OBSTETRICAL BRACHIAL PLEXUS INJURY: A GUIDELINE

OBSTETRICAL BRACHIAL PLEXUS INJURY: A NATIONAL CLINICAL PRACTICE GUIDELINE

By:

CHRISTOPHER JAMES CORONEOS, BHSc, MD

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AUTHOR:	Christopher James Coroneos, BHSc (McMaster University), MD (The University of Western Ontario)
SUPERVISOR:	Dr. Melissa C. Brouwers, BSc, MA, PhD
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ABSTRACT

Purpose

The objective of this thesis is to establish an evidence-based clinical practice guideline for the primary management of obstetrical brachial plexus injury (OBPI). Four gaps are identified for management of OBPI in Canada: 1) The historic poor use of evidence, 2) Timing of referral to multidisciplinary care, 3) Indications and timing of operative nerve repair, and 4) Distribution of expertise in Canada.

Methods

The guideline is intended for all providers delivering perinatal care, and all specialists delivering care to OBPI patients. The consensus group was composed of clinicians representing each of Canada's ten multidisciplinary centres. An original systematic review comparing the effectiveness of primary operative versus nonoperative management, and a review of Canadian OBPI epidemiology were completed. Quality indicators for referral to a multidisciplinary centre were established. Recommendations were based on best evidence, and interpretation of this evidence by clinical experts. An electronic modified Delphi approach was used for consensus, with agreement criteria defined a priori following RAND procedures.

Results

Nerve repair reduces functional impairment in OBPI versus nonoperative management of similar patients, and modern microsurgery has low incidence of major adverse events. The quality of evidence was low. Residual impairment is underestimated and uncharacterized in nonoperative literature. OBPI incidence was at least 1.24 per 1000 births in Canada, and consistent over the study period. The strongest risk factors for OBPI were comorbid humerus fracture, shoulder dystocia and comorbid clavicle fracture. Most patients were not referred to a multidisciplinary centre. The guideline group approved seven recommendations.

Discussion

Recommendations address the identified gaps in care, and guide identification, referral, treatment and outcome assessment for OBPI. The process established a new network of opinion leaders and researchers for further guideline development, and multicentre research. The next step is to facilitate the implementation of the recommendations.

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LIST OF ABBREVIATIONS

AGREE-II	Appraisal of Guidelines for Research & Evaluation - II
AMS	Active Movement Scale
ARR	Absolute risk reduction
BMI	Body mass index
BPOM	Brachial Plexus Outcome Measure
CI	Confidence interval
CIHI	Canadian Institute for Health Information
CIHR	Canadian Institutes of Health Research
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CT	Computed tomography
EMBASE	Excerpta Medica database
EMG	Electromyography
ER	External rotation
ICF	International Classification of Function, Disability and Health
IKT	Integrated Knowledge Translation
IR	Internal rotation
KT	Knowledge translation
KTA	Knowledge-to-action
MEDLINE	Medical Literature Analysis and Retrieval System Online
MINORS	Methodological Index for Non-Randomized Studies
MRC (M)	Medical Research Council Muscle Grading System
MRI	Magnetic resonance imaging
NCS	Nerve conduction study
NNT	Number needed to treat

OBPI	Obstetrical brachial plexus injury
OIS	Optimal information size
OR	Odds ratio
Primary care	Health care professionals that are the first point of contact for newborns in the healthcare system. This includes but is not limited to: general practitioners, family physicians, obstetricians and gynaecologists, paediatricians, general physical and occupational therapists, nurses, midwives, etc.
RCT	Randomized controlled trial
RR	Relative risk
Specialist	Health care professionals that newborns are referred to for OBPI management. This includes but is not limited to: peripheral nerve surgeons, physical medicine and rehabilitation physicians, other specialized physical and occupational therapists, other physicians and surgeons, radiologists, specialized nurses, etc.

CHAPTER 1: INTRODUCTION

1.1 Statement of Problem

The brachial plexus is a network of peripheral nerves providing innervation to the upper extremity. It is composed of the ventral rami of the fifth to eighth cervical, and first thoracic spinal nerves. Obstetrical brachial plexus injury (OBPI) is an injury in newborns, caused by traction on the neck-shoulder angle during labour and delivery.(1) Traction leads to lesions typically at the root and truck levels of the brachial plexus. Incidence is estimated between 0.5 to 2 in 1000 births.(2) Shoulder dystocia is the main risk factor; others are related to fetal size, prolonged labour, difficult/instrumented delivery and presence of other fetal trauma.(3) Clinical presentation immediately following delivery is consistent regardless of injury severity; newborns experience flaccid paralysis of the upper extremity.(4) Given the absence of a gold-standard baseline investigation,(5) serial examination over time is required to determine injury severity.

Most cases of OBPI are transient,(6) with complete spontaneous recovery expected. However, children with incomplete recovery suffer lifelong functional impairment, with joint involvement dictated by the root levels injured. Long-term sequelae include weakness, joint contracture, joint architecture deformity, and limb length discrepancy.(7,8) Residual, central nervous system mediated, developmental morbidity(9) has been identified in children with intact nerves.(10,11) Beyond physical impairment, OBPI impacts the family dynamic,(12) and the child's global development.(7)

OBPI management is limited by four gaps.

1.1.1 Historic Poor Use of Evidence

Residual deficits with nonoperative therapy are underestimated,(6,13) and surgical outcomes of OBPI are evaluated inconsistently.(14) Moreover, operative indications and timing have not been compared with a randomized controlled trial,(15) despite acknowledgment of the need for a high quality study.(16,17) No review has addressed the existing cohort studies comparing microsurgical repair versus nonoperative recovery. The dearth of conclusive evidence, and incomplete and inappropriate analyses of the existing data, may have allowed historic attitudes to remain among primary care providers.

1.1.2 Timing of Referral to Multidisciplinary Care

While most injuries spontaneously recover,(6) they are not discernible at baseline from severe injuries that require operative nerve repair.(18) Primary care providers for newborns likely lack the expertise to monitor peripheral nerve recovery,(19,20) and often provide guardians with inaccurate information and education.(21) Recovery is often overestimated, causing guardian distress and delayed specialist referral.(18) Early referral to a multidisciplinary centre addresses guardian education,(21) treatment by specialized therapists,(8,22) serial assessment for recovery and operative planning if necessary;(18) however, ideal referral timing is not established. The optimal window for operative reconstruction is three months of age for the most severe injuries, and the latest surgical indications are applied at nine months.(22) However, for example, 12% of referrals to

McMaster University's multidisciplinary clinic are patients three years of age or older with residual functional impairment.(23)

1.1.3 Indications and Timing of Operative Nerve Repair

Surgeons agree mild injuries (eg. Narakas I) with immediate evidence of improvement and significant recovery by one month, do not require repair.(23) Conversely, severe total plexus injuries with clinical evidence of root avulsion and poor hand function (eg. Narakas IV), require early repair to preserve distal function.(22,23) However, 50-90% of OBPI patient referrals to specialty centres have injuries between these extremes, with surgical indications and timing varying between centres.(24–28) As a result, treatment may not be optimized.

1.1.4 Distribution of Expertise in Canada

OBPI expertise is not evenly distributed across the country, with ten multidisciplinary centres in Canada located at academic institutions in large cities. In the health care system, a physician must generate patient referrals to specialists at multidisciplinary centres. For these centres, communication with primary care and patient logistics are challenging; centres serve expansive geographic areas and diverse populations (eg. Saskatchewan and the Territories do not have a centre, with treatment provided in neighbouring provinces). Given the historic lack of evidence and significant practice variation among Canadian centres,(22,23,29) primary care is not well informed

about how to optimally manage and refer these patients. Unified recommendations from OBPI specialists do not exist to guide practice.

Networking opportunities are rare between multidisciplinary centres themselves. The need for multicenter trials has been demonstrated in the literature.(16,17) Individually, and within the scope of their individual expertise, each of Canada's OBPI centres has contributed high-level research recognized on the international level. However, no single institution treats the clinical volume of patients to power its own large trial in a practical timeframe. Collaboration between the centres is required to advance quality of care more rapidly, and address aforementioned system-level issues.

1.2 Objectives

The overall objective of this study is to develop an evidence-based clinical practice guideline for the primary management of OBPI. To address this objective, the study is divided into three parts.

1.2.1 Part I: Systematic Review and Meta-analysis of Primary Management

1.2.1.1 Primary Objectives

1. To assess the effect of primary operative and nonoperative management on physical function in patients with OBPI.
2. To determine if one strategy is superior to the other and for which patients.

1.2.2 Part II: Review of Canadian Epidemiology

1.2.2.1 Primary Objectives

1. To measure volume and timing of OBPI referral to Canadian multidisciplinary centres.

1.2.2.2 Secondary Objectives

1. To determine the incidence of OBPI in Canada.
2. To measure OBPI risk factors for identified cases.

1.2.3 Part III: Clinical Practice Guideline

1.2.3.1 Primary Objectives

1. To develop evidence-based recommendations for the primary management of OBPI.

1.3 Rationale

OBPI treatment has evolved since the adoption of microsurgery.(30) The role of physical and occupational therapists has been established for assessment(22) and rehabilitation therapy.(31) Numerous operative algorithms,(22,23,25,28,32,33), novel repair techniques(14,34–41) and evaluation methods(42) exist for patients. Still, gaps exist; evidence in the literature is weak,(16,17) referral from primary care(18) and surgical indications vary,(23) and expertise is concentrated. The need for guidelines

encompassing the initial evaluation, diagnostic investigation, management and outcome evaluation has been demonstrated.(43)

Integrating care for this patient population is challenging. A diverse group of physicians and other health care providers are involved in perinatal care. The relationship and timing between injury identification, referral, assessment and management are critical; surgery is performed as early as three month of age. Given this clinical background, where practice is heterogeneous and evidence is unclear, rigorous approaches to knowledge synthesis and application have the greatest capacity to impact practice.(44) Development and application of a clinical practice guideline has the potential to improve knowledge among clinicians, improve educated referral, influence care processes at tertiary care centres, minimize practice variation, inform policy and establish criteria for evaluation/quality review for OBPI.(45) If applied, these factors will contribute to optimizing care and improving clinical outcomes.

Beyond providing deliverable recommendations to address practice variation, clinical gaps in referral and operative indications, the process of guideline development itself can facilitate the development of an "evidence culture" of OBPI management in Canada. By forming a "network of opinion leaders and researchers", stages of guideline development foster collaboration and cohesion among national specialists, improve their acceptance and application of evidence, and create opportunities to facilitate an integrative research environment.(44) This may address the distribution of expertise in the country. Opinion leaders are same group of individuals who will ultimately influence dissemination, implementation, and health policy in their clinical settings. A clinical

practice guideline can improve transparency,(46) by providing a consistent message to primary care providers and guardians. Finally, guideline development can advance a program of research to address known gaps,(45) by establishing priorities for a national research program and facilitating the formation of new research teams with the skills and motivation to pursue, for example, the types of multicentre trials required in the OBPI field to advance quality.

CHAPTER 2: BACKGROUND

2.1 Clinical Background

2.1.1 Nerve Injury Classification

Patterns and corresponding severity of nerve traction can be classified into "stretch" (neuropraxia, Sunderland I), degrees of "rupture" (axonotmesis/neurotmesis, Sunderland II-V) and "root avulsion".(8,47) Stretch injuries are least severe; the nerve sustains a conduction block with traction. Nerve structures remain intact, spontaneous recovery begins immediately, and complete recovery is expected without surgery.(23) Conversely, avulsion is most severe; the nerve root is physically separated from the motor cell body within the spinal cord. No motor spontaneous recovery is expected.(8) These nerve distributions do not recover function without surgery.(23)

Degrees of rupture are between these extremes. In contrast to adult injuries, complete ruptures with a physical "gap" are uncommon.(5) Typically, the nerve axon is disrupted with variable involvement of the connective tissue framework (axonotmesis and neurotmesis). Wallerian degeneration occurs distal to the lesion in both cases. Neurotmesis is more severe; the axon and its connective tissue framework are completely disrupted. There is no recovery potential without nerve repair. In axonotmesis, the axon is disrupted with incomplete involvement of the connective tissue framework. Subsequent axon regeneration occurs at approximately one millimetre per day. Recovery is slow and ultimate function is uncertain; it is dependent on the extent of neuroma-in-continuity scar

formation. The proportion of injuries ultimately with poor function may be improved with nerve repair.(23)

Root involvement defines clinical presentation of brachial plexus injury. Narakas provides an ordinal classification.(48) Injuries most commonly involve the "upper plexus". Narakas I (C5-6), is the classic Erb's palsy,(49) with the shoulder internally rotated and adducted, elbow extended, and forearm pronated. Narakas II (C5-C7) adds C7 injury with the historic "policeman's tip", later termed "waiter's tip"(4) hand position, characterized by wrist and metacarpophalangeal joint flexion, and proximal and distal interphalangeal joint extension. Narakas III (C5-T1) includes total plexus injury. Narakas IV (C5-T1) adds Horner's syndrome, indicative of preganglionic T1 injury,(22) and likely root avulsion. Isolated "lower plexus" injuries (C8-T1) are not included in Narakas classification and are exceptionally rare.(50)

2.1.2 Intervention Options

All OBPI patients receive physical and/or occupational therapy to maintain full range of motion and strength, and prevent fixed contractures, muscle imbalance, and poor motor patterns.(51–53) Often, this is as simple as teaching parents positioning, handling, and exercises to perform at home with their infant.(52,54) Limb visualization and developmental exercises aim to maintain milestone progression and prevent neglect.(31) Therapy begins immediately to facilitate spontaneous recovery, and is adjusted both prior to and following other treatments to optimize results. A specialized physical or occupational therapist within the multidisciplinary team typically supervises programs

and aids in clinical decision-making.(8,22) Additional nonoperative treatments include splinting, taping, neuromuscular electrical stimulation, postural therapy and biofeedback.(53–55)

Early surgical intervention is critical for peripheral nerve lesions without potential for recovery; it limits loss of motor-end plate density and atrophy at distal muscles.(56) By basic principles of peripheral nerve surgery, surgeons repair injuries with poor prognosis, and avoid surgery in injuries destined to spontaneously recover.(23) Neurotmesis or avulsion injuries have no potential to recover, and require early repair. Axonotmesis injuries with limited axon regeneration may preclude functional recovery.(34) Reported options for nerve repair include direct end-to-end neurorraphy, neurolysis, nerve transfer, and neuroma excision and grafting.(8)

In both operative and nonoperative approaches, sequelae of incomplete recovery are approached with secondary surgery. These procedures include tendon transfers and osteotomies targeted to functional limitations, joint contractures, and joint architecture deformities.(8)

2.1.3 Evolution of OBPI Management

The surgical principles of OBPI surgery, neuroma excision and nerve repair, were established in the early 1900s.(57,58) However, subsequent series failed to demonstrate improvement, while reporting high risk of morbidity and mortality consistent with paediatric surgery during the era. Nonoperative management was subsequently favoured through to the 1970s, with literature focusing on “natural history” of recovery.(59,60)

OBPI deficits were considered transient and without important sequelae in the primary care literature,(19,61,62) making nerve repair "unwarranted".(63) "Full recovery" was reported in 70-95% of cases.(23,63–66) However, definitions of full recovery were broad and inconsistent(7) or not reported,(23) thus biasing toward overestimation. Contemporary series indicate full recovery in approximately 66% of cases.(13,67,68) While children may be described as "recovered", mild sequelae cause important functional impairment (eg. deficits in shoulder external rotation or forearm supination).(69) Moreover, residual, centrally mediated OBPI morbidity(9) has been identified in children with intact nerves.(10,11)

In the 1980s, the emergence of microsurgery,(60) success of adult brachial plexus repair,(70) and safety of paediatric anaesthesia(27) led to increased application of peripheral nerve repair techniques to OBPI. Early series reported success of primary nerve repair; their operative indications are still commonly applied.(30) However, after 30 years, there remains disagreement among specialists and an absence of definitive evidence for surgical timing, operative indications and type of nerve procedure to perform.(8,71)

2.1.4 Summary

Based on the aforementioned factors, OBPI management is complex. Perinatal primary care providers do not have the expertise to evaluate recovery of peripheral nerve injuries and are often uncertain of care algorithms.(20) Parents find management "confusing and time-consuming".(20) Timing of referral to specialized physicians and

therapists is critical, peripheral nerve injuries require timely repair. However, specific indications and timing of repair of intermediate severity injuries is uncertain. Management can be improved with an optimized and coherent practice approach to referral and subsequent management. Failing timely nonoperative and operative management, there is an increased burden of disease; the injury impacts physical function, aesthetic form, the child's development, and the family dynamic.(7)

2.2 Increasing the Use of Knowledge in Clinical Practice

2.2.1 Use of Evidence

The literature consistently reports a gap between best evidence and care actually delivered.(72) In 2001, "Crossing the Quality Chasm"(73) reported the overuse of inappropriate treatments, and underuse of proven interventions. These were both identified as deficiencies in the delivery of high quality care.(73) Interventions do not reflect best practice and healthcare resources are wasted.(72) These issues occur simultaneously in the same region(74) and independently of procedure volume.(75) Adoption of findings from high quality research into practice is delayed for years following publication.(76) Canadian health policy processes do not consistently utilize health services research.(77) Overall, gaps represent a risk to patients.(76) While care delivered does not reflect best evidence in 30-45% of cases, in 20-25% of cases it is ineffective or harmful.(78)

2.2.2 Knowledge Translation

Uncertainty in OBPI management among primary care providers, parents and specialists is attributable, in part, to a deficiency in the evidence base. Existing evidence has not been synthesized to support clinically relevant decision-making. Primary research is lacking to inform aspects of care (eg. nonoperative therapy).(79,80) Parents and primary care providers would benefit from consistent and unified education and communication from specialists. Reflecting these limitations, OBPI care would likely benefit from approaches to synthesis, knowledge application, dissemination and exchange.(78)

The field of knowledge translation (KT) attempts to bridge gaps by directing how to put best evidence into practice, or "knowledge into action".(81) KT is synonymous with a number of terms, including implementation science, research utilization, knowledge transfer, exchange diffusion and dissemination.(78) From a Canadian perspective, the Canadian Institutes of Health Research (CIHR) uses the term KT and provides a robust definition: "a dynamic and iterative process that includes the synthesis, dissemination, exchange and ethically sound application of knowledge to improve health, provide more effective health services and products and strengthen the healthcare system."(82) This definition is relevant to health care providers, health policy personnel, patients and the public.(78) The science and practice of KT provides a framework, evidence-based tools, and interventions to improve OBPI management.

2.2.3 Knowledge-to-Action Cycle

To understand KT and the process of engineering change, many planned-action theories, conceptual frameworks, and theoretical models are described.(78) CIHR

supports the knowledge-to-action (KTA) cycle to define KT processes and design research (Figure 2-1).(82) KTA is a conceptual framework, empirically based on over 30 planned action theories.(78) Planned action theory is well suited, as it encompasses the prediction and explanation of behaviour.(83) While change is simply described in diffusion theory(84) and conceptualization,(85) it is engineered and deliberate in KTA. Knowledge creation is illustrated centrally in three stages. The action cycle is illustrated peripherally in seven stages, reflecting planned action theory to drive change in a specific setting. These stages are dynamic and integrated, with each influencing the others.(82)

Knowledge creation is divided into three distinct phases: 1) Knowledge inquiry, 2) Knowledge synthesis, and 3) Knowledge tools. These phases conceptualize the progression of knowledge from primary research (eg. clinical trials) to knowledge syntheses (eg. systematic reviews) and finally knowledge tools (eg. clinical practice guidelines). In each stage, knowledge is distilled to be more accessible to end users.(82)

KTA provides an organizing framework to help us focus our efforts. This program of research is centred at the cusp of the knowledge creation and action cycle. Review of Canadian OBPI epidemiology provides knowledge inquiry. Systematic review of operative versus nonoperative management provides a high-level knowledge synthesis. With this evidence base established, a clinical practice guideline can be produced.

2.2.4 Clinical Practice Guidelines

"Evidence-based clinical practice guidelines are knowledge tools defined as systematically developed statements that help clinicians and patients make decisions

about appropriate health care for specific clinical circumstances."(45) This definition can be expanded to include decisions made by healthcare managers and health policy personnel.(45,86) Guidelines represent a refined facet of knowledge creation in KTA, systematically summarizing and appraising primary research and syntheses, and creating actionable messages to guide best practice. Clinical practice guidelines are distinct from the compulsory steps and actions in health care protocols or clinical pathways.(46) Instead, they are tools to facilitate decision-making,(45) by interpreting the evidence for management options, and balancing their risks and benefits. In addition, to clinical decision-making, clinical practice guidelines influence policy in detecting strengths and limitations in research, defining cost effective practice and resource allocation, and providing quality indicators.(45,46)

From a developmental perspective, the structure and methodology for clinical practice guidelines are well established.(44) They are increasingly popular and adopted into practice.(87,88) Tools exist to advance the development and application of clinical practice guidelines. For example, the AGREE-II instrument (Appraisal of Guidelines for Research & Evaluation), is an international standard used to direct the development, reporting, and evaluation of guidelines,(89) and the ADAPTE tool is available to direct adaptation of existing guidelines to new settings.(90)

Clinical practice guidelines have potential for multiple beneficial impacts, both in development and implementation. Knowledge among health care providers, and intent of their behaviours improve.(44) Unwanted practice variation is minimized, and processes of care are influenced with changes toward recommendation content.(44) Patients may be

better informed by transparent reporting of distilled evidence, highlighting management options and risk versus benefit trade-offs.(46,91) Policy deliberations are impacted; clinical practice guidelines inform quality indicators, access to care and funding decisions.(45) Ultimately, implementation likely results in improved outcomes.(92) Guideline development produces a rigorous review of current literature, highlighting strengths and gaps.(46,93) Moreover, development engages opinion leaders, developing a network to engage stakeholders, enhance implementation and spur primary research.(45) Currently, no comprehensive guideline exists in Canada, or elsewhere, to guide the management of OBPI.

2.2.5 Identifying Practice Gaps

High quality evidence and tools such as clinical practice guidelines are necessary but not sufficient to impact practice.(94) For implementation to be successful, elements of the knowledge-to-action cycle should be considered during guideline development.(46) The first stage following knowledge creation is identifying the "problem", the knowledge-practice gap.

At this stage, the discrepancy between knowledge contained in syntheses and guidelines, and care ultimately delivered can be objectively quantified using quality indicators.(95) Ideally, these measures are valid, reliable, clinically relevant, sensitive to change, and feasible to obtain in practice.(96) Measures, acceptable variation, and the definitions of "good", "satisfactory" and a "gap" can be identified by stakeholders through a dedicated consensus process,(97) or within a clinical practice guideline.(95)

With quality indicators and definitions established, gaps can be quantified at every level of the healthcare system. From a population perspective, data are typically available from sources such as government health insurance plans; information is generated secondary to reimbursement instead of primarily for research, and is limited to standard diagnostic codes and the population and services eligible for coverage.(98) From an organizational perspective, data are typically available from hospitals and healthcare networks.(95) They are often more robust in demonstrating the organizational structure (eg. providers involved), process (eg. referrals, times) and outcomes (eg. investigations, clinical) associated with a disease diagnosis.(95) Finally, from a single provider perspective, data are available for patient outcomes, and provider practice patterns, knowledge and competencies.(95)

In Canada, the burden of health for OBPI has not been investigated. Moreover, while timely referral to multidisciplinary care is a clinically important limitation in management of OBPI, quality indicators for referral timing are not defined; their establishment would allow this gap to be reliably measured and monitored.

2.2.6 OBPI in the KTA Cycle

OBPI care may be improved with approaches to synthesis, knowledge application, dissemination, and communication. The KTA framework provides a guide to this program of research. Products of this program (review of epidemiology, systematic review of management, clinical practice guideline and generation of quality indicators) provide the tools and means to address defined gaps in OBPI management.

Components of this thesis provide the foundation to an integrative process to improve OBPI care in Canada by applying principles and tools from the KT field. Primary data and quality indicators, not previously utilized in OBPI research, can characterize gaps in care. Results of the systematic review and guideline recommendations, both currently absent in OBPI, will direct clinical care and demonstrate gaps to address with a research enterprise. The social aspect of guideline creation provides a network to execute multicentre research, and unified information to primary care providers and patient guardians. Applying KT to OBPI in Canada provides an opportunity to improve the quality of care, health services, patient outcomes and health policy.

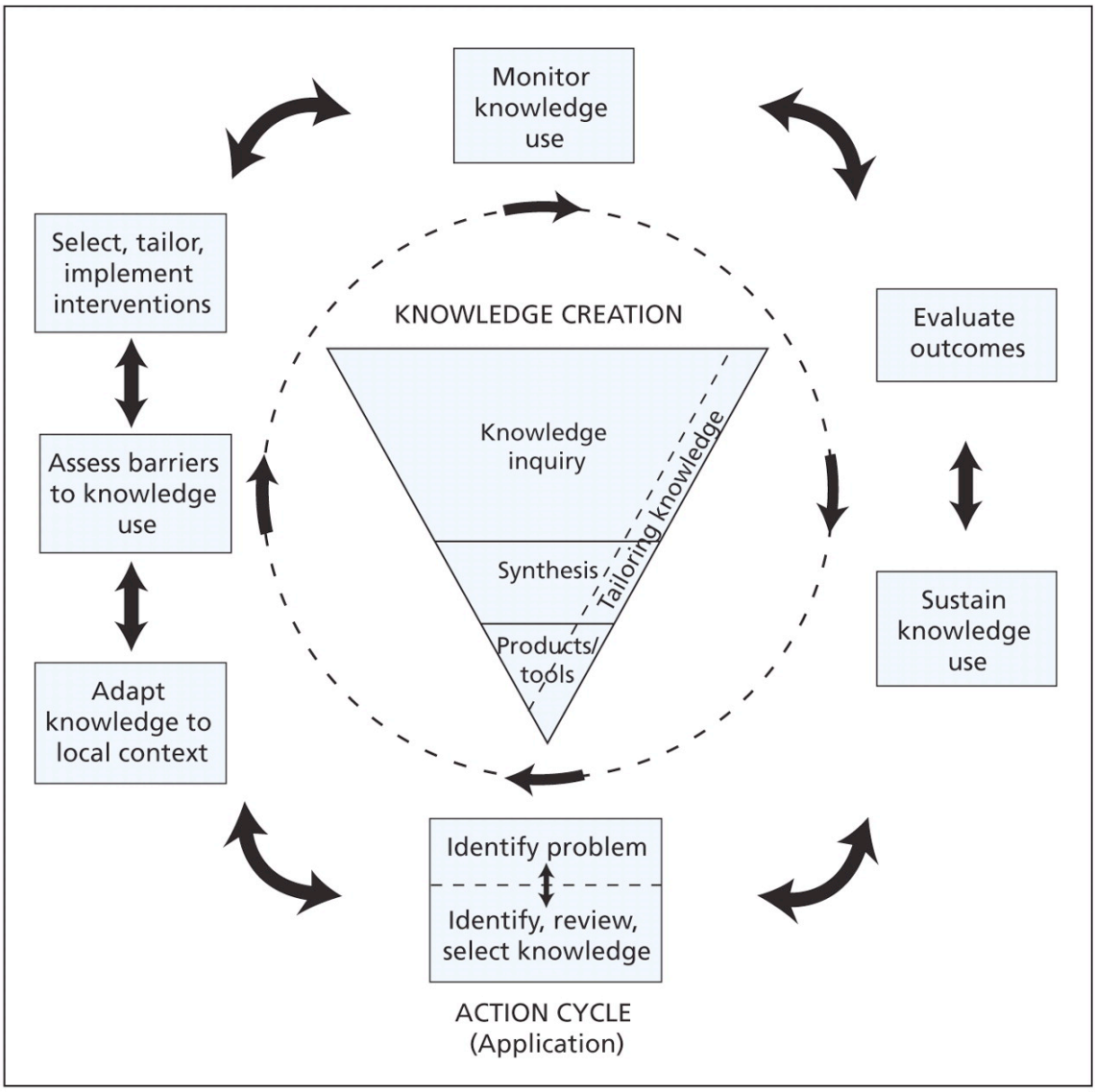
Ultimately, implementation of the clinical practice guideline is critical; without an approach to implementation, recommendations often fail to achieve potential benefits in care process, use of best evidence, and consistency in practice.(99–101) As a specialty, plastic surgery is beginning to measure guideline adherence at hospital and physician levels.(102) A review found inconsistency, with practices failing to meet recommendations following carpal tunnel release, screening mammography for breast augmentation and deep vein thrombosis (DVT) prophylaxis in lower extremity reconstruction.(103) High quality clinical practice guidelines themselves are not sufficient to most effectively implement the recommendations.(104) While guidelines are more "usable" than the set of studies they are based on, context improves implementation.(94)

There is insufficient evidence to support one guideline implementation strategy, or cluster of strategies, over another.(105) However, integrated knowledge translation (IKT)

interventions may be well suited to OBPI. IKT integrates relevant end-users and researchers in intervention design, and dissemination.(101) IKT is particularly relevant to OBPI given the range of primary care providers involved in perinatal care, and the multidisciplinary team involved in OBPI assessment and therapy.(101) Collaboration between primary care providers, parents, specialists, and resource managers is critical to the timely and optimized OBPI care. The systematic review of primary management begins by providing the first comparative synthesis of OBPI treatment. An updated evidence base is the first step in reconciling the divergence in opinion between primary care providers and OBPI specialists for prognosis and interventions, and providing consistent information to guardians.

Figure 2-1: The Knowledge to Action Framework

(from http://www.cmaj.ca/content/181/3-4/165/F1.large.jpg, retrieved June 27, 2014)



CHAPTER 3: PRIMARY MANAGEMENT OF OBSTETRICAL BRACHIAL PLEXUS INJURY: A SYSTEMATIC REVIEW AND META-ANALYSIS

3.1 Abstract

3.1.1 Purpose

The purpose of this review was to determine the effectiveness of primary nerve repair compared to nonoperative management for physical function in obstetrical brachial plexus injury (OBPI). This is the first review comparing operative and nonoperative outcomes.

3.1.2 Methods

Electronic databases were searched (MEDLINE, EMBASE, CINAHL, Cochrane Central). Included studies were randomized controlled trials, observational studies and case series (n>9) of patients under two years old undergoing nerve repair and/or nonoperative management of OBPI and reporting incidence of functional impairment. Two reviewers independently screened articles and extracted study, population, intervention and outcome data using objective a priori criteria. Bias was assessed for each study. Overall quality of evidence was evaluated for each outcome. Subgroup analyses explored clinical and methodological heterogeneity.

3.1.3 Results

Nine cohort studies including 222 patients directly compared nerve repair and nonoperative management in patients meeting intervention criteria as defined in each study. Nerve repair significantly reduces functional impairment, RR 0.58, 95%CI 0.43-0.79, $p<0.001$, $I^2=0\%$. Thirty case series including 1128 patients undergoing operative management were indirectly compared to 19 case series including 444 "gray zone" patients with nonoperative management. With nerve repair, functional impairment remains in 23% (95%CI 17-30%) versus nonoperative, 58% (95%CI 42-73%); RR 0.39, (95%CI 0.33-0.45%). With operative management, death was not reported. Major adverse events were reported in 1.5% of cases and minor in 5.0%.

3.1.4 Conclusion

Low quality evidence suggests nerve repair reduces functional impairment in OBPI. Nonoperative management in author-defined gray zone patients leads to a high proportion of functional impairment. Residual impairment with nonoperative management is underreported in the literature. Mortality is not a common risk of modern paediatric microsurgical nerve repair.

3.2 Rationale

Commonly cited studies of operative and nonoperative management for OBPI are limited to cohort studies and case series.(23,68) Studies of natural history and nonoperative therapy are not rigorous; no single report includes a demographic patient sample, prospective outcome collection, objective outcome assessment, or appropriate tactics to address loss to follow-up at sufficient time horizons.(6,106) Superiority of microsurgical repair is reported with comparison to historic controls.(25,27,34,47) Operative indications and timing of surgery have not been compared with a randomized controlled trial,(15) despite acknowledgment of its need.(16,17) Previous reviews are inconclusive and of poor quality. No review has addressed existing cohort studies of microsurgical repair versus nonoperative recovery. Steps in the systematic review process are generally not performed in duplicate, as is common in international standards. Operative and nonoperative outcomes are not compared in patients with similar prognosis making the conclusions of limited clinical utility. Analyses are descriptive and are generally not pooled.

McNeely and Drake(107) reviewed outcomes of nerve repair and nonoperative management separately, concluding no benefit with operative management. Quality assessment was limited to each study's overall level of evidence. Pondaag et al.(6) reviewed nonoperative outcomes using four methodological inclusion criteria. Of 1020 reports, none met all criteria; outcomes were limited to seven studies meeting two criteria, with conclusions based on two studies meeting three criteria. The review concluded nonoperative recovery is overestimated, and the OBPI literature is of poor quality.

Bialocerkowski et al.(55,80) reviewed operative and nonoperative interventions (excluding "natural history") in separate publications. This was the only previous review to perform steps in duplicate. The review concluded evidence and descriptions are scarce for nonoperative interventions, and clinical heterogeneity in operative studies precludes comparison. No operative or nonoperative intervention was supported. Finally, Foad et al.(68) reviewed nonoperative outcomes. This was the only previous review to pool results. Analysis of 11 reports concluded recovery is worse in Narakas III and IV injuries compared to Narakas I and II. Reviews consistently conclude the evidence is insufficient to guide treatment recommendations.

Previous reviews focus on operative and nonoperative management separately without direct comparison, given the lack of randomized controlled trials for this effective surgical intervention. While surgeons agree severe total plexus injuries require early repair, and neuropraxic injuries require only nonoperative therapy, there is a proportion of patients between these extremes that is often the focus of research.(22,23) The body of OBPI literature contains cohort studies comparing operative and nonoperative management in patients with defined impairment at specific ages. Moreover, case series of operative and nonoperative interventions exist with similar definitions of impairment at specific time points. No previous author has applied methodological solutions to pool similar patients from these studies for an estimate of treatment effect.

Reviews consider reported full recovery and functional recovery interchangeably in some instances, while criticizing original reports for inconsistent outcome definitions. A number of physical assessment scales exist for OBPI, assessing specific functional

movements of the upper extremity. No previous author has pooled different scales based on similar definitions of "impaired" or "not impaired" derived from original scale design.

The dearth of conclusive evidence may have allowed historic attitudes to remain in primary care: "permanent sequelae are rare",(19,61,62) and operative repair is "unwarranted".(63) However, there are methodological solutions to address the inherent limitations of the OBPI literature. In clinical situations where evidence is unclear, "gray zones",(23) such as the case for management of OBPI, rigorous approaches to knowledge syntheses have the highest capacity to impact practice.(45) Overall, the quality and completeness of existing reviews have not been optimized and do not provide direction to support the decisions of the clinical community, and may compromise the patient outcomes.

3.3 Objectives

3.3.1 Primary Objectives

1. To assess the effect of primary operative and nonoperative management on physical function in patients with OBPI.

2. To determine if one strategy is superior to the other and for which patients.

3.4 Methods

3.4.1 Protocol

A systematic review protocol was developed a priori. This protocol was not published.

3.4.2 Eligibility Criteria

3.4.2.1 Types of studies

This review included published full reports of primary research and systematic reviews in English. Primary research studies included randomized controlled trials (RCTs), observational trials and case series (n>9). Abstracts, grey literature and reports in other languages were excluded.

3.4.2.2 Types of participants

This review included all patients with OBPI, regardless of severity, demographics, or comorbidities.

3.4.2.3 Types of interventions

All studies including primary operative and nonoperative management were included. “Primary” management was defined as first-order, received within the first 24 months of life. “Operative management” was defined as any nerve surgery: direct end-to-end neurorrhaphy, neurolysis, neuroma excision and grafting, and nerve transfer. All operative indications were included. “Nonoperative management” was defined as the absence of surgical intervention. Co-intervention including physical, occupational or rehabilitation therapy(55) was permitted for both groups. Pharmacologic interventions

(eg. Botulinum toxin)(53) were excluded. Patients undergoing secondary surgical management were excluded (eg. late nerve transfer after 24 months of age, tendon transfers, osteotomies).

3.4.2.4 Primary outcome measures

3.4.2.4.1 Physical function (Functional impairment)

Physical function of the upper extremity is both patient and surgeon-important. It was chosen since existing generic paediatric outcome measures are not well suited to OBPI deficits,(42,108) and fail to guide therapy.(108) Further, a disease specific Brachial Plexus Outcome Measure (BPOM)(108) was validated only recently, and thus is not yet reflected in the literature.(109) Given inconsistent definitions of recovery in the literature,(23) the outcome of interest for physical function was defined as prevention of functional impairment.

For inclusion, studies reported functional impairment using one of the following measures: Mallet Score,(110) Active Movement Scale (AMS),(111) Narakas Grading System,(112) Gilbert Shoulder Classification,(113) Gilbert-Raimondi Elbow Classification,(113) Raimondi Hand and Wrist Classification,(113) Medical Research Council Muscle Grading System (MRC),(114) Gilbert and Tassin modified MRC,(33) other categorical physical outcome score defined in same report, or subjective categorical physical recovery on examination.

3.4.2.5 Secondary outcome measures

3.4.2.5.1 Full recovery

Full recovery is patient and surgeon-important. It was chosen to inform health policy, providing an estimate of proportion and timing of full recovery. Definition of outcome was full scale (same measures as defined in functional impairment), or subjective assessment of recovery without author-defined residual deficit. For inclusion, only reports with a demographic patient sample were analyzed to provide a reliable denominator for proportions.

3.4.2.5.1 Adverse events

Adverse events are patient and surgeon-important. All author-defined adverse events reported in an operative study were included. Adverse events were categorized for analysis: mortality, major (requiring operative or inpatient intervention) and minor (self-limiting).

3.4.3 Literature Search Strategy

3.4.3.1 Electronic search

Electronic search strategy was reviewed with a reference librarian, N. Bhatnagar, McMaster University, executed February 7, 2013: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present, Ovid MEDLINE Daily Update February 07, 2013, EMBASE 1980 to 2013 Week 6, CINAHL 1982-Present and Cochrane Register for Randomized Controlled Trials 2013, Issue 1 (Appendix 1).

3.4.3.2 Hand Search

Citations of included studies from identified systematic reviews were hand searched to ensure all eligible studies were captured.

3.4.3.3 Title and Abstract Screening

Titles and abstracts were screened independently and in duplicate for eligibility by the primary reviewer (CJC) and one of five second reviewers (SV, MKC, NA, SRG, LIW). Screening was highly sensitive; any potentially relevant references were included in full-text review. Articles were retrieved. The primary reviewer and a second reviewer reviewed full text articles independently and in duplicate. Reviewers used a standardized electronic eligibility form, pilot tested with two articles by each reviewer. Reason for report exclusion was recorded in each case (population, intervention, outcome, study type). Disagreements were resolved with discussion, and review with a supervisor if necessary. Agreement for full text inclusions was calculated using Cohen's unweighted kappa.

3.4.4 Data Extraction

The primary reviewer and a second reviewer extracted data independently and in duplicate, guided by standardized electronic forms with a data dictionary designed a priori. Pilot testing was completed with two articles by each second reviewer. Disagreements were resolved with discussion, and review with a supervisor if necessary.

Study and methodological characteristics included country of origin, specialty of corresponding author, study objective and study design. Population characteristics included type of sample (demographic birth sample, hospital birth series or referral) year beginning recruitment, total series size, number of patients with outcome assessment, baseline severity, incidence in population, and clinical distribution of injury. Intervention characteristics included number of centres participating, centre setting, centre team, diagnostic investigations, type of intervention, operative indication and timing if applicable, and therapy details. Outcome characteristics included timing of assessment, criteria applied, functional impairment, and adverse events.

Author, study, population, and intervention characteristics were compared to detect multiple reports from the same trial or series. If overlap could not be excluded, the most recent report of the complete patient series was used. Country of origin was attributed to corresponding author or centre location. If patients were followed for different periods (eg. minimum two years, range 2-5 years), the minimum length of follow-up was recorded. The unit of analysis was the limb (ie. bilateral injury). Patients requiring secondary surgery were considered functionally impaired if no scale outcome was available. To analyze recovery in studies with multiple reported outcomes, the order of preference was: shoulder, elbow, hand, and global outcome.

3.4.5 Quality Assessment

RCTs were assessed with The Cochrane Collaboration's risk of bias tool.(115) Non-randomized studies were assessed with the Methodological Index for Non-

Randomized Studies (MINORS) instrument, with eight items applied to non-comparative studies and twelve applied to comparative.(116) The primary reviewer and a second reviewer assessed each article independently and in duplicate. Agreement was calculated with weighted kappa, given ordered responses in each tool.

3.4.6 Measures of Treatment Effect

Physical assessments were converted to binary outcomes with events defined as functional impairment. Review Manager 5.2 was used to analyze comparative reports.(117) Relative risks were calculated with 95% confidence intervals(118) using a random effects model. Optimal information size (OIS) was calculated with alpha=0.05, beta=0.20, relative risk reduction=0.20 and nonoperative event rate.(119) StatsDirect was used to analyze non-comparative reports.(120) Operative and nonoperative functional impairment were analyzed separately with proportional meta-analyses using 95% confidence intervals and a random-effects model.

For operative management, all included interventions were pooled. There is currently insufficient evidence to preclude pooling nerve repair techniques.(121) Similarly, all nonoperative management protocols were pooled; descriptions of individual nonoperative interventions and protocols are poor.(55,79) There is currently insufficient evidence to preclude pooling.

Sources of heterogeneity were defined a priori: length of follow-up (over two years vs. under) with worse outcomes anticipated in short follow-up; joint assessment (shoulder abduction vs. external rotation vs. elbow) with worse outcomes anticipated in

external rotation; and clinical injury pattern (upper vs. total plexus) with worse outcomes anticipated in total plexus. Heterogeneity was explored with I^2, where: 0%-30% "heterogeneity might not be important", 30%-50% "may represent moderate heterogeneity", 50%-75% "may represent substantial heterogeneity" and 75%-100% "considerable heterogeneity". Funnel plots were used to explore publication bias for each outcome if at least 10 articles were found.(122)

3.4.7 Data Analysis

Comparing all operative outcomes to all nonoperative outcomes would be biased; a proportion of patients with neuropraxic injuries achieve full recovery spontaneously. Including these patients would confound analyses by inflating estimates of outcomes in favour of patients in the non-operative group. The most appropriate analysis, therefore, is comparing operative to nonoperative outcomes for patients more likely not to recover spontaneously. In order to address this, objective methodology was applied to facilitate comparison of similar patients. A "gray zone" of prognosis was defined previously, where "the decision as to the benefits and risks of surgery versus no surgery is not clear".(23) Patients in the gray zone meet author-defined criteria for poor prognosis as reported in the article itself. These criteria are often used as surgical indications (eg. no recovery of biceps at three months). Identifying studies reporting outcomes for gray zone patients allowed nonoperative outcomes for patients in the gray zone to be compared to operative outcomes as an indirect control; thus a more appropriate and clinically relevant analytical model. Outcomes for gray zone patients were identified in cohort studies and case series.

OBPI studies report a variety of outcomes.(42) An objective methodological solution was applied to allow combination of all relevant studies. To pool outcomes across the multiple scales, all physical recovery scores were converted to binary outcomes to determine functional impairment. The definition of a "functional" outcome was identified in the source reporting of each scale. All scores below the "functional" score were considered "impaired". Scale physical recovery is defined as in the literature for "functional" scores as follows: Mallet Score (III),(70) AMS (6),(40) Narakas Grading System (as described),(112) Gilbert Shoulder Classification (III),(113,123) Gilbert-Raimondi Elbow Classification (2-3), Raimondi Hand and Wrist Classification (III),(27,123) MRC (M3=functional),(28,59) and Gilbert and Tassin modified MRC (M3).(33)

3.5 Results

3.5.1 Search results

Search strategy resulted in 4177 unique citations, with 391 articles selected for full text review (Figure 3-1). There were 105 primary studies and six systematic reviews selected.(6,55,68,79,80,107) Citation review of the previous systematic reviews identified two additional articles. Thus, 107 articles were selected for data extraction. Unweighted kappa for agreement is 0.67. Eight articles were excluded during data extraction: population (surgery after 24 months),(35,121,124,125) intervention (secondary procedures), and outcome (continuous range of motion).(126,127) There were 99 articles

included in analysis.(1,4,13–15,18,19,23,25–28,32,34,36–39,41,51,52,59–67,69,70,106,123,128–192) Articles included no RCTs, 17 cohort studies, and 82 case series (n>9). Operative outcomes were available in 39 articles, and nonoperative in 73 (13 articles included both operative and nonoperative outcomes).

3.5.2 Characteristics and quality

Characteristics and quality scores are illustrated for nonoperative studies in Table 3-1 and operative studies in Table 3-2. MINORS quality assessment factors for all outcomes are summarized in Table 3-3. Reflecting previous reviews,(6,55,68,80,107) quality of the OBPI literature identified was poor. In cohort studies, control groups were unequal at baseline, including fewer severe injuries, and thus having a better prognosis. This biases against the operative group. Further, sample size was not calculated, and the follow-up period was variable. Operative series were typically retrospective and not consecutive. Only one series reported outcomes with a subjective measure. Nonoperative demographic series were similarly retrospective and endpoints were typically subjective.

Referral samples represent specialized centres. Among 65 studies with a referral sample, the care team was multidisciplinary in 43, specialist only in 12 and not described in 10. Three studies with a referral sample provided timing and criteria for referral from primary care: no recovery at six months,(149) impaired deltoid and biceps at 2 to 3 months,(159) and absence of active elbow extension at one month or absence of active elbow flexion with EMG absence of biceps motor unit potentials at one month.(18)

Routine investigations included myelogram (preoperatively in 3 reports), CT

myelogram (preoperatively in 8), MRI (preoperatively in 4, all patients in 1), EMG (preoperatively in 12, all patients in 14), and plain films (preoperatively in 3, all patients in 5).

3.5.3 Publication Bias

Funnel plots for primary outcomes with at least ten studies are illustrated in Figure 3-2. Egger's regression test is significant for operative outcomes ($p<0.01$). The plot for operative management indicates absence of imprecise positive results; publication bias is not suspected. Visual appearance of the funnel plots is likely due to the considerable heterogeneity in both cases.

3.5.4 Primary Outcomes

3.5.4.1 Functional impairment: Direct comparison of operative versus nonoperative

Functional impairment data for direct comparisons of operative versus nonoperative management in patients with an author-defined impairment ("gray zone") were available for 222 patients from nine articles (Table 3-4).(15,25,26,28,34,59,106,138,153) All studies were small. Operative indications, control group characteristics and outcome assessments are described in Table 3-4. Tendon transfers were considered poor outcomes in two studies.(15,26) Gray zone criterion was extrapolated from a median value in one study.(106) Operative management was compared to outcomes in children whose parents refused surgery in two studies.(28,153)

Operative management significantly reduces functional impairment, RR 0.58, 95% CI 0.43-0.79, p<0.001, I^2=0% (Figure 3-3). There is no statistical heterogeneity between studies though sample sizes are small. The comparison is underpowered after pooling; OIS of 514 patients per group is not met. Studies are consistent in direction of effect with point estimates equivocal in favouring operative management.

3.5.4.2 Functional impairment: Case series and indirect comparison

3.5.4.2.1 Operative series

Functional impairment data for series of operative management alone were available for 1128 patients from 30 articles. (Table 3-5).(13–15,19,25,27,34,38,39,41,59,106,136,138,145,161,162,164,167,171,172,174,175,178,179,181,183,184,188,189) The nerve repair groups alone from 12 cohort studies were included. Nine articles were excluded for series overlap.(28,32,36,37,51,70,147,153,156) Operative indications, nerve repair, postoperative physical therapy and outcome assessment are illustrated in Table 3-5. With operative management, functional impairment occurs in 23% (95% CI 17-30%, I^2=78%) of patients (Figure 3-4). There is considerable heterogeneity among studies.

3.5.4.2.2 Nonoperative gray zone series

Nonoperative management of gray zone series are analyzed separately from other nonoperative management (Sections 3.5.4.3 and 3.5.5.1). Patients in the gray zone meet author-defined criteria for poor prognosis as reported in the article itself.

Functional impairment data for series of nonoperative management alone in gray zone patients were available for available for 444 patients from 19 articles (Table 3-6).(15,23,25,26,28,34,59,60,64,67,69,106,123,138,146,148,155,159,166) One article was excluded for series overlap.(153) The nonoperative groups alone from 10 cohort studies were included. Gray zone criteria, nonoperative management and outcome assessment are illustrated in Table 3-6. With nonoperative management of the gray zone, functional impairment occurs in 58% of patients (95% CI 42-73%, I^2=91%) (Figure 3-5). There is considerable heterogeneity among studies.

3.5.4.2.3 Indirect comparison of operative versus nonoperative

Nonoperative management of gray zone patients serves as a comparison group to operative series data. These patients are similar given their author-defined impairment at a specific time point, analogous to surgical indications in operative series, serving as an appropriate and clinically relevant comparison.

With indirect comparison to nonoperative gray zone patients, operative management reduces functional impairment, RR 0.39, 95% CI 0.33-0.45. Heterogeneity in operative versus gray zone nonoperative series was explored with subgroup analyses (Table 3-7). Results are similar to overall outcomes. In these indirect comparisons, relative risks do not exclude less effective operative management outcomes with short follow-up, total plexus injury, and assessment of shoulder external rotation.

3.5.4.2.4 Nonoperative management in referral samples

Nonoperative management of referral samples is distinct from gray zone and demographic samples (Sections 3.5.4.2.2 and 3.5.5.1). In contrast to gray zone patients, no criterion for author-defined impairment was applied; prognosis is better versus gray zone. In contrast to demographic samples, referral samples do not represent the entire spectrum of OBPI cases. Instead, referral samples are composed simply of patients referred to specialty care. It is likely that many neuropraxic injuries recover spontaneously, and are not referred to specialists. Thus prognosis in referral samples is worse than demographic samples.

Functional impairment data for nonoperative management in patients referred to a specialist were available for 2732 patients from 31 articles (Table 3-8).(15,18,23,25,28,34,52,59,61,67,69,128,129,131–134,137,138,146,148,155,157,159,162,166,169,183,185,187,190) Nine articles were excluded for series overlap.(26,60,144,153,156,164,165,182,186) Eleven studies used subjective outcome assessment. Care team, nonoperative management, availability of operative management, and outcome assessment are illustrated in Table 3-8. Availability of nerve repair was mentioned in 18 studies and secondary musculoskeletal procedures in seven; surgery was not detailed in six studies. With nonoperative management of referral sample patients, functional impairment occurs in 32% of patients (95% CI 25-40%, I^2=94%) (Figure 3-6). There is considerable heterogeneity among studies. Details of nonoperative interventions and therapy protocols are poorly described.

3.5.5 Secondary Outcomes

3.5.5.1 Functional impairment, nonoperative management in demographic samples

Demographic samples include the entire spectrum of OBPI severity. These studies identify all OBPI cases, and capture neuropraxic injuries likely to recover spontaneously. These samples provide an indication of the proportion of impairment in the overall population.

Functional impairment data for nonoperative management in demographic patient samples (demographic population or hospital birth series) were available for 1604 patients from 27 articles (Table 3-9).(1,4,62–66,106,123,130,135,139,141–143,149–152,154,158,168,170,173,177,191,192) Six articles were excluded for series overlap.(13,140,160,163,176,180) Corresponding author's specialty, management details and outcome assessment are illustrated in Table 3-9. Functional impairment occurs in 18% of patients (95% CI 14-23%, I^2=81%) (Figure 3-7). Full recovery occurs in 73% of patients overall (95% CI 64-81%, I^2=93%) (Figure 3-8). Post hoc analysis of 510 patients from 10 articles demonstrates full recovery by one month in 35% of patients (95% CI 23-48%, I^2=89%) (Figure 3-9). These studies represent samples with a cumulative OBPI incidence of 2.1/1000 births (95% CI 1.6-2.6, I^2=98%) (Figure 3-10).

Heterogeneity was explored with subgroup analyses (Table 3-10). Results are similar to overall outcomes for short and long-term follow-up.

3.5.5.3 Adverse events

Among the 30 operative studies, 19 explicitly described incidence of 30 adverse events in 512 patients. No deaths were reported. Six major, and 24 minor events were

reported. Major events included persistent hemidiaphragm paralysis, laryngeal edema/reintubation, and disconnection of transferred nerves. The most common minor event was transient hemidiaphragm paralysis, with wound infection, nerve transfer deficits, co-contraction, and intraoperative positioning events also described. Among operative studies, major events occur in 1.5% of cases (95% CI 0.6-2.7%) (Figure 3-11) and minor in 5.0% (95% CI 2.5-8.3%) (Figure 3-12).

3.6 Discussion

3.6.1 Primary Outcomes

3.6.1.1 Functional impairment

Primary operative management for OBPI patients meeting author-defined surgical indications is associated with a lower risk of functional impairment versus nonoperative management of similar patients based on best available evidence. Pooled analysis of 222 patients from nine cohort studies shows nerve repair reduces impairment versus gray zone nonoperative; RR 0.58, 95% CI 0.43-0.79, $p<0.001$, $I^2=0\%$. This converts to an absolute risk reduction (ARR) of 19% (42% impairment among nonoperative patients versus 23% among operative). Number needed to treat (NNT) is 6. This outcome is low quality. Cohort designs are typically defined as low quality and case series as very low quality, given inherent sources of bias in their designs.(193)

This outcome may underestimate the effectiveness of primary nerve repair; study characteristics potentially bias findings against the operative group (Table 3-3). Of the

nine studies, five had an adequate control using the same criteria applied to both treatment groups.(28,59,138,153) Three studies used different criteria,(15,25,26) with the nonoperative group having a better prognosis. Further, only two reports defined injury severity at baseline.(26,34) A range of surgical indications and nerve repair techniques (including direct neurorraphy) were used (Table 3-4). The earliest indications were applied at three months. Despite clinical and methodological heterogeneity (Table 3-4), pooled results demonstrate no statistical heterogeneity. Sample sizes were small; the largest study included 45 patients, and only one included at least 10 patients in both treatment groups. The pooled comparison is underpowered, not meeting OIS of 514 patients per group.

Thirty series of operative management were indirectly compared to 19 series including gray zone nonoperative patients. Operative management shows a statistical risk reduction in functional impairment (RR 0.39, 95% CI 0.33-0.45). However, the nature of the study designs and the indirect analysis yields this finding as very low quality. As has been found in studies examining the impact of lower quality study designs, the estimate of treatment effect in this analysis is greater compared to that yielded from the better quality cohort data.(194)

Operative and gray zone outcomes show considerable heterogeneity. Sources of clinical and methodological heterogeneity are listed for each in Tables 3-5 and 3-6, and summarized in Table 3-3. Heterogeneity is not explained through analysis of a priori subgroups. On visual assessment, funnel plots for publication bias reflect considerable heterogeneity. In subgroup analyses, indirect comparisons of relative risks do not exclude

improved outcomes among patients followed long term, supporting surgical dogma of slow recovery following nerve repair. Total plexus injuries may have worse outcome with operation versus upper plexus injuries, attributed to their worse baseline function. Elbow assessment may have improved outcome versus shoulder in both operative and nonoperative gray zone patients. Elbow outcomes may overestimate recovery versus shoulder outcomes. External rotation may show no difference with operative management, possibly explained by typical high incidence of internal rotation contractures in both operative and nonoperative groups.(79)

Details of nonoperative interventions and therapy protocols were poorly described in studies. Intervention details, therapy protocol details, and definitions were variable. Reliably abstracted nonoperative details were limited to the delivery of nonoperative therapy, its provider, and guardian education for therapy performed with the child at home. The level of detail presented precludes the ability to reliably replicate therapy protocols. Despite the poor evidence for nonoperative management, it remains likely all OBPI infants benefit from early specialized assessment, and education versus primary care follow-up alone (see Section 3.6.2.1).

3.6.2 Secondary Outcomes

3.6.2.1 Functional impairment, demographic samples

Twenty-seven reports of nonoperative management in demographic populations show functional impairment in 18% of patients (95% CI 14-23%). This outcome may underestimate the incidence of impairment. Primary care physicians authored the majority

of studies, investigating natural history (Table 3-9). Only three reports assessed outcomes with physical scales; the remainder relied on subjective assessment. This reflects traditional reports of OBPI from primary care reporting transient injury without sequelae.(19,61,62)

Full recovery was identified a priori to inform health policy. Given the proportion of studies assessing outcomes subjectively and known inconsistent definitions of impairment,(23) author-defined "full recovery" analysis was compared to functional impairment post-hoc. Full recovery occurs in 73% (95% CI 64-81) of patients from demographic samples. Interpreted inversely, the author-defined incidence of any subjective residual impairment is 27% (19-36%). This proportion demonstrates at least 19-36% of OBPI cases have an uncharacterized residual impairment. While these patients may not all be operative candidates, they may benefit from specialized assessment and therapy instead of "natural history". This outcome is very low quality. Outcomes are consistent in subgroup analyses.

Analysis of full recovery by one month of age was added post hoc; 35% (95% CI 23-48%) of patients from demographic samples are classified as fully recovered without residual deficit by one month. Outcomes reflect considerable heterogeneity among studies. Outcomes are reported by one month, however five studies indicate full recovery was assessed on discharge. Recovery at one month has potential healthcare system implications since algorithms for specialist referral are applied at this time.(18,23,195)

3.6.2.2 Adverse events

Adverse events were reported in 19 series of operative management. No deaths were reported. Major events occur in 1.5% of cases, and minor in 5.0%. Adverse events were inconsistently reported across series. This outcome is incomplete; events were recorded only from reports of operative series. This outcome is very low quality. The proportion and type of events are focused only on surgical technique. This differs from a dedicated review of complications alone,(196) where the overall complication rate was 33.5% and events related to accidental extubation, and perioperative care.

3.6.3 Agreements and Disagreements with Other Reviews

McNeely and Drake(107) is the only previous review including operative and nonoperative management. Authors reported descriptive analysis of 23 series, compared to our indirect comparison of 30 operative and 19 gray zone series. McNeely and Drake did not compare operative outcomes with similar patients treated nonoperatively (ie. gray zone), possibly introducing bias in favour of nonoperative since neuropraxic injuries inherently recover. In contrast, and more clinically and methodologically appropriate, we compared operative and nonoperative gray zone patients with author-defined physical deficits, providing a comparison with similar baselines prognosis and targeting the clinical scenarios in which there is greatest confusion about how to proceed. McNeely and Drake stated the literature does not provide conclusive evidence of improvement with operative management versus nonoperative, but both approaches are valid. In contrast, we believe our findings support the conclusion that nerve repair improves outcomes for infants with impairment beginning at three months.

Bialocerkowski et al.(80) reviewed operative management alone. Search strategy resulted in 21 series with multiple reports from centres, versus our 30 series after identifying, and eliminating series overlap. The review concluded no estimate of effectiveness could be made on nerve repair. In contrast to Bialocerkowski at al., we performed an exhaustive search of the historical literature, with objective definitions of impairment for outcome assessment. We provide a pooled estimate of effect supporting nerve repair based on best available evidence.

Pondaag et al.(6) performed an exhaustive review of nonoperative management screening 1020 articles in multiple languages. Inclusion criteria were strict: prospective, demographic sample, complete follow-up for three years, and objective outcome assessment protocol. No study met all criteria. We agree with conclusions based on two series with demographic samples; nonoperative recovery is overestimated with residual deficit in 20-30% of patients. Our review included 27 demographic samples, and attention to outcome definitions, with a similar estimate of residual impairment at 27% (19-36%).

Foad et al.(68) reviewed biceps and full recovery with nonoperative management at six months, results of 11 series were pooled. Referral and demographic samples were not differentiated in analyses. In contrast, our review included outcomes at two years, and 19 gray zone and 27 demographic sample studies of nonoperative management. We agree with selection of an objective outcome and overall estimate of results. Our review differentiates recovery in demographic and referral populations given the latter likely have worse prognosis.

Bialocerkowski et al.,(55) and ter Steeg et al.(79) reviewed "conservative treatment" of OBPI, reporting nonoperative management alone. In contrast to our review, these reviews excluded natural history. Each review highlighted the importance of therapists delivering nonoperative treatment(24,55) and suggested all infants be assessed by a therapist,(79) and for parent/guardian education.(10) Nonoperative treatments and protocols were descriptively reviewed. Similar to our review, both reviews found details of interventions were poor, prohibiting replication.(55) Insufficient evidence exists to support specific treatment recommendations beyond therapist referral itself.(55,79) Historic application of routine bracing/splinting is not endorsed by previous reviews,(55,79) and was thus not included in our review.

3.6.4 Limitations

This review has limitations. First, we included only full reports in English. Limiting the search strategy may have introduced publication bias.(197) However, funnel plots likely reflect heterogeneity in the included studies. Visual inspection of the funnel plot for operative management indicates absence of imprecise positive results. This is the opposite of what is expected with publication bias, where small negative papers are missed. Gilbert is a notable author absent in cohort study analysis. Upon review, Gilbert and Tassin's(30) comparative study (reported in French) favours operative management for patients without biceps recovery at three months. However, operative outcomes are reported from a subset of the total series. Further, the number of subjects in the conservative group and their specific physical deficit for gray zone inclusion are not

reported. Assuming balance between groups, addition of the study would not change our pooled estimate.

Second, analysis of cohort studies was based on negative events using relative risk. Negative events (functional impairment) were selected a priori given inconsistency in definitions of recovery.(23) Given the low number of patients in this analysis, a post-hoc sensitivity analysis of statistical methods is considered. Results are consistent if reanalyzed with positive or negative events, and odds ratio. However, statistical significance of benefit for nerve repair among cohort studies is lost if analyzed with positive events, and relative risk. This is attributed to three control groups having "zero events" (ie. no "recoveries" with positive event analysis) and a loss of statistical power.

Lastly, the definitiveness of the conclusions is not firm, given the evidence base is low quality. No RCT has been completed for OBPI management. Cohort studies were small and pooled analysis was underpowered based on OIS. Our conclusions are based on the best available evidence. This review was designed with rigorous methodology a priori to address limitations of the low quality studies. Given clinical and methodological heterogeneity, we focused on combining similar study designs, population types and prognoses.

3.6.5 Strengths

This review has several strengths. Above all, we applied a number of methodological solutions to address the inherent limitations of the OBPI literature. This review succeeded in combining the body of OBPI literature, and preventing confounding.

Simply comparing outcomes of nerve repair to all nonoperative patients would be biased; the proportion of infants with neuropraxic injury will spontaneously recover. We relied on a previously established gray zone definition,(23) to establish an objective comparison group of nonoperative management. To pool outcomes assessed with different scales, all physical recovery scores were converted to binary functional impairment outcomes based on the original scale descriptions. Data were analyzed on the basis of study design and population sample. This allowed comparison of operative and nonoperative management directly from cohort study data, and indirectly from data derived from case series. Moreover, demographic samples were analyzed to estimate the proportion of residual impairment for the entire spectrum of OBPI. Infants with neuropraxic injuries and complete recovery in the first month are not reliably referred to specialists; analyzing referral populations for spontaneous recovery would be biased.

This is the first review to pool results of operative management for OBPI. It is also the first to compare operative and nonoperative management directly and indirectly. This is the first review to demonstrate benefit of nerve repair, a treatment practiced at specialized centres worldwide.(8) This is also the first review to demonstrate proportion of residual deficit for nonoperative management in a large sample of demographic populations.

Lastly, this review is methodologically rigorous. This is especially important given the low quality of literature. Steps were performed in duplicate. Search strategy was extensive. Each study was assessed for quality and bias, and quality of evidence for each outcome was summarized. Outcomes were investigated for inconsistency, imprecision,

power and publication bias. Heterogeneity was investigated with subgroup analyses. Statistical assumptions were tested with sensitivity analyses. Assumptions were tested and reporting is transparent.

3.7 Conclusions

3.7.1 Implications For Practice

Based on low quality evidence, operative management is beneficial for OBPI patients meeting surgical criteria applied beginning at three months of age. Nonoperative management in the subset of gray zone patients leads to a high proportion of functional impairment. Incidence of residual impairment with nonoperative management is underreported in the literature. Therapist assessment, treatment, and guardian education are likely appropriate for all patients. There is no evidence to support specific nonoperative therapy protocols. Mortality and major adverse events are not common risks of modern microsurgical nerve repair.

3.7.2 Implications For Research

The body of OBPI evidence is low to very low quality, limited to small cohort studies with potential bias and case series. This is unacceptable. While operative management demonstrates benefit, a variety of surgical algorithms are studied. Future studies should determine optimal surgical criteria and timing with higher quality study designs and larger sample sizes. Studies should have prospective design, independent

outcome assessment, and long-term follow-up of at least two years. Evidence and consensus for nonoperative interventions are lacking. Shoulder external rotation may remain a deficit with operative management.

Figure 3-1: Flow diagram of search and study selection

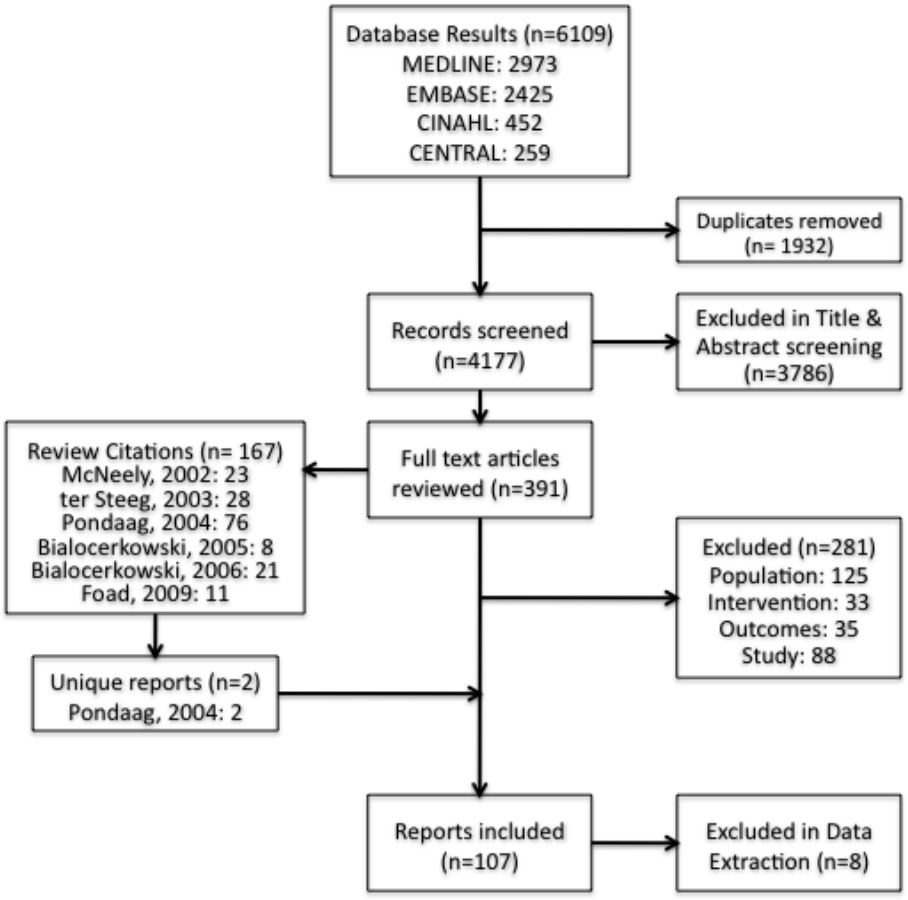


Table 3-1: Nonoperative report characteristics

				MINORS									Comparisons			
Report	Study Type	Study Aim	Sample	Clear Aim	Consecutive patients	Prospective Data	Endpoints	Unbias Assessment	Follow-up Period	Loss to Follow-up	Sample Size	Adequate Control	Contemporary	Baseline Equivalence	Analyses
Aitken 1952	Case series	Clinical OBPI	Referral	0	1	0	1	0	0	1	0	-	-	-	-
Wickstrom 1962	Case series	Clinical OBPI	Referral	1	0	0	1	0	1	2	0	-	-	-	-
Rubin 1964	Case series	Incidence/Risk OBPI	Hospital Birth Series	0	1	0	1	0	0	2	0	-	-	-	-
Gjorup 1966	Case series	Clinical OBPI	Hospital Birth Series	2	1	0	1	0	1	2	0	-	-	-	-
Alder 1967	Case series	Clinical OBPI	Referral	1	1	1	1	0	1	1	0	-	-	-	-
Eng 1971	Case series	Clinical OBPI	Referral	0	0	0	1	0	1	1	0	-	-	-	-
Gordon 1973	Case series	Clinical OBPI	Demographic Population	2	0	1	1	2	2	1	0	-	-	-	-
Tan 1973	Case series	Incidence/Risk OBPI	Hospital Birth Series	0	1	0	1	0	1	1	0	-	-	-	-
Bennet 1976	Case series	Clinical OBPI	Referral	0	1	0	1	0	1	2	0	-	-	-	-
Srivastava 1979	Case series	Clinical OBPI	Referral	0	1	0	1	0	1	2	0	-	-	-	-
Hardy 1981	Case series	Clinical OBPI	Hospital Birth Series	1	1	0	1	0	1	2	0	-	-	-	-
Greenwald 1984	Case series	Clinical OBPI	Hospital Birth Series	2	1	0	1	0	1	1	0	-	-	-	-
Tada 1984	Case series	Clinical OBPI	Referral	2	0	0	2	0	2	1	0	-	-	-	-
Soni 1985	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	1	1	1	0	1	1	0	-	-	-	-
Mabogunje 1986	Case series	Clinical OBPI	Referral	1	0	0	1	0	0	1	0	-	-	-	-
Meyer 1986	Cohort	Clinical OBPI	Referral	0	1	0	2	0	1	2	0	2	0	0	0
Boome 1988	Cohort	Clinical OBPI	Referral	1	2	0	2	0	1	1	0	2	2	1	0
Jackson 1988	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	2	2	1	0	2	1	0	-	-	-	-
Sjoberg 1988	Case series	Incidence/Risk OBPI	Demographic Population	1	1	0	1	0	2	2	0	-	-	-	-
Al-Najashi 1989	Case series	Incidence/Risk Birth Injury	Hospital Birth Series	1	1	0	1	0	2	0	0	-	-	-	-
Hentz 1991	Case series	Clinical OBPI	Referral	0	2	0	1	0	2	2	0	-	-	-	-
Morrison 1992	Case series	Incidence/Risk Birth Injury	Hospital Birth Series	2	1	0	1	0	1	2	0	-	-	-	-
Laurent 1993	Cohort	Clinical OBPI	Referral	1	2	1	2	0	1	1	0	2	2	1	2
Walle 1993	Case series	Incidence/Risk Birth Injury	Hospital Birth Series	1	1	2	1	0	2	2	0	-	-	-	-
Michelow 1994	Cohort	Clinical OBPI	Referral	2	1	0	2	0	1	2	0	2	2	2	2
Baskett 1995	Case series	Incidence/Risk Birth Injury	Hospital Birth Series	2	1	0	1	0	1	2	0	-	-	-	-
Lipscomb 1995	Case series	Incidence/Risk Birth Injury	Hospital Birth Series	1	1	0	1	1	1	0	0	-	-	-	-
Al-Qattan 1996	Case series	Incidence/Risk OBPI	Referral	0	2	0	1	0	0	1	0	-	-	-	-
Eng 1996	Case series	Clinical OBPI	Referral	2	0	0	1	0	1	1	0	-	-	-	-
Lindell-Iwan 1996	Case series	Clinical OBPI	Referral	2	1	0	2	0	1	0	0	-	-	-	-
Narchi 1996	Case series	Incidence/Risk OBPI	Hospital Birth Series	1	1	0	1	0	1	2	0	-	-	-	-
Bager 1997	Case series	Incidence/Risk OBPI	Demographic Population	1	1	0	2	0	2	2	0	-	-	-	-
Dawodu 1997	Case series	Incidence/Risk OBPI	Hospital Birth Series	1	2	2	1	0	1	2	0	-	-	-	-
Kolderup 1997	Case series	Incidence/Risk Birth Injury	Demographic Population	2	1	0	1	0	1	1	0	-	-	-	-
Sherburn 1997	Cohort	Clinical OBPI	Referral	0	1	2	2	0	2	1	0	2	2	1	0
Gherman 1998	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	1	0	1	1	1	2	0	-	-	-	-
Waters 1999	Cohort	Clinical OBPI	Referral	2	1	1	2	0	2	2	0	1	2	1	2
Yilmaz 1999	Case series	Invesitgation OBPI	Referral	1	0	0	2	0	1	0	0	-	-	-	-
Al-Qattan 2000	Cohort	Clinical OBPI	Referral	1	0	2	2	0	1	0	0	1	2	2	2
Al-Qattan 2000	Case series	Clinical OBPI	Referral	2	2	0	2	0	1	0	0	-	-	-	-
Basheer 2000	Case series	Clinical OBPI	Referral	2	0	1	2	0	2	0	0	-	-	-	-
Hoeksma 2000	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	1	0	1	0	0	1	0	-	-	-	-
Strombeck 2000	Cohort	Clinical OBPI	Referral	1	1	1	1	0	2	1	0	1	1	1	2
Wolf 2000	Case series	Clinical OBPI	Hospital Birth Series	1	1	0	1	0	1	2	0	-	-	-	-
Xu 2000	Cohort	Clinical OBPI	Referral	2	0	0	2	0	2	0	0	1	1	2	2
Leblebicioglu 2001	Case series	Clinical OBPI	Referral	1	0	0	2	0	1	1	0	-	-	-	-
Noetzel 2001	Case series	Clinical OBPI	Referral	2	0	2	2	0	1	1	0	-	-	-	-
Donnelly 2002	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	1	2	1	0	1	2	0	-	-	-	-
Nehme 2002	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-
Al-Qattan 2003	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-
Bisinella 2003	Case series	Clinical OBPI	Referral	1	2	0	2	0	2	2	0	-	-	-	-
Bisinella 2003	Case series	Clinical OBPI	Referral	1	1	2	1	0	2	2	0	-	-	-	-
Evans-Jones 2003	Case series	Incidence/Risk OBPI	Demographic Population	2	2	2	1	0	1	1	0	-	-	-	-
Kao 2003	Case series	Invesitgation OBPI	Referral	2	0	2	1	2	1	0	0	-	-	-	-
DiTaranto 2004	Case series	Clinical OBPI	Hospital Birth Series	1	1	0	2	0	2	2	0	-	-	-	-
Hoeksma 2004	Case series	Clinical OBPI	Hospital Birth Series	2	1	1	2	0	1	1	0	-	-	-	-
Smith 2004	Cohort	Clinical OBPI	Referral	1	0	2	2	0	2	2	0	1	2	1	2
Chauhan 2005	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	1	0	1	0	1	2	0	-	-	-	-
Gurewitsch 2006	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	1	0	1	0	2	1	0	-	-	-	-
Mollberg 2007	Case series	Incidence/Risk OBPI	Demographic Population	2	2	2	1	1	1	2	2	-	-	-	-
AlAwari 2008	Case series	Clinical OBPI	Hospital Birth Series	1	0	0	1	0	2	1	0	-	-	-	-
Mollberg 2008	Case series	Incidence/Risk OBPI	Demographic Population	2	1	2	1	1	1	1	0	-	-	-	-
Al-Qattan 2009	Cohort	Clinical OBPI	Referral	1	0	0	1	0	2	0	0	2	2	1	2
Badr 2009	Cohort	Clinical OBPI	Referral	0	1	0	2	0	1	1	0	1	2	1	1
Bain 2009	Cohort	Clinical OBPI	Referral	1	1	2	2	0	1	2	0	2	2	0	1
Al-Qattan 2010	Case series	Incidence/Risk OBPI	Referral	2	1	0	1	0	2	0	0	-	-	-	-
Al-Qattan 2010	Case series	Incidence/Risk OBPI	Referral	1	1	1	1	0	2	0	0	-	-	-	-
Ashrafzadeh 2010	Case series	Incidence/Risk OBPI	Referral	1	0	0	2	0	1	2	0	-	-	-	-
Lagerkvist 2010	Cohort	Incidence/Risk OBPI	Demographic Population	2	1	2	2	0	1	1	0	1	2	1	1
Toupchizadeh 2010	Case series	Clinical OBPI	Referral	2	0	1	1	0	2	1	0	-	-	-	-
Malessy 2011	Case series	Clinical OBPI	Referral	2	0	2	1	1	1	2	0	-	-	-	-
Walsh 2011	Case series	Incidence/Risk OBPI	Hospital Birth Series	2	1	2	1	0	1	0	0	-	-	-	-
Lindqvist 2012	Case series	Incidence/Risk OBPI	Hospital Birth Series	1	1	0	1	0	1	0	0	-	-	-	-

Table 3-2: Operative report characteristics
MINORS scoring: 0 (not reported), 1 (reported but inadequate), 2 (reported and adequate)

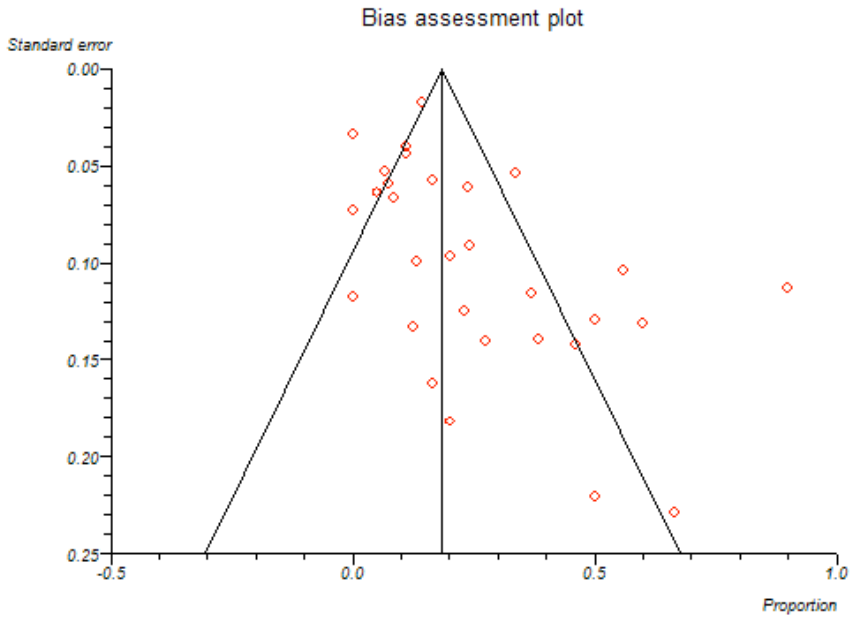
				MINORS									Comparisons			
Report	**Study Type**	**Study Aim**	**Sample**	**Clear Aim**	**Consecutive patients**	**Prospective Data**	**Endpoints**	**Unbias Assessment**	**Follow-up Period**	**Loss to Follow-up**	**Sample Size**	**Adequate Control**	**Contemporary**	**Baseline Equivalence**	**Analyses**
Alanen 1986	Case series	Clinical OBPI	Referral	1	0	0	1	0	1	2	0	-	-	-	-
Meyer 1986	Cohort	Clinical OBPI	Referral	0	1	0	2	0	1	2	0	2	0	0	0
Boome 1988	Cohort	Clinical OBPI	Referral	1	2	0	2	0	1	1	0	2	2	1	0
Gilbert 1991	Case series	Clinical OBPI	Referral	0	1	0	2	0	2	0	0	-	-	-	-
Laurent 1993	Cohort	Clinical OBPI	Referral	1	2	1	2	0	1	1	0	2	2	1	2
Kawabata 1994	Case series	Clinical OBPI	Referral	1	0	0	2	0	1	1	0	-	-	-	-
Laurent 1994	Case series	Clinical OBPI	Referral	1	0	0	2	0	1	2	0	-	-	-	-
Gilbert 1995	Case series	Clinical OBPI	Referral	1	1	0	2	0	2	0	0	-	-	-	-
Clarke 1996	Cohort	Clinical OBPI	Referral	2	2	0	2	0	1	1	0	2	2	1	2
Geutjens 1996	Case series	Clinical OBPI	Referral	0	1	0	2	0	1	0	0	-	-	-	-
Laurent 1997	Case series	Clinical OBPI	Referral	1	2	0	2	0	2	0	0	-	-	-	-
Sherburn 1997	Cohort	Clinical OBPI	Referral	0	1	2	2	0	2	1	0	2	2	1	0
Waters 1999	Cohort	Clinical OBPI	Referral	2	1	1	2	0	2	2	0	1	2	1	2
Al-Qattan 2000	Cohort	Clinical OBPI	Referral	1	0	2	2	0	1	0	0	1	2	2	2
Xu 2000	Cohort	Clinical OBPI	Referral	2	0	0	2	0	2	0	0	1	1	2	2
Kawabata 2001	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	1	0	-	-	-	-
Leblebicioglu 2001	Case series	Clinical OBPI	Referral	1	0	0	2	0	1	1	0	-	-	-	-
Xu 2001	Case series	Clinical OBPI	Referral	1	1	0	2	1	2	0	0	-	-	-	-
Al-Qattan 2003	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-
Blaauw 2003	Case series	Clinical OBPI	Referral	1	0	0	2	0	1	0	0	-	-	-	-
Hoeksma 2004	Case series	Clinical OBPI	Hospital Birth Series	2	1	1	2	0	1	1	0	-	-	-	-
Smith 2004	Cohort	Clinical OBPI	Referral	1	0	2	2	0	2	2	0	1	2	1	2
Chuang 2005	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-
Pondaag 2005	Cohort	Clinical OBPI	Referral	2	0	0	2	0	2	0	0	2	2	1	2
Grossman 2006	Case series	Clinical OBPI	Referral	0	0	0	2	0	2	2	0	-	-	-	-
Konig 2006	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-
Pondaag 2006	Case series	Clinical OBPI	Referral	1	0	1	2	0	2	1	0	-	-	-	-
Ashley 2007	Case series	Clinical OBPI	Referral	2	2	0	2	0	2	2	0	-	-	-	-
El-Gammal 2008	Case series	Clinical OBPI	Referral	1	0	0	2	0	1	0	0	-	-	-	-
Kirjavainen 2008	Case series	Clinical OBPI	Demographic Population	1	1	1	2	0	2	1	0	-	-	-	-
Pondaag 2008	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-
Vekris 2008	Case series	Clinical OBPI	Referral	0	0	0	2	0	1	2	0	-	-	-	-
Badr 2009	Cohort	Clinical OBPI	Referral	0	1	0	2	0	1	1	0	1	2	1	1
Wellons 2009	Case series	Clinical OBPI	Referral	1	0	0	2	0	1	1	0	-	-	-	-
Gosk 2010	Cohort	Clinical OBPI	Referral	0	0	0	2	0	2	0	0	1	2	1	0
Lagerkvist 2010	Cohort	Incidence/Risk OBPI	Demographic Population	2	1	2	2	0	1	1	0	1	2	1	1
Terzis 2010	Case series	Clinical OBPI	Referral	1	2	0	2	0	2	0	0	-	-	-	-
Lin 2011	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-
Luo 2011	Case series	Clinical OBPI	Referral	1	0	0	2	0	2	0	0	-	-	-	-

Table 3-3: Quality assessment summarized by outcome
MINORS scoring: 0 (not reported), 1 (reported but inadequate), 2 (reported and adequate)

						MINORS								Comparisons			
Group	**Total Patients (n)**	**Total Reports**	**Outcome Assessment**	**Follow-up (months)**	**Report Quality Score**	**Clear Aim**	**Consecutive patients**	**Prospective Data**	**Endpoints**	**Unbias Assessment**	**Follow-up Period**	**Loss to Follow-up**	**Sample Size**	**Adequate Control**	**Contemporary**	**Baseline Equivalence**	**Analyses**
Functional Impairment: Operative vs. Gray Zone Nonoperative																	
					0	2	3	3	0	9	0	2	9	0	1	1	3
Cohort			**Scale:** 9	**>24:** 4	**1**	4	4	2	0	0	5	4	0	4	1	6	1
Studies	222	9	**Subjective:** 0	**<24:** 5	**2**	3	2	4	9	0	4	3	0	5	7	2	5
					0	5	18	25	0	30	0	13	30	0	1	1	3
Operative			**Scale:** 29	**>24:** 17	**1**	18	7	3	1	0	13	10	0	5	1	8	2
Series	1128	30	**Subjective:** 1	**<24:** 13	**2**	7	5	2	29	0	17	7	0	5	8	1	5
Gray Zone					**0**	1	9	11	0	18	0	6	19	0	1	2	2
Nonoperative			**Scale:** 16	**>24:** 8	**1**	10	8	3	3	0	10	6	0	6	2	5	2
Series	444	19	**Subjective:** 3	**<24:** 11	**2**	8	2	5	16	1	9	7	0	4	7	3	6
Functional Impairment and Full Recovery: Nonoperative																	
					0	2	2	19	0	24	2	4	27	0	0	0	0
Demographic			**Scale:** 3	**>24:** 9	**1**	11	22	2	24	2	16	11	0	1	0	1	1
Samples	1604	27	**Subjective:** 24	**<24:** 18	**2**	14	3	6	3	1	9	12	0	0	1	0	0
Adverse Events: Operative																	
					0	3	13	19	0	19	0	8	19	0	0	0	1
Operative			**Minor:** 19	**>24:** 9	**1**	14	1	0	1	0	10	7	0	1	0	3	1
Series	512	19	**Major:** 19	**<24:** 10	**2**	2	5	0	18	0	9	4	0	2	3	0	1

Figure 3-2: Funnel plot for A) operative management series and B) nonoperative management series

A)



B)

Table 3-4: Characteristics for reports of operative versus nonoperative management

Study	Care Team	Indication	Timing (mo)	Procedures	Non-op Group Comparison	Subjects (n)	Assessment	Timing (mo)	Functional Impairment
Meyer 1986	Surgeon	No return of function and myelogram	3	Excision and grafting	Onset biceps function >3 months	Nonop:6 OR:4	Mallet Score, Gilbert and Tassin MRC	Nonop:NR OR:6	Nonop:3 OR:2
Boome 1988	Surgeon	No recovery C5/6	3	Neurolysis, excision and grafting	No recovery C5/6 at 3 months	Nonop:6 OR:20	MRC (deltoid)	Nonop:12 OR:9	Nonop:1 OR:1
Laurent 1993	Multidisciplinary	For upper plexus: improvement in 2 of deltoid, biceps, triceps	4	Exploration, end-to-end, neurolysis,excision and grafting	Refused OR	Nonop:4 OR:25	MRC (deltoid)	Nonop:12 OR:18	Nonop:4 OR:0
Sherburn 1997	Multidisciplinary	Antigravity strength biceps, triceps, deltoid	4	Neurolysis, neurotization, excision and grafting	Refused OR	Nonop:9 OR:18	MRC (deltoid)	Nonop:24 OR:7	Nonop:9 OR:10
Waters 1999	Surgeon	Recovery of biceps	6	Excision and grafting	Recovery of biceps 3-6 months	Nonop:39 OR:6	Mallet Score (global abduction)	Nonop:24 OR:24	Nonop:3 OR:0
Al-Qattan 2000	Multidisciplinary	Elbow flexion against gravity	4	Excision and grafting	Recovery elbow flexion against gravity 3-4 months	Nonop:11 OR:3	AMS (abduction)	Nonop:18 OR:18	Nonop:6 OR:1
Xu 2000	Surgeon	No biceps function	3	Neurolysis, (then change to) transfer, excision and grafting	Recovery of biceps after 3 months	Nonop:12 OR:19	Mallet Score (abduction)	Nonop:36 OR:40	Nonop:8 OR:7
Smith 2004	Surgeon	Absence of elbow flexion with plateau in neurological recovery	6	Neurolysis, neurotization, excision and grafting	Absent biceps muscle function at 3 months	Nonop:22 OR:6	Mallet Score (abduction)	Nonop:60 OR:60	Nonop:8 OR:1
Lagerkvist 2010	Multidisciplinary	NR	NR	NR	Stregth elbow flexion <MRC 2.5 at 3 months	Nonop:9 OR:3	MRC (deltoid)	Nonop:18 OR:18	Nonop:9 OR:2

Figure 3-3: Functional outcomes in operative versus nonoperative reports

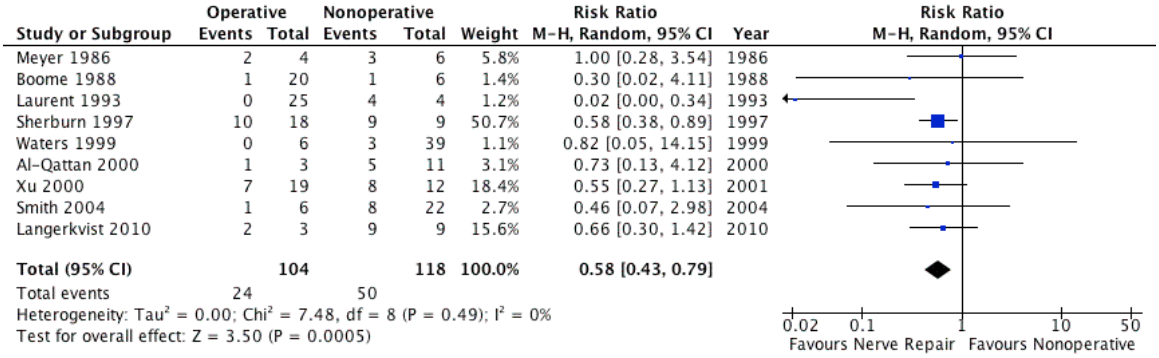


Table 3-5: Characteristics for reports of operative management

	Indication				Outcome			
Study	**Exam**	**Timing (mo)**	**Procedures**	**Postop physical therapy described**	**Assessment**	**Timing (mo)**	**Subjects (n)**	**Functional Impairment**
Alanen 1986	Clinical improvement, grossly defective EMG, juxtaganglionar affection	2	Direct end-to-end, neurolysis	Yes	Subjective "functional deficit"	6	11	3
Meyer 1986	No return of function and myelogram	3	Excision and grafting	Yes	Mallet Score, Gilbert and Tassin MRC	6	4	2
Boome 1988	No recovery C5/6	3	Neurolysis, excision and grafting	Yes	MRC (deltoid)	9	20	1
Kawabata 1994	No recovery of deltoid, biceps, triceps or wrist extensors	3	Accessory nerve neurotization	No	MRC (multiple)	12	13	5
Gilbert 1995	Absent biceps, complete palsy, flail arm + Horner's (1 mo)	3	Excision and grafting, neurolysis, neurotization	Yes	Mallet Score	24	436	62
Clarke 1996	Toronto Test score <=3.5, elbow flexion AMS 6 (9 mo)	3	Neurolysis	Yes	AMS (shoulder abduction)	12	16	8
Laurent 1997	Improvement of 1 MRC grade in 2/3 of deltoid, biceps, triceps or plateau less than antigravity	4	Excision and grafting, neurolysis	Yes	MRC (deltoid)	24	73	8
Waters 1999	Recovery of biceps	6	Excision and grafting	No	Mallet Score (global abduction)	24	6	0
Xu 2000	No biceps function	3	Neurolysis (then change to) transfer, excision and grafting		Mallet Score (abduction)	40	19	7
Kawabata 2001	Gilbert criteria	3	ICN to MCN neurotization	Yes	MRC (biceps)	36	31	2
Leblebicioglu 2001	Absence of deltoid and/or biceps function	4	Neurolysis, excision and grafting	Yes	Mallet Score	12	13	3
Al-Qattan 2003	Active elbow flexion against gravity	4	Transfer, excision and grafting	No	AMS shoulder abduction	24	5	1
Blaauw 2003	Not given	-	Pectoral to MSC transfer	No	Mallet (hand to mouth)	7	25	6
Hoeksma 2004	Persistent paralysis of the whole arm, absence of any active external rotation and supination	3	Neurosurgical repair	No	Narakas Motor Scale	12	8	1
Smith 2004	Absence of elbow flexion with plateau in neurological recovery	6	Neurolysis, neurotization, excision and grafting	No	Mallet Score (abduction)	60	6	1
Chuang 2005	Absence of biceps function with little or no hand function	3	Neurolysis, grafting, transfer of avulsions, muscle stim	Yes	Own scale (shoulder)	48	49	8
Pondaag 2005	Biceps less than M3 (MRC)	3	AN transfer, excision and grafting	No	Mallet Score (hand-head)	24	86	29
Grossman 2006	Not given	-	SAN to SSN with graft	No	Gilbert shoulder	30	26	0
Konig 2006	Antigravity in elbow flexion and shoulder abduction	6	Neurolysis, excision and grafting	Yes	Gilbert shoulder	30	10	9
Ashley 2007	Not given	-	Neurolysis, excision and grafting	Yes	MRC (composite)	24	63	7
El-Gammal 2008	Not given	-	ICN transfer	No	AMS	12	55	13
Kirjavainen 2008	Not given	-	Neurolysis, direct end-to-end, excision and grafting, transfer	No	Raimondi Hand	60	25	14
Vekris 2008	No spontaneous recovery	6	Excision and grafting, transfer	Yes	Mallet Score	6	11	0
Badr 2009	Lack of satisfactory biceps or shoulder function	6	Neurolysis, excision and grafting, transfer	No	Impairment rating (Eng)	12	15	2
Wellons 2009	Elbow flexion	7	MPN to MCN neurotization, neurolysis, excision and grafting	Yes	Mallet Score (hand-mouth)	9	20	4
Gosk 2010	Not given	-	Direct end-to-end, excision and grafting	No	Gilbert shoulder	36	13	6
Lagerkvist 2010	Not given	-	Not given	Yes	MRC (deltoid)	18	3	2
Terzis 2010	Not given	-	Excision and grafting, transfer	No	MRC (elbow, Terzis mod)	24	27	2
Lin 2011	Poor shoulder or elbow function	12	Contralateral C7 transfer	Yes	MRC (deltoid, biceps)	36	15	9
Luo 2011	No function biceps	3	ICN transfer	Yes	MRC (biceps)	24	24	2

Figure 3-4: Functional impairment in operative management

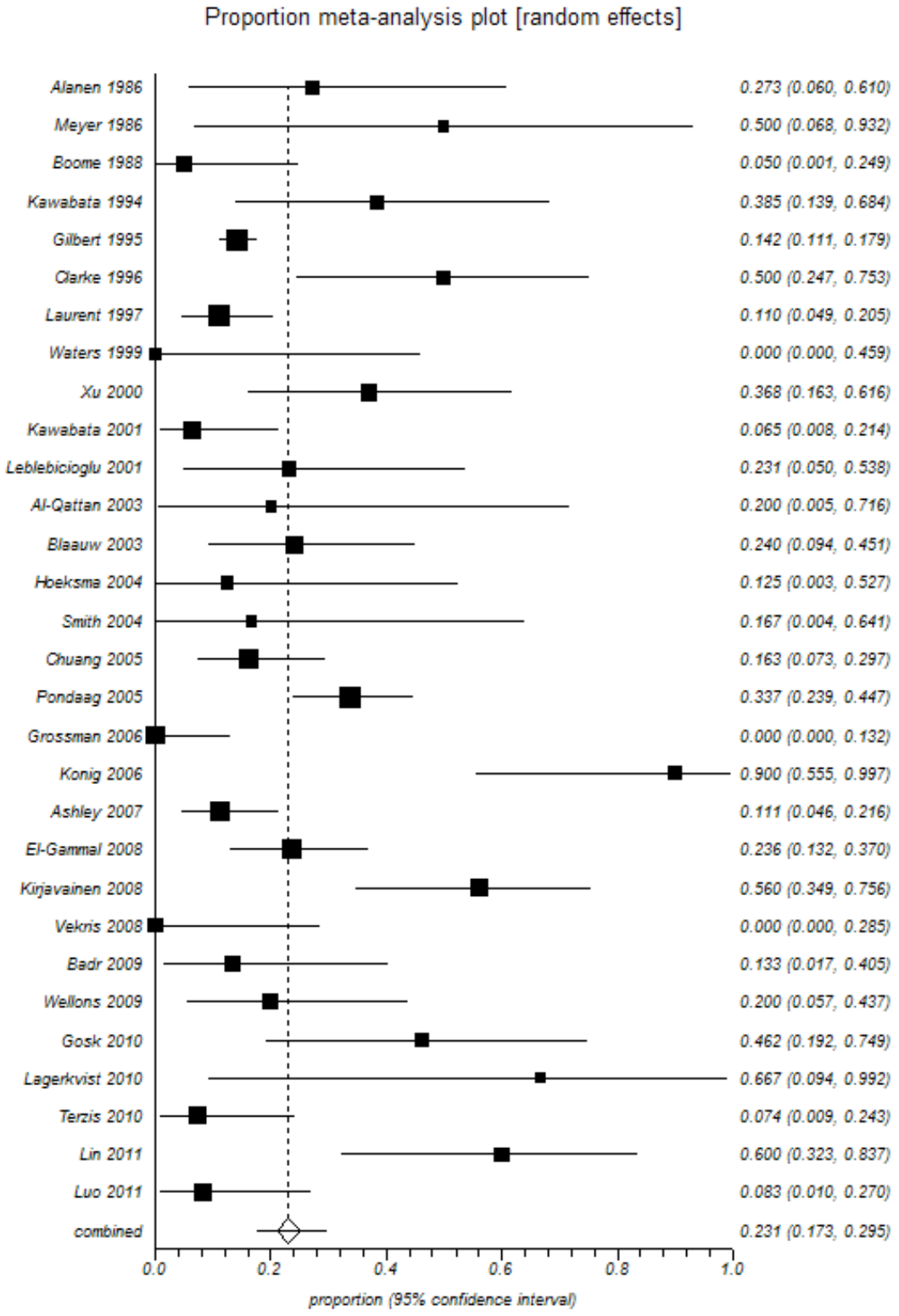


Table 3-6: Characteristics for reports of "gray zone" patients with nonoperative management

		Gray Zone				Outcome			
Study	**Care Team**	**Criteria**	**Timing (mo)**	**Management**	**Home Therapy**	**Assessment**	**Timing (mo)**	**Subjects (n)**	**Functional Recovery**
Gordon 1973	Not given	"Still paralyzed"	4	Natural history	No	Subjective categorical	48	6	4
Meyer 1986	Surgeon	Onset biceps function	3	Therapy at own multidisciplinary centre	Yes	Mallet Score, Gilbert and Tassin MRC	-	6	3
Boome 1988	Surgeon	No recovery C5/6	3	Home Therapy	Yes	MRC (deltoid)	12	6	5
Laurent 1993	Multidisciplinary	Improvement in 2 of deltoid, biceps, triceps; Refused OR	4	Therapy at own multidisciplinary centre	No	MRC (deltoid)	12	4	0
Michelow 1994	Multidisciplinary	Elbow flexion less than or equal to 1.3 (more than half range) (Toronto Test Score)	3	Therapy at own multidisciplinary centre	No	AMS (initial)	12	29	23
Eng 1996	Multidisciplinary	Elbow flexion not antigravity, shoulder abduction <90	3	Therapy at own multidisciplinary centre	Yes	Impairment rating (Eng)	18	68	45
Lindell-Iwan 1996	Multidisciplinary	Biceps to M3	3	Therapy at own multidisciplinary centre	No	Mallet Score	18	20	17
Waters 1999	Surgeon	Recovery of biceps	3	Natural history	No	Mallet Score (global abduction)	24	39	36
Yilmaz 1999	Surgeon	Toronto Test Score	3	Natural history	No	AMS	12	5	0
Al-Qattan 2000	Multidisciplinary	Recovery elbow flexion against gravity	3	Therapy at own multidisciplinary centre	No	AMS (abduction)	18	11	5
Strombeck 2000	Multidisciplinary	No biceps function	3	Therapy at own multidisciplinary centre	No	Subjective categorical	60	47	7
Xu 2000	Surgeon	Recovery of biceps	3	Therapy unknown site	No	Mallet Score (abduction)	36	12	4
Noetzel 2001	Multidisciplinary	Biceps M3	4.5	Therapy at own multidisciplinary centre	Yes	MRC (biceps)	6	27	16
Nehme 2002	Multidisciplinary	Elbow ROM <90deg, or biceps <M3, or shoulder abduction <120deg or weak ER, or an IR contracture, or absence of recovery	3	Therapy at own multidisciplinary centre	No	Mallet Score	24	28	15
Bisinella 2003	Multidisciplinary	No or minimal recovery, neurophysiology	3	Therapy at own multidisciplinary centre	No	Mallet Score (shoulder)	36	73	36
DiTaranto 2004	Multidisciplinary	No recovery of biceps deltoid	6	Therapy at own multidisciplinary centre	Yes	Gilbert shoulder	24	28	0
Smith 2004	Surgeon	Absent biceps muscle function	3	Therapy unknown site	No	Mallet Score (abduction)	60	22	14
Bain 2009	Multidisciplinary	AMS composite cutoff scores, plateau, Refused OR	3	Therapy at own multidisciplinary centre	Yes	AMS (composite)	12	4	0
Lagerkvist 2010	Multidisciplinary	Stregth elbow flexion <MRC 2.5	3	Therapy at own multidisciplinary centre	No	Subjective categorical	18	9	0

Figure 3-5: Functional impairment in gray zone patients with nonoperative management

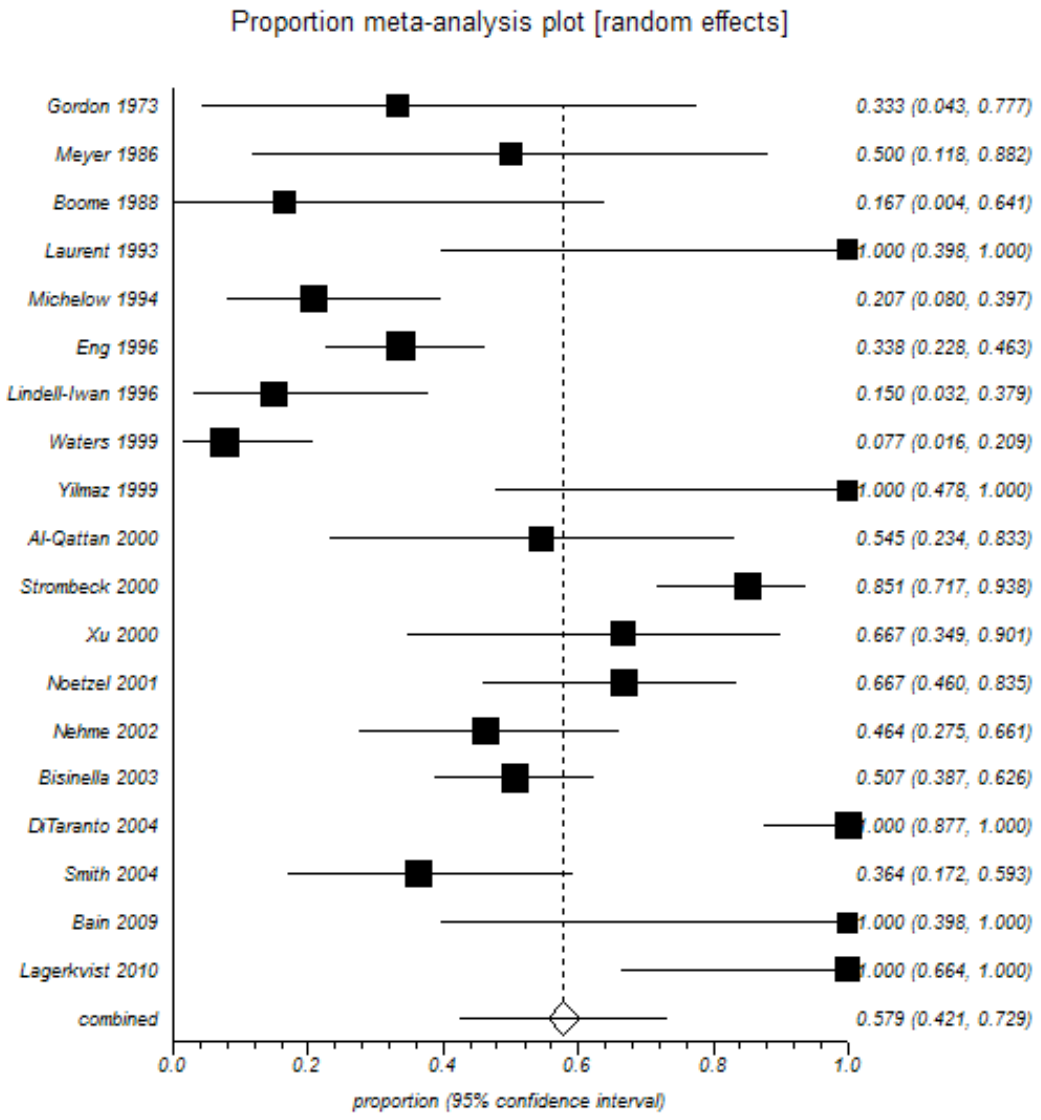


Table 3-7: Subgroup analyses of operative versus nonoperative management
OR (Operative management), Nonop GZ (Nonoperative management of gray zone patients)

Subgroup		Functional Impairment /Patients (n/n)		Functional Impairment (Pooled proportions)		Relative Risk (95% CI)
		OR	Nonop GZ	OR	Nonop GZ	
Follow-up						
	>24 months	167/914	139/255	23% (15-31%)	56% (30-80%)	0.34 (0.28-0.40)
	<24 months	50/214	79/183	24% (16-33%)	60% (39-80%)	0.54 (0.40-0.72)
Injury Level						
	Upper Plexus	80/517	45/86	25% (17-35%)	57% (23-87%)	0.30 (0.22-0.39)
	Total Plexus	70/277	32/78	28% (17-40%)	66% (22-98%)	0.61 (0.44-0.86)
Assessment						
	Shoulder	141/769	142/294	27% (18-36%)	52% (33-71%)	0.38 (0.31-0.46)
	External Rotation	115/218	49/90	49% (33-65%)	55% (42-68%)	0.97 (0.78-1.23)
	Elbow	91/522	78/261	19% (15-24%)	40% (18-63%)	0.58 (0.45-0.76)

Table 3-8: Characteristics for reports of nonoperative management in referral samples

						Outcome			
Study	Care Team	OR Available	Management	Details	Home Therapy	Assessment	Timing (mo)	Subjects (n)	Functional Impairment
Aitken 1952	Not given	Secondary	Therapy at own multidisciplinary centre	Relax paralysed muscles to prevent contractures, day then night splinting, active/purposeful movements	Yes	Subjective categorical	-	87	41
Wickstrom 1962	Multidisciplinary	Secondary	Therapy at own multidisciplinary centre	Splinting/protection until tone, twice daily passive or assist range of motion, night splint to improve shoulder int rotation	Yes	Subjective categorical	18	75	33
Alder 1967	Surgeon	Secondary	Therapy at own multidisciplinary centre	Splinting and home ROM parents, frequent diligent and gentle exercise, full ROM to prevent contracture	Yes	Subjective categorical	12	88	82
Eng 1971	Multidisciplinary	No	Therapy at own multidisciplinary centre	Splinting, ROM, electrotherapy and home electrotherapy, avoidance of substitution	Yes	Subjective categorical	12	22	5
Bennet 1976	Surgeon	Secondary	Natural history	ROM to prevent contractures. Parental teaching	Yes	Subjective categorical	12	24	6
Srivastava 1979	Multidisciplinary	No	Therapy at own multidisciplinary centre	Prevent contractures, active ROM (wrist/fingers extension, shoulder abduction), heat, effleurage, parental teaching	Yes	Subjective categorical	9	25	7
Tada 1984	Surgeon	Secondary	Natural history	Natural history	No	MRC	60	15	5
Mabogunje 1986	Surgeon	No	Therapy at own multidisciplinary centre	PROM, active range, resistance, play, stiffness prevention, splints for muscle imbalance, parental teaching	Yes	Subjective categorical	-	26	14
Meyer 1986	Surgeon	Yes	Therapy at own multidisciplinary centre	Rest for 2-3 weeks, gentle PROM	Yes	Mallet Score, Gilbert and Tassin MRC	6	11	3
Boome 1988	Surgeon	Yes	Natural history	Home stretching	Yes	MRC (deltoid)	12	42	4
Hentz 1991	Multidisciplinary	Yes	Natural history	Occupational therapy, splinting	No	Subjective categorical	42	25	7
Laurent 1993	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Physical therapy	No	MRC (deltoid)	12	48	4
Eng 1996	Multidisciplinary	No	Therapy at own multidisciplinary centre	Gentle PROM, shoulder sling if shoulder injured, holding and massage for awareness, weight bearing, AROM, wrist-cock up splint, elbow dynamic/static elbow splints,strengthening	Yes	Impairment rating (Eng)	18	149	23
Lindell-Iwan 1996	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Dynamic traction to stimulate early learning, voluntary movment and development of body image	No	Mallet Score	18	46	3
Waters 1999	Surgeon	Yes	Natural history	Natural history	No	Mallet Score (global abduction)	24	61	4
Yilmaz 1999	Surgeon	No	Natural history	Natural History	No	AMS	12	13	5
Basheer 2000	Multidisciplinary	Secondary	Therapy at own multidisciplinary centre	Physiotherapy to prevent the development of contractures	No	Own scale	24	52	7
Strombeck 2000	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Physiotherapy, excercises, home exercises	Yes	Subjective categorical	60	247	75
Xu 2000	Surgeon	Yes	Therapy unknown site	Physiotherapy recommended	No	Mallet Score (abduction)	36	12	8
Leblebicioglu 2001	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Neutral position for 3 weeks, PROM at 4 weeks, natural play	Yes	Mallet Score	12	88	11
Noetzel 2001	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Physical and occupational therapy at centre and away	Yes	MRC (deltoid)	6	80	18
Nehme 2002	Multidisciplinary	Secondary	Therapy at own multidisciplinary centre	All these patients were initially treated with simple range of motion exercises and orthotic devices	No	Mallet Score	24	30	13
Bisinella 2003	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Occupational therapy	No	Mallet Score (shoulder)	36	248	90
Kao 2003	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Physical and occupational therapy	No	Need for surgical intervention	9	109	43
Smith 2004	Not given	Yes	Therapy unknown site	Range of motion	No	Mallet Score (abduction)	60	22	8
Badr 2009	Not given	Yes	Natural history	No details	No	Impairment rating (Eng)	12	135	40
Bain 2009	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Physical and occupational therapy	Yes	AMS	12	75	22
Al-Qattan 2010	Multidisciplinary	Yes	Natural history	None provided	No	Subjective categorical	36	708	417
Ashrafzadeh 2010	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Physiotherapy and occupational therapy since the first week of life and during the study	No	Mallet Score	12	20	5
Toupchizadeh 2010	Multidisciplinary	No	Therapy at own multidisciplinary centre	Physiotherapy three sessions/weekx50mins, gentle and frequent exercise, full range of motion, massage, motivation of parents	Yes	Subjective categorical	24	28	13
Malessy 2011	Multidisciplinary	Yes	Therapy at own multidisciplinary centre	Physical therapy	No	Predictive outcome	6	121	61

Figure 3-6: Nonoperative functional impairment in referral samples

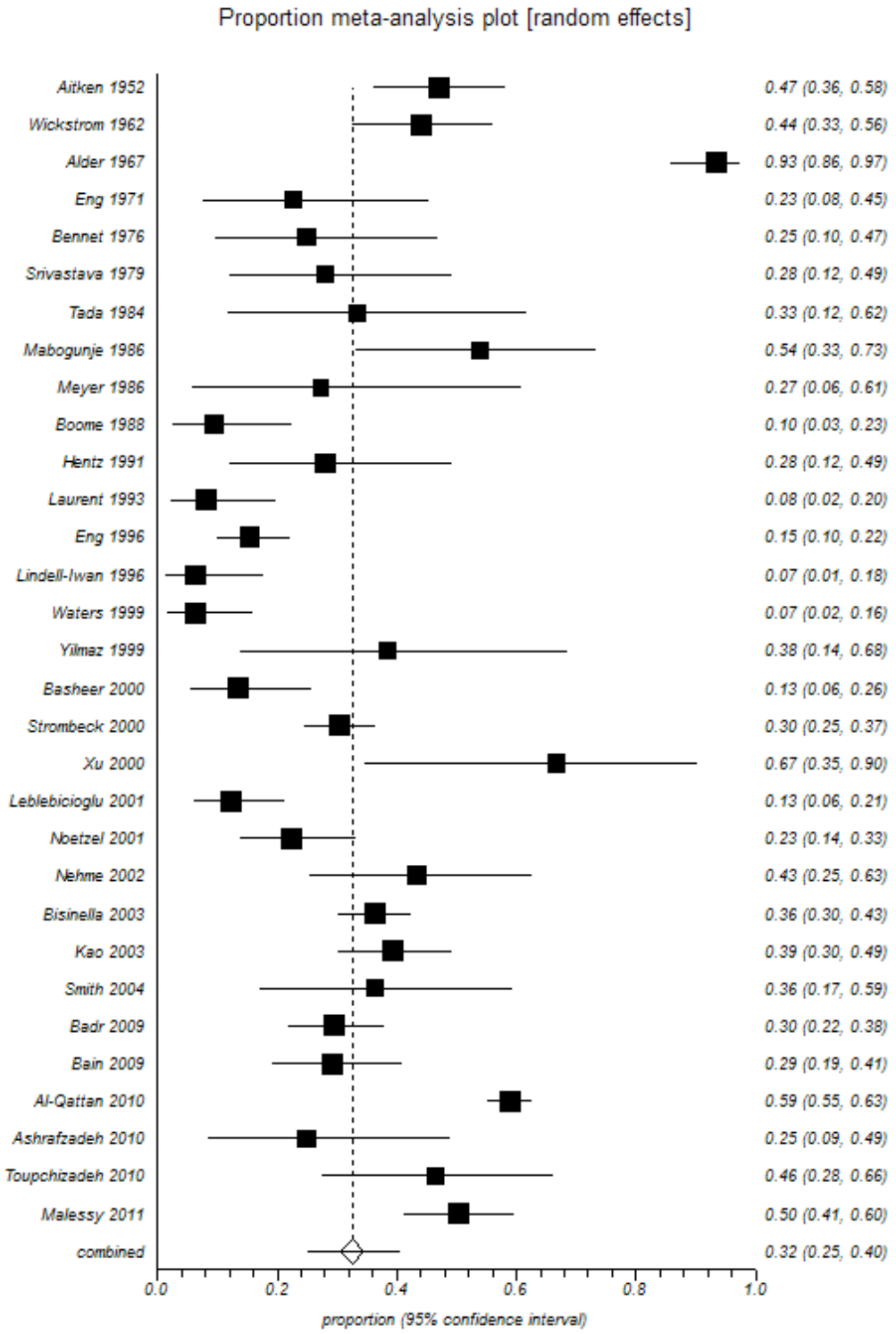


Table 3-9: Characteristics for non-operative demographic populations

					Outcome					
Study	**Specialty**	**Management**	**Home Therapy**	**Incidence per 1000**	**Assessment**	**Timing (mo)**	**Subjects (n)**	**Functional Impairment**	**Full Recovery**	**Full recovery one month**
Rubin 1964	Primary Care	Natural history	No	1.17	Subjective categorical	-	17	3	11	-
Gjorup 1966	Not Stated	Therapy at own multidisciplinary centre	Yes	NR	Subjective categorical	<1	104	45	32	32
Gordon 1973	Primary Care	Natural history	No	1.89	Subjective categorical	48	56	3	53	-
Tan 1973	Primary Care	Therapy at own multidisciplinary centre	No	0.63	Subjective categorical	9	35	4	24	15
Hardy 1981	OBPI Surgeon	Therapy at own multidisciplinary centre	Yes	0.88	Subjective categorical	13	36	8	27	6
Greenwald 1984	OBPI Surgeon	Natural history	No	2.00	Subjective categorical	12	38	2	36	25
Soni 1985	Primary Care	Natural history	Yes	3.58	Subjective categorical	18	18	6	12	-
Jackson 1988	OBPI Surgeon	Therapy at own multidisciplinary centre	Yes	2.54	Subjective categorical	26	19	4	15	7
Sjoberg 1988	Primary Care	Therapy at own multidisciplinary centre	Yes	1.87	Subjective categorical	36	48	13	35	12
Al-Najashi 1989	Primary Care	Natural history	No	NR	Subjective categorical	24	11	1	10	-
Walle 1993	Primary Care	Natural history	No	1.97	Subjective categorical	48	10	1	9	-
Baskett 1995	Primary Care	Natural history	No	0.81	Subjective categorical	<1	33	7	6	6
Lipscomb 1995	Primary Care	Therapy at own multidisciplinary centre	No	0.82	Subjective categorical	2	12	0	12	-
Narchi 1996	Primary Care	Natural history	Yes	4.18	Subjective categorical	18	37	1	36	28
Bager 1997	OBPI Physician or Therapist	Therapy at own multidisciplinary centre	No	1.72	Own defined scale	48	41	9	20	-
Dawodu 1997	Primary Care	Natural history	No	2.92	Subjective categorical	6	27	6	21	-
Kolderup 1997	Primary Care	Natural history	No	1.48	Subjective categorical	6	22	5	17	-
Gherman 1998	Primary Care	Natural history	No	4.41	Subjective categorical	12	40	9	31	-
Hoeksma 2000	OBPI Physician or Therapist	Therapy at own multidisciplinary centre	Yes	4.64	Subjective categorical	-	62	17	45	22
Evans-Jones 2003	Primary Care	Natural history	No	0.42	Subjective categorical	6	276	21	160	-
DiTaranto 2004	OBPI Surgeon	Therapy at own multidisciplinary centre	Yes	2.36	Gilbert Shoulder Classification	24	91	28	21	-
Chauhan 2005	Primary Care	Therapy at own multidisciplinary centre	No	0.99	Subjective categorical	12	85	10	75	-
Gurewitsch 2006	Primary Care	Natural history	No	5.80	Subjective categorical	24	135	11	124	-
AlAwari 2008	Primary Care	Therapy at unknown site	No	NR	Subjective categorical	24	29	12	13	-
Lagerkvist 2010	Primary Care	Natural history	No	2.94	MRC	18	98	13	80	12
Walsh 2011	Primary Care	Therapy at other multidisciplinary centre	No	1.72	Subjective categorical	12	72	9	63	-
Lindqvist 2012	OBPI Surgeon	Therapy at own multidisciplinary centre	No	3.24	Subjective categorical	12	152	36	116	-

Figure 3-7: Nonoperative functional impairment in demographic samples

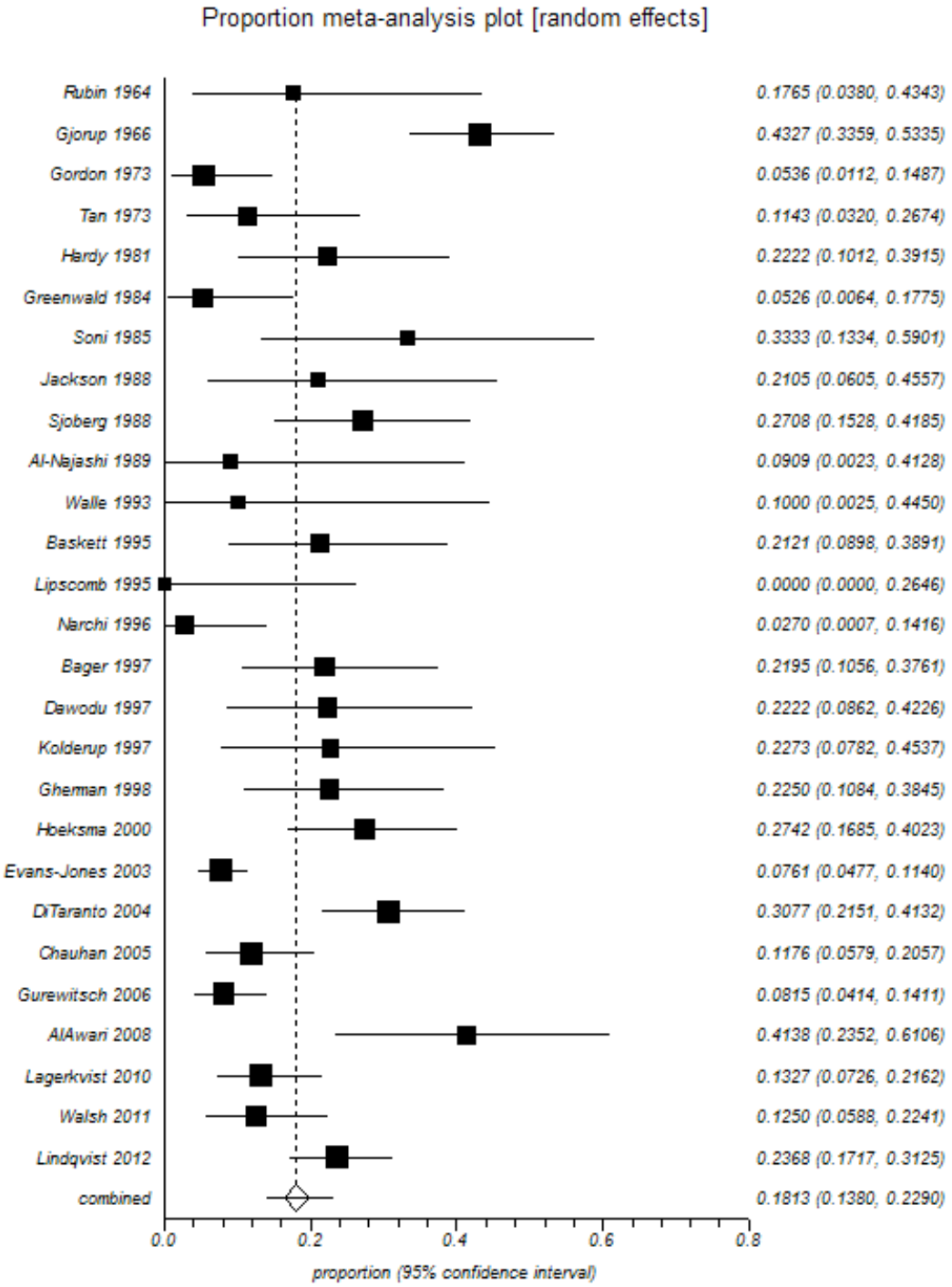


Figure 3-8: Nonoperative "full" recovery in demographic samples

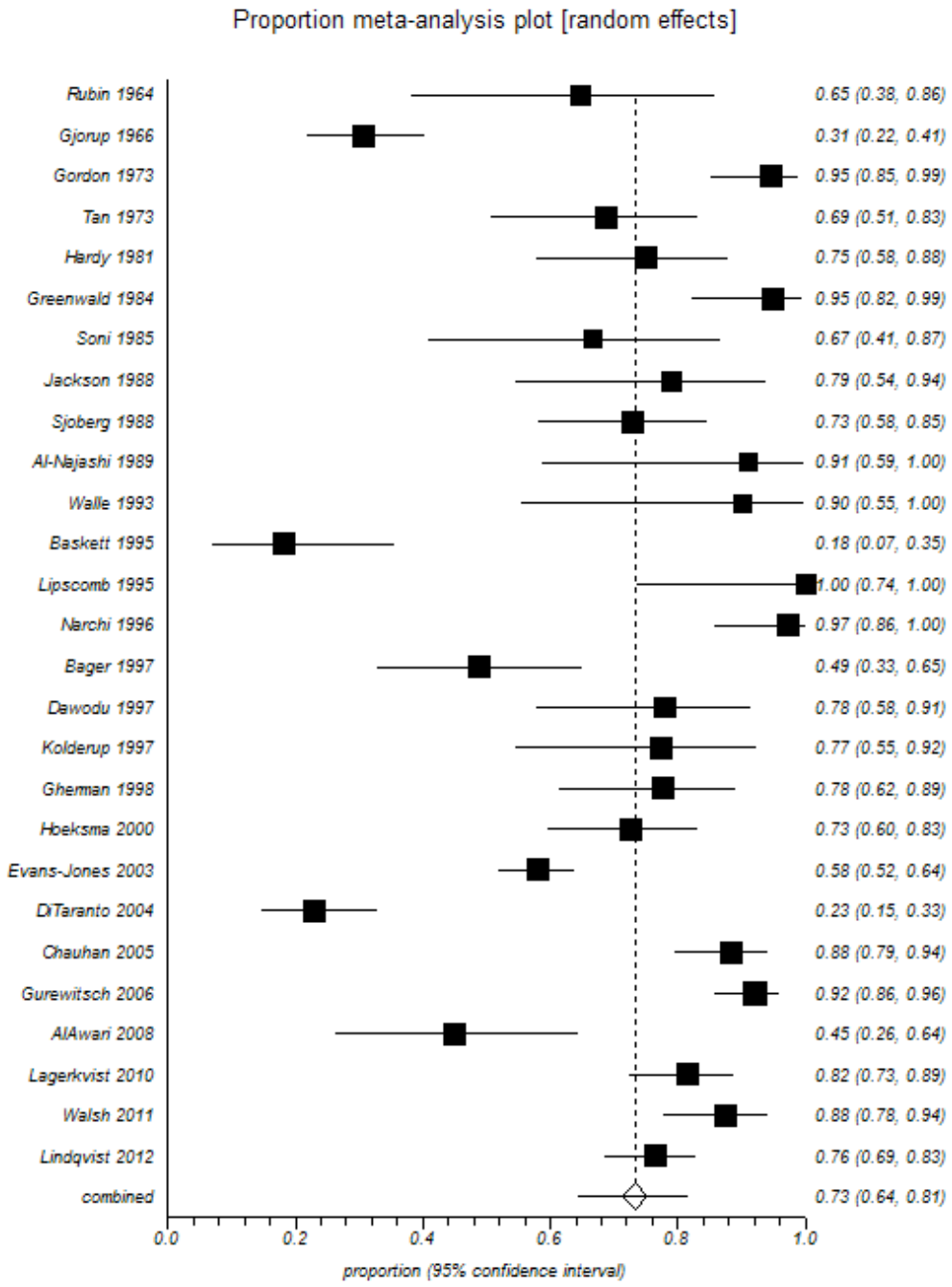


Figure 3-9: Full recovery at one month in demographic samples

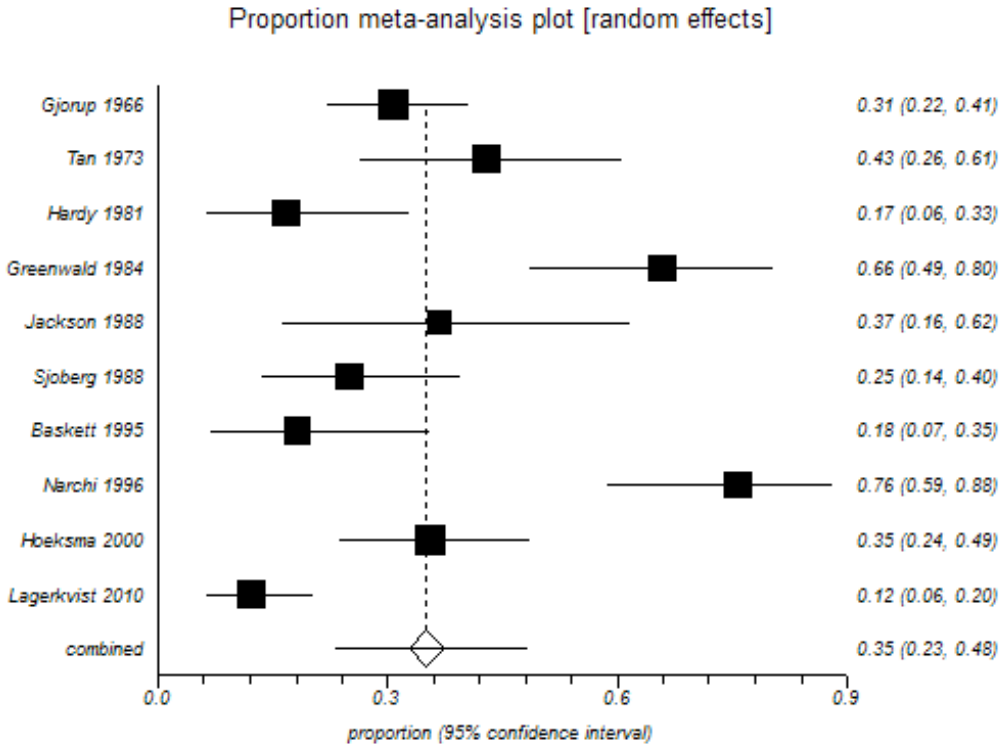


Figure 3-10: OBPI incidence reported in demographic samples

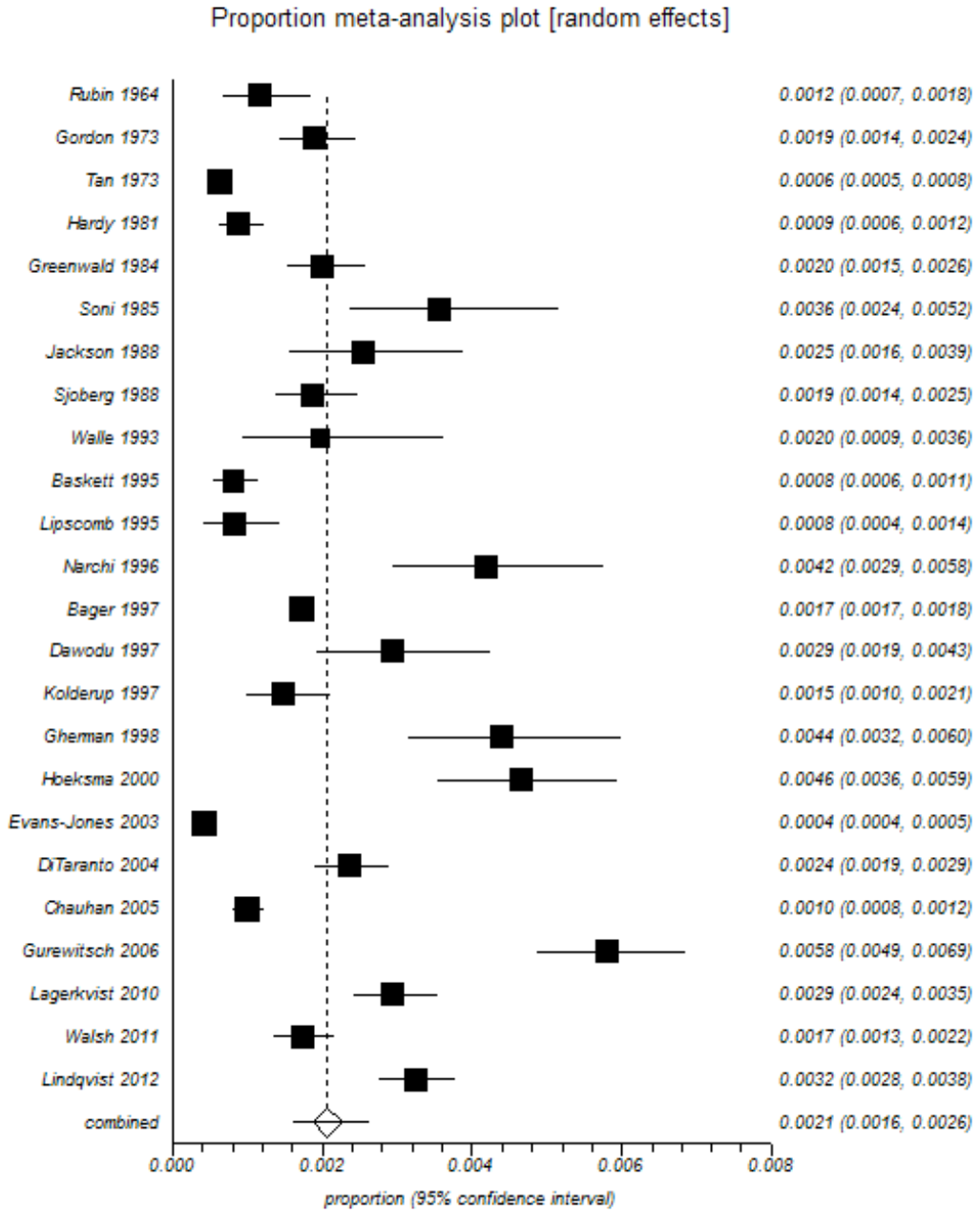


Table 3-10: Subgroup analyses for nonoperative management in demographic populations

Subgroup		Subjects (n)	Functional Impairment (Pooled proportions)	Full Recovery (Pooled proportions)
Follow-up				
	>24 months	440	20% (12-29%)	72% (49-89%)
	<24 months	1164	17% (12-23%)	74% (64-83%)

Figure 3-11: Major adverse events in operative series

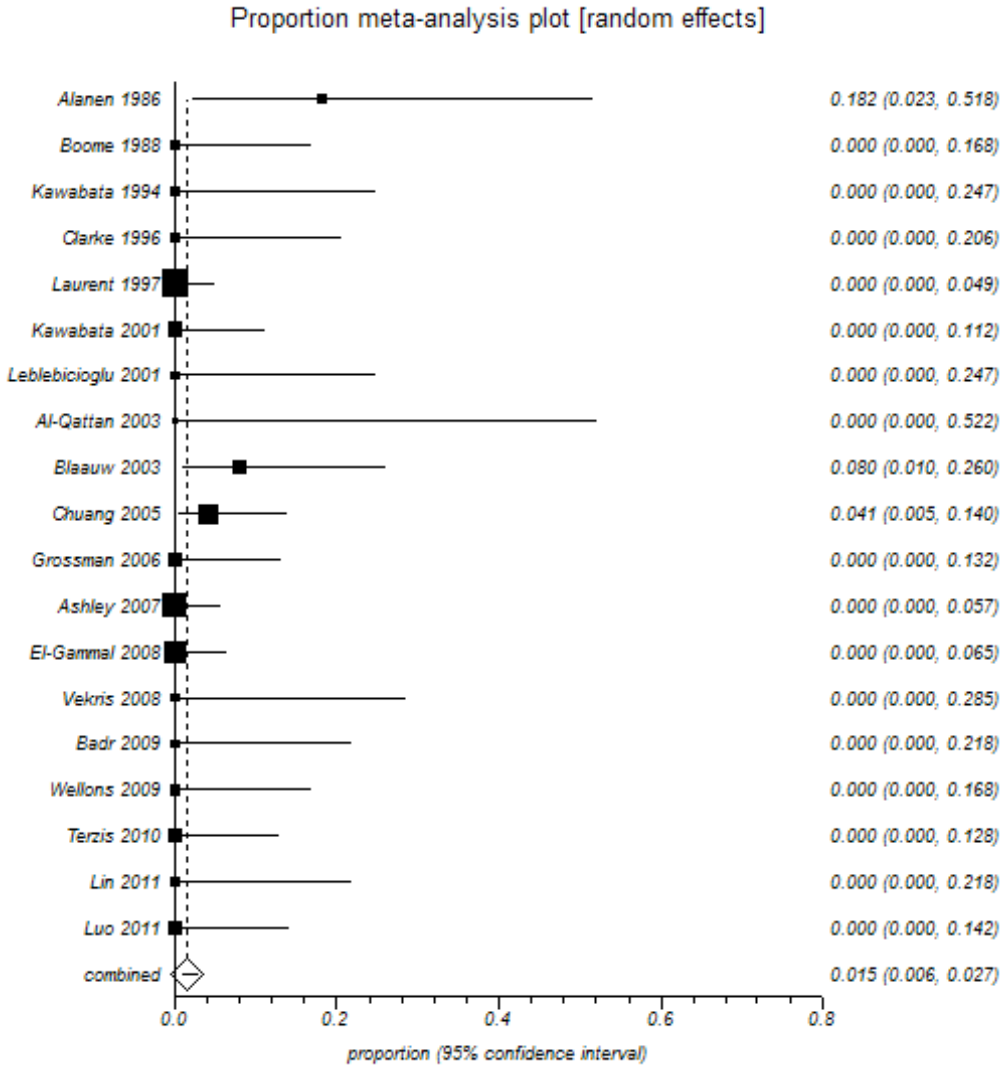
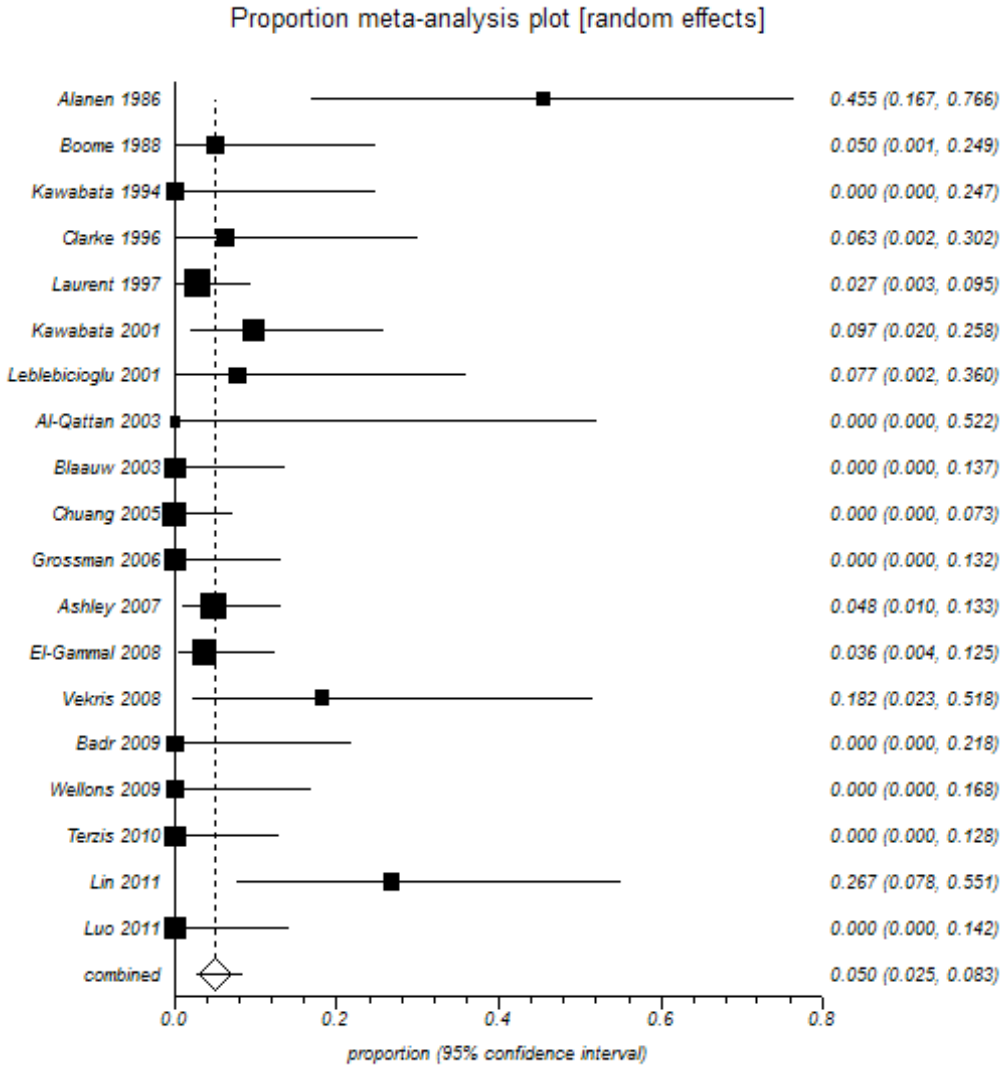


Figure 3-12: Minor adverse events in operative series



CHAPTER 4: OBSTETRICAL BRACHIAL PLEXUS INJURY: INCIDENCE, RISK FACTORS AND REFERRAL PATTERNS IN CANADA

4.1 Abstract

4.1.1 Introduction

The epidemiology and burden of disease for OBPI have been established in a number of populations worldwide; no data is available in Canada. Timing and volume of referral to multidisciplinary centres are unknown. The objective of this study is to determine the volume and timing of OBPI referrals to multidisciplinary centres.

4.1.2 Methods

OBPI diagnoses and risk factors were identified from newborn and corresponding maternal records in the CIHI Discharge Abstract Database and Hospital Morbidity Database from 2004-2012. Risk factors were generated from studies of OBPI epidemiology. Pearson's chi-squared test compared crude annual incidence during the time period. Identified risk factors were used to calculate odds ratios. Referral data were obtained from Canada's ten multidisciplinary centres over the same timeframe. Quality indicators were approved by the guideline consensus group, defined by the child's age on presentation to a multidisciplinary centre; "good" by one month, "satisfactory" by three months, and "poor" thereafter.

4.1.3 Results

OBPI incidence was at least 1.24 per 1000 live births in Canada. All potential biases underestimate injury identification. Incidence was consistent from 2004-2012. The risk factors with the strongest odds for OBPI were humerus fracture, shoulder dystocia and clavicle fracture. The majority (55-60%) of identified cases were likely not referred to multidisciplinary centres. Among those that were, timing was "good" in 28%, "satisfactory" in 66% (including those classified as good within one month), and poor in the remaining 34%.

4.1.4 Discussion

This is the first analysis of OBPI incidence, risk factors and referral timing in Canada. OBPI incidence is stable. Shoulder dystocia is the strongest modifiable risk factor. Quality indicators for referral are established for analysis of health processes. Most children are likely not referred to multidisciplinary carem, and those that are referred are likely referred late.

4.2 Rationale

Reported incidence of OBPI is approximately 2.1 in 1000 births (Section 3.5.5.1). It is reported between 0.4-5.8 per 1000 births,(168,173) varying with study type and availability of maternal-fetal care.(63,149,163) Incidence is consistent over decades in similar settings.(168,191) Incidence is equivalent to that of autism,(198) and congenital profound hearing loss (congenital deafness);(199) it is greater than the highest estimated incidence of type 1 diabetes mellitus,(200) cystic fibrosis,(201) and the combined incidence of congenital disorders in routine newborn screening.(199) Obstetrical trauma and risk factors can be measured by population-based administrative databases.(98) Accepted risk factors relate to dystocia, increased fetal size, prolonged labour, difficult/instrumented delivery and comorbid fetal trauma.(3)

One of the management "gaps" identified for OBPI is timely referral to multidisciplinary care. From our own review (Chapter 3) and the literature,(18) primary care providers underestimate and fail to objectively characterize residual impairment, and provide guardians with inaccurate information and education.(21) This results in guardian distress and delayed specialist referral.(18)

Incidence and associated risk factors have been established nationally in the United States,(3) but they have not been measured in Canada. While early referral algorithms have been investigated internationally,(18) volume of referrals to multidisciplinary centres, and process indicators and are not been established in the Canadian healthcare system.

National administrative databases exist to quantify incidence and risk factors for birth trauma in Canada. Clinic-based audit has been demonstrated to improve perinatal care.(202) Organizational databases are maintained for institutions' OBPI clinics, reflecting clinic processes and single-provider surgeon and therapist outcomes. This is a retrospective study of OBPI incidence in Canada and its risk factors. Identified cases were correlated with referrals to Canada's OBPI centres to generate quality indicators, and provide a baseline measurement of referral processes.

4.3 Objectives

4.3.1 Primary

1. To measure volume and timing of OBPI referral to Canadian multidisciplinary centres.

4.3.2 Secondary

1. To determine the incidence of OBPI in Canada.
2. To measure OBPI risk factors for identified cases.

4.4 Methods

4.4.1 Personnel

The Canadian OBPI Working Group was established for the purposes of participating in clinical practice guideline development, enhancing implementation, and

forming a network for future research (see Section 5.4.3). It is composed of 12 national OBPI opinion leaders; the lead physicians at each of Canada's ten OBPI multidisciplinary centres. They reviewed primary research (Chapters 3 and 4), provided aggregate patient data for referral volume and timing, approved quality indicators, and composed the consensus group for the formal recommendations consensus process (Chapter 5).

4.4.2 Data Sources

4.4.2.1 Incidence and Risk Factors

National incidence and risk factor data were obtained from newborn and associated maternal records in the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) and Hospital Morbidity Database (HMDB),(203) from 2004 to 2012. This database contains administrative, clinical and demographic data from all acute care facility discharges; thus children born outside of hospitals are not reliably captured. Reporting is mandatory across Canada except in the province of Quebec. Excluding Quebec, reporting has been nationally consistent since 2004-2005 using International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada (ICD-10-CA) and the Canadian Classification of Health Interventions (CCI). Quebec adopted ICD-10-CA in 2006-2007; data prior to this fiscal year are inconsistent with current reporting. Each fiscal year is defined between April 1 and March 31.

4.4.2.2 Referral to Multidisciplinary Centres

Referral data were obtained from all ten of Canada's multidisciplinary OBPI clinics. Data were generated from available organizational and single provider databases.

4.4.3 Variables

4.4.3.1 Incidence and Risk Factors

Database search strategy and ICD-10-CA codes were reviewed with the Program Lead of Decision Support Services, Clinical Administrative Databases at CIHI. All newborn records were identified in the national database, limited to acute inpatient care. Stillbirths and therapeutic abortions were excluded. Associated maternal records for all newborn records were identified. Records were stratified by province/territory to enable comparison with multidisciplinary centre referrals. OBPI cases were identified with the following codes:

- P14.0 Erb's paralysis due to birth injury
- P14.1 Klumpke's paralysis due to birth injury
- P14.2 Phrenic nerve paralysis due to birth injury
- P14.3 Other brachial plexus birth injuries
- P14.8 Birth injuries to other parts of peripheral nervous system
- P14.9 Birth injury to peripheral nervous system, unspecified

Risk factors were generated from a previous epidemiological study,(3) and studies from our systematic review with a primary outcome of OBPI incidence or risk.(1,62,63,106,130,135,144,149–151,154,158,163,168,170,173,176,180,185–187,191,192) For all newborn records, the following codes were identified:

- P08.0 Exceptionally large baby (macrosomia, >4500g)
- P13.4 Fracture of clavicle due to birth injury
- P13.30 Birth injury to humerus (fracture)

For all maternal records, in cases of twin or other multiple births, the mother's record was only associated with the first newborn's chart number. There were additional instances of an inability to link newborn and maternal charts, which resulted in undercounting. The database does not collect factors related to maternal weight (eg. body mass index, weight gained during pregnancy, etc.). In the database, an elective caesarean section is defined to be carried out as a planned intervention where the decision is made prior to the onset of labour. An emergency caesarean section is defined to be required due to an emergency situation posing a threat to the maternal or fetal health, and the mother may or may not be in labour. The following risk factor codes were identified:

- O66.001 Obstructed labor due to shoulder dystocia
- 5.MD.53.** Forceps traction and rotation delivery
- 5.MD.54.** Vacuum traction delivery
- 5.MD.56.** Breech delivery
- 5.MD.60.** Caesarean section delivery

Maternal impaired glucose tolerance

- O99.801 Other specified diseases and conditions complicating pregnancy, childbirth and the puerperium
- O99.802 Other specified diseases and conditions complicating pregnancy, childbirth and the puerperium +R73.0 Abnormal glucose tolerance test

Maternal gestational diabetes

- O24.4*1 Diabetes mellitus arising in pregnancy….delivered, with or without mention of antepartum condition (2004-2006)
- O24.4*2 Diabetes mellitus arising in pregnancy…delivered, with mention of postpartum condition (2004-2006)
- O24.9*1 Diabetes mellitus in pregnancy, unspecified…delivered, with or without mention of antepartum condition (2004-2006)
- O24.9*2 Diabetes mellitus in pregnancy…delivered, with mention of postpartum condition (2004-2006)
  The codes O24.9-1 and O24.9-2 would be assigned if documentation did not identify if the diabetes mellitus was pre-existing or gestational
- O24.801 Diabetes mellitus arising in pregnancy (gestational), delivered, with or without mention of antepartum condition (2006-2012)
- O24.802 Diabetes mellitus arising in pregnancy (gestational), delivered, with or without mention of antepartum condition (2006-2012)

Maternal pre-existing diabetes mellitus
The codes O24.9-1 and O24.9-2 would be assigned if documentation did not identify if the diabetes mellitus was pre-existing or gestational

- O24.0*1 Pre-existing diabetes mellitus, of unspecified type…delivered with or without mention of antepartum condition (2004-2006)
- O24.0*2 Pre-existing diabetes mellitus, of unspecified type…delivered with or without mention of antepartum condition (2004-2006)
- O24.1*1 Pre-existing diabetes mellitus, of unspecified type…delivered with or without mention of antepartum condition (2004-2006)
- O24.1*2 Pre-existing diabetes mellitus, of unspecified type…delivered with or without mention of antepartum condition (2004-2006)
- O24.2*1 Pre-existing diabetes mellitus, of unspecified type…delivered with or without mention of antepartum condition (2004-2006)
- O24.2*2 Pre-existing diabetes mellitus, of unspecified type…delivered with or without mention of antepartum condition (2004-2006)
- O24.3*1 Pre-existing diabetes mellitus, of unspecified type…delivered with or without mention of antepartum condition (2004-2006)
- O24.3*2 Pre-existing diabetes mellitus, of unspecified type,…delivered, with mention of postpartum condition (2004-2006)
- O24.501 Pre-existing type 1 diabetes mellitus in pregnancy, delivered, with or without mention of antepartum condition (2006-2012)
- O24.502 Pre-existing type 1 diabetes mellitus in pregnancy, delivered, with mention of postpartum condition (2006-2012)
- O24.601 Pre-existing type 2 diabetes mellitus in pregnancy, delivered, with or without mention of antepartum condition (2006-2012)
- O24.602 Pre-existing type 2 diabetes mellitus in pregnancy, delivered, with mention of postpartum condition (2006-2012)
- O24.701 Pre-existing diabetes mellitus of other or unspecified type in pregnancy, delivered, with or without mention of antepartum condition (2006-2012)
- O24.702 Pre-existing diabetes mellitus of other or unspecified type in pregnancy, delivered, with mention of postpartum complication (2006-2012)

Given resource limitations in CIHI's Graduate Student Data Access Program (GSDAP),(204) some risk factors were only made available for Ontario newborn and associated maternal records. The following newborn factor codes were provided for Ontario records only:

- P08.1 Other heavy for gestational age infants (heavy for dates, not macrosomia)
- P20.* Fetal asphyxia
- P21.* Birth asphyxia
- P52.* Intracranial nontraumatic hemorrhage of fetus and newborn

The following maternal factor codes were provided for Ontario records only:

Twin or multiple births

- Z37.2 Twins, both liveborn
- Z37.3 Twins, one liveborn and one stillborn
- Z37.5 Other multiple births, all liveborn
- Z37.6 Other multiple births, some liveborn

Episiotomy

- 5.MD.53.** Episiotomy with forceps traction and rotation delivery
- 5.MD.54.** Episiotomy with vacuum traction delivery
- 5.MD.55.** Episiotomy with combination of vacuum and forceps delivery
- 5.MD.56.** Episiotomy with breech delivery
- 5.MD.50.** Episiotomy with manually assisted vaginal delivery

4.4.3.2 Referral to Multidisciplinary Centres

No quality indicators for primary management of OBPI exist. Without indicators generated by consensus,(97) we relied on best available evidence and current practice patterns.(96) The guideline working group defined quality indicators, approved by the 12 members of the consensus group. Indicator selection was guided by criteria suggested by Mainz:(96)

i. Indicator is based on agreed definitions, and described exhaustively and exclusively
ii. Indicator is highly or optimally specific and sensitive, i.e. it detects few false positives and false negatives
iii. Indicator is valid and reliable
iv. Indicator discriminates well
v. Indicator relates to clearly identifiable events for the user (e.g. if meant for clinical providers, it is relevant to clinical practice
vi. Indicator permits useful comparisons
vii. Indicator is evidence-based.

In general, indicators are valuable where management timeframes are short, indicators address low volume providers and patient prognosis cannot be stratified.(96) These conditions are met in OBPI; early referral is critical, referrals are generated by primary care without expertise in peripheral nerve injury and no diagnostic investigation can indicate prognosis. Early referral to a multidisciplinary centre provides guardian

education,(21) early treatment by specialized therapists,(8,22) serial assessment for recovery and appropriate operative management.(18) Centres and providers with high volumes of the same diagnosis (ie. specialized centres) generally deliver higher quality care in the paediatric population.(205)

Indicators were defined by the child's age at initial assessment at a multidisciplinary centre; "good" by one month of age, "satisfactory" by three months of age and "poor" thereafter. The selection of one month was informed by practice patterns,(22,23) algorithms for referral,(18) and previous position statements.(195) The selection of three months was informed by our systematic review (Chapter 3), and surgical indications.(22,23)

Each Canadian multidisciplinary centre provided the number of cases seen in initial consultation/primary assessment whose birth dates were within the time range as the cases identified by the CIHI incidence data, April 1 2004 to March 31 2012. Further, each centre provided the proportion of cases seen in consultation by one month of age, and by three months of age (including those seen by one month). Referrals to multidisciplinary centres within the same province were pooled to facilitate comparison with total provincial cases identified in the national database. The Maritime provinces (Newfoundland and Labrador, Prince Edward Island, Nova Scotia and New Brunswick) were pooled to facilitate comparison with the single multidisciplinary centre servicing these provinces.

4.4.4 Analysis

Methodology was advised by Dr. F. Farrokyhar, epidemiologist and research methodologist, Department of Surgery, McMaster University. Incidence was calculated as a proportion of all available newborn records, and expressed per 1000 cases. Pearson's chi-squared test (one-way goodness-of-fit) was used to compare crude annual incidence during the time period. Identified newborn and maternal risk factors were used to calculate odds ratios (OR) to determine comorbidities associated with OBPI. Referrals to multidisciplinary centres were pooled by province/territory, and expressed as a proportion of identified OBPI cases in the national database. Quality indicators for referral were calculated and expressed as proportions of cases referred to each individual centre. For calculation of quality indicators, OBPI cases in Quebec for 2004 and 2005 were imputed using the means of the available years (2006-2011).

Quebec's multidisciplinary centre assessed more children in consultation during the study period than indexed for Quebec in the CIHI dataset. Quebec data were removed from incidence and risk factor analyses post hoc, given absence of 2004-2005 OBPI cases prior to the adoption of ICD-10-CA coding, and low reporting. Reporting is not mandatory in the province, and no cases were reported in 2004-2005. Quebec had the lowest cumulative incidence during this two-year period, 0.33 per 1000 births.

4.5 Results

4.5.1 Incidence

The CIHI Discharge Abstract Database (DAD) and Hospital Morbidity Database (HMDB) included 2,762,996 newborn records from April 1, 2004 to March 31, 2012. Of these newborns, 2968 were coded with a brachial plexus injury (Tables 4-1 a and b). Total OBPI incidence was 1.07 per 1000 live births (95% CI 1.04-1.11 per 1000) during the study period (Table 4-1 c). Excluding Quebec's data, OBPI incidence is 1.24 per 1000 births (95% CI 1.20-1.29 per 1000) (Table 4-1 d). There was no change in annual crude incidence, χ^2=6.885, df=7, p=0.44. The probability of observing this or a more extreme difference if incidence was equal between years is approximately 0.44.

4.5.2 Risk Factors

Odds ratios were calculated for identified OBPI risk factors from the available national and Ontario data; "heavy for dates", birth asphyxia, fetal asphyxia, intracranial haemorrhage, twin/multiple births and episiotomy were analyzed from Ontario data only. Odds ratios were sorted in descending order with confidence intervals Table 4-2. To summarize, risk factors were consistent with a large fetus, difficult labour and comorbid birth trauma. The strongest risk factors for OBPI were birth injury to humerus, shoulder dystocia and clavicle fracture, each with odds ratios greater than 30. Twin and multiple births, and caesarean delivery were protective factors. While caesarean delivery was a protective factor, the incidence of OBPI in caesarean deliveries was not zero.

4.5.3 Referral Processes

Referral data were available from nine of Canada's ten OBPI multidisciplinary centres (Table 4-3). Referrals were pooled by province and their respective multidisciplinary centres. Within Ontario, Western University referral data were not available, and data for the University of Ottawa were available from 2008 when the centre's surgeon began practice. The surgeon representing Dalhousie, the Maritimes' only centre, began practice after the reference timeframe and no data were available. Overall, multidisciplinary centres accounted for 1188 OBPI referrals, 40% of total cases identified by the database during the time period (Table 4-3).

Proportions of provincial OBPI cases referred to each multidisciplinary centre are illustrated in Table 4-3. Universite de Montreal referrals accounted for 153% of Quebec's incident cases during the time period. Data for incident cases were inconsistent in Quebec, and absent in 2004-2005. If the mean annual cases from 2006-2011 were imputed for 2004-2005, Quebec's total referrals would be 220, 115% of provincial cases. In Ontario, 41% of incident cases were seen in referral at a multidisciplinary centre. Data were unavailable for Western University; referrals can be estimated using McMaster University's data given similar centre sizes and surgeons. This would increase total national referrals to 1327 (45% of national cases), and Ontario centres' total referrals to 715, (51% of provincial cases).

Referral timing by quality indicator criteria is illustrated in Table 4-4. Overall, 28% of OBPI patients referred were assessed by multidisciplinary teams by one month of age ("good"), and 66% by three months of age ("satisfactory"). No centre assessed the majority of its consultations prior to one month of age; range 4% (Universite de

Montreal) to 47% (University of Alberta). Conversely, six of the eight centres reporting (excluding Dalhousie and Western) assessed the majority of their consultations by three months of age; range 38% (University of Ottawa) to 82% (University of Alberta).

4.6 Discussion

Among mandatory reported data sets in Canada, incidence of OBPI is 1.24 per 1000 live births at minimum. All potential biases underestimate OBPI identification. Incidence was consistent during the study period. The strongest OBPI risk factors were humeral injury (fracture), shoulder dystocia, and clavicle fracture. Most (55-60%) were not referred to multidisciplinary centres for specialized assessment and therapy. Among those referred, timing was "good" for only 28% (seen by one month of age). Timing was "satisfactory" for 66% (seen by three months of age). This is the first analysis of OBPI epidemiology in Canada.

4.6.1 Incidence

Incidence among demographic samples (demographic population or hospital series) was pooled in our systematic review; 2.1 per 1000 births (95% CI 1.6-2.6, I^2=98%). Incidence is reported to vary with study methodology and population.(63,149,163) Canadian incidence is at least 1.24 per 1000 births, similar to many other well-known childhood conditions and disabilities.(198–201) Our data was derived from an administrative population database; it is not kept for research and

excludes newborns born outside of hospital. Moreover, the database relies on diagnostic codes on hospital discharge from primary care. These providers may not accurately assess peripheral nerve injury,(206) and incidence may be underestimated.

Still, our estimated Canadian incidence is consistent with similar study samples; retrospective demographic populations,(62,150,152) large samples from the United States(3,168) and hospital series reviewing birth trauma where OBPI incidence or risk was not the primary outcome.(141–143) The largest epidemiological study of OBPI estimated incidence at 1.51 per 1000 births based on a national (United States) sample of discharge records in a national cost utilization database.(3) A previous Canadian retrospective series analyzing shoulder dystocia estimated OBPI incidence at 0.81 per 1000 births.(142)

Evidence from historical North American reports,(64,130), modern studies spanning decades,(170,191) and clinical environments with dedicated educational intervention, and increased awareness,(173) demonstrate incidence is unaffected over time. The exception is Foad et al.,(3) who reported decreased annual incidence in 1997 versus 2003; from 1.7 per 1000 births to 1.3 per 1000. Conclusions were based only on samples of births from these two years. While the study demonstrated statistical significance, it relied on a large sample size and may not be clinically significant or consistent. It compared only two years with a difference of 0.4 in 1000, similar to the difference in our data if only 2011 and 2004 are compared (1.38 vs. 1.03 in 1000) rather than a more robust analysis.

Obesity rates are rising; the largest increase in obesity for Canadian women is the 20-39 year age group.(207) Being overweight or obese increases the risk of a large for gestational age newborn,(208) and subsequent complications(209) including shoulder dystocia.(210) Rates of induction and preterm caesarean delivery in Canada have increased in response to newborn size.(211) Despite advances in perinatal care and decreased incidence in other birth trauma, the literature consistently reports no change in OBPI incidence.(168) Predicting fetal size in individual cases remains difficult, and consequently a reliable prognostic model for OBPI prevention is elusive.(212) Predicting birth-weight becomes more important since it is correlated with OBPI neurological severity and need for nerve repair.(213)

4.6.2 Risk Factors

Risk factors are consistent with a previous epidemiological study,(3) and studies from our systematic review.(1,62,63,106,130,135,144,149–151,154,158,163,168,170,173,176,180,185–187,191,192) Identified risk factors related to shoulder dystocia,(214) a large fetus, and comorbid birth trauma (Table 4-2).(3) Beyond those available in the national database, maternal BMI or obesity,(209,210) and maternal risk in previous deliveries(144) are considerations in practice. While comorbid birth trauma (ie. humerus and/or clavicle fracture) correlated with OBPI, these factors themselves are not identified prior to labour.

Dystocia is the most significant modifiable risk factor, both from the perspective of prevention and effective management. OBPI following dystocia is mechanically

distinct and results in greater residual impairment;(173) over 90% of "permanent" injuries are secondary to shoulder dystocia. Increasing the rate of caesarean delivery is not considered feasible, with the number of caesareans needed to prevent one OBPI exceeding 100.(214) While predicting fetal size and deliverability remain difficult, awareness and dedicated training of dystocia manoeuvres may improve OBPI outcomes.(215) It is accepted that increased force and downward traction in dystocia worsen the severity of OBPI.(180) High fidelity training models can characterize the magnitude and vector of force,(216) and decrease incidence of both overall and "permanent" OBPI in practice.(217)

4.6.3 Referral Processes

At best, only 45% of OBPI cases were referred to multidisciplinary care. This statistic includes an optimistic imputation of Western University's referral volume, and a "denominator" of total OBPI likely underestimated given that it relied on recorded primary care diagnoses in the national database and missing data in Quebec. The proportion of cases referred was consistent between provinces with a centre. Universite de Montreal's proportion in excess to incident provincial cases was likely due to the province's missing CIHI data and referrals from the Maritimes. Children from other provinces and territories without a centre may have been assessed at centres with a large catchment (ie. University of Alberta, University of Manitoba). We were unable to reliably determine if referrals were generated in the same province as each multidisciplinary centre. Provinces and territories without a centre may have lower referral proportions.

Among those referred, only 28% were assessed at multidisciplinary centres by one month of age. These newborns were referred within a good timeline, allowing assessment, investigations, therapy, and education to be optimized. Worse, 34% of patients were assessed later than three months of age. Given that these infants were referred late in their recovery course, they were almost certainly referred due to a deficit identified at three months of age or later. Assessment, investigations, nonoperative, and operative therapy modalities in this population were delayed. Despite the existence of ten multidisciplinary centres, a large proportion of Canadian children with OBPI were referred late, and care was not optimized.

Referral was consistent with an study of adult brachial plexus injuries in Ireland;(206) 48.6% of cases were referred to specialized centres, with 53.7% referred late. This is the first study to analyze OBPI referrals