CAM) QUESTIONNAIRE

OBSERVATIONS BY INTERVIEWER

Interviewer: Immediately after completing the interview, please answer the following questions based on what you observed during the interview, Modified Mini-Cog Test (Pg 25), and Digit Span Test.

ACUTE ONSET

1. a. Is there evidence of an acute change in mental status from the patient's baseline?

Yes	- 1
No	- 2
Uncertain	- 8

b. (IF YES) Please describe change and source of information:

_____

_____

INATTENTION

2. a. Did the patient have difficulty focusing attention, for example being easily distractible, or having difficulty keeping track of what was being said?

Not present at any time during interview	- 1
Present at some time during interview, but in mild form	- 2
Present at some time during interview, in marked form	- 3
Uncertain	- 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase and decrease in severity?

Yes	- 1
No	- 2
Uncertain	- 8
Not Applicable (NA)	- 9

c. (IF PRESENT) Please describe this behavior:

_____

_____

_____

DISORGANIZED THINKING

3. a. Was the patient's thinking disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow or of ideas, unpredictable switching from subject to subject?

Not present at any time during interview	- 1
Present at some time during interview, but in mild form	- 2
Present at some time during interview, in marked form	- 3
Uncertain	- 8

b. (IF PRESENT) Did this behavior fluctuate during the interview, that is, tend to come and go or increase or decrease in severity?

Yes	- 1
No	- 2
Uncertain	- 8
NA	- 9

c. (IF PRESENT) Please describe this behavior:

_____

_____

_____

ALTERED LEVEL OF CONSCIOUSNESS

4. a. Overall, how would you rate this patient's level of consciousness?

GO TO Q5 ←	Alert (Normal)	- 1
	Vigilant (Hyperalert, overly sensitive to environmental stimuli, startled very easily	- 2
	Lethargic (Drowsy, easily aroused)	- 3
	Stupor (Difficult to arouse)	- 4
	Coma (Unarousable)	- 5
	Uncertain	- 8

APPENDIX III- DATA COLLECTION SHEET

Patient name ________________ Medical Record #___________ Study ID # ______

✂- -

Study ID # ____________________ **Pre-op Date** ___/___/____ **Education level:** ______

Age: _______ **Gender:** □ Male □ Female **Diagnosis:** _____________

Comorbidities:

______________________ ______________________ ______________________

______________________ ______________________ ______________________

______________________ ______________________ ______________________

Pre-op MOCA: __________ **Pre-op MMSE:** __________ **Pre-op CAM:** ______

Procedure Date: ___/___/____ **Procedure:**____________________________

ASA Score □ 1 □ 2 □ 3 □ 4 □ 5

Intra-op complications: ____

Clavien Grade ( )

COMPLICATIONS □ **NO**

□ Urinary Tract Infection ( )	□ Superficial Thrombophlebitis ( )	□ C. diff Colitis ( )
□ Wound Disruption ( )	□ CVA/Stroke ( )	□ Graft/Prosthesis/Flap Failure ( )
□ Pneumonia ( )	□ Coma > 24 Hours ( )	□ Deep Vein Thrombosis ( )
□ Unplanned Intubation ( )	□ Cardiac Arrest requiring CPR ( )	□ Sepsis ( )
□ Pulmonary Embolism ( )	□ Myocardial Infarction ( )	□ Septic Shock ( )
□ On Ventilator > 48 Hours ( )	□ Peripheral/Cranial Nerve Injury ( )	□ Return to Operating Room ( )
□ Acute Renal Failure ( )	□ Bleeding > 4 Units ( )	□ Mortality ( )
□ SSI: Superficial Incisional ( )	□ SSI: Deep Incisional ( )	□ SSI: Organ Space ( )
□ Other: ________________________ ( )		

Restraints Physical: □ Yes □ No **Chemical:** □ Yes □ No

- Fall(s): □ Yes □ No **- Sitter:** □ Yes □ No

Delirium

	POD 1	POD 2	POD 3	POD 4	POD 5	POD 6	POD 7
+ CAM							

APPENDIX IV- Consent Form

SMBD - Jewish General Hospital
Department of Surgery
Dr. Simon Bergman, MD, MSc, FRCSC

Consent Form
CAN THE MONTREAL COGNITIVE ASSESSMENT PREDICT POST-OPERATIVE DELIRIUM? A PILOT STUDY

Introduction
You are being invited to participate in a clinical research study which is designed to look at delirium in older patiens who are undergoing major surgery. You have the right to know about the purpose and procedures that are to be used in this research study, and to be informed about the potential benefits, risks, compensation, and discomfort of this research.

Before you give your consent to be a participant, it is important that you read the following information and ask as many questions as is necessary in order to understand what you will be asked to do, should you decide to participate. It is also important that you understand that you do not have to take part in this study.

Purpose of study
Delirium is a state of confusion and of increased or decreased mental or motor activity. This is brought on by stress to the body and often occurs after surgery. This can be because of the surgery and anesthesia, because of complications, or simply from being in an unfamiliar place. Delirium can be dangerous, because it puts an older person at risk for falls, a slower recovery, and even a higher chance of dying in the hospital. Also, an older person can take days to even weeks to recover his or her usual mental function once the stress on the body has been removed. Unfortunately, delirium is difficult to prevent, because it is unclear which patients are most at risk of developing it. We believe that older patients with early memory and attention problems, or "mild cognitive impairment" (MCI for short) are a group particularly at risk for delirium after surgery.

The purpose of this study is to determine whether people with MCI, as diagnosed by a questionnaire called the Montreal Cognitive Assessment, are at higher risk of developing delirium. To do this, we will compare how often delirium occurs after surgery in those with MCI and in those *without* MCI.

Procedures
This is what you can expect if you decide to participate in this study:

1) Before Surgery (at the pre-operative clinic)
   - 2 short memory and attention tests (about 20 minutes total)

2) After Surgery (while you are in the hospital)

- Every day that you are in the hospital for the first week, you will receive a visit from the same investigator. He/she will give you a short memory and attention test (about 15 minutes per visit).

Your hospital charts will also be look at for relevent information while you are on the study.

Risks, Discomforts and Side-Effects
There are no risks, discomforts or side-effects associated with this study. If you are found to have mild cognitive impairment or delerium this information will be given to to either the pre-operative clinic physician or the surgical team who will follow up with your care.

Benefits
The potential benefit to participating in this study is that the questionnaires that you answer may help you uncover certain medical conditions (cognitive impairment, delirium) that may have otherwise gone undetected.

This study will help us better understand how to predict delirium after surgery, which may benefit other elderly patients undergoing surgery in the future.

Voluntary participation/withdrawal
Your participation in this study is voluntary. You may choose to participate now and decide to stop your participation at any time. Your future medical care and your patient-doctor relationship will not be affected in any way. If you wish to stop taking part in this study, it is very important that you inform your study doctor. He/she will explain to you the best way for you to end your participation in this study.

Confidentiality
All information obtained about you during this research will be treated confidentially within the limits of the law. This information will be coded, and kept under lock and key. Decoding can only be performed by the principal researcher or a person authorized by the principal researcher. The study files will be kept at the Lady Davis Institute under the responsibility of Dr. Simon Bergman, for 5 years, and then destroyed. Access to your identifying information will be restricted and supervised by the principal researcher. No information that discloses your identity will be allowed to leave this institution.

The results of this research may be published or communicated in other ways; however, your identity or any other identifying information will not be disclosed in any reports or publications.

If you withdraw (or are withdrawn) from this study, any information collected up to the point of withdrawal for the purpose of this research may still be used in order to protect the scientific integrity of the study.

Costs and compensation

You will not be paid for your participation in this study.

Contact information or questions

If you have any questions about the research now or later, if you notice anything unusual, you should call Dr. Simon Bergman at 514-340-8222 ext. 4611. If you have questions about your rights as a research participant, you may call the Jewish General Hospital Local Commissioner of Complaints & Quality of Services, Rosemary Steinberg, at (514) 340-8222 ext. 5833.

STATEMENT OF CONSENT
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I have read the above information and my questions were answered to my satisfaction. A copy of this signed consent form will be given to me. My participation is voluntary and I can withdraw from the study at any time without giving reasons, without it affecting my medical care now or later. I do not give up any of my legal rights by signing this consent form. I agree to participate in this study.

I agree that my family doctor will be told about my participation in this research (please circle one):

YES **NO** INITIALS: _____

Signature: _____ Date: _____

Name of Participant: _____

Consent form administered and explained in person by:

Signature: _____ Date: _____

Name of Investigator (or delegate): _____

RESEARCH ETHICS
04 MAI 2010
APPROVAL
INITIALS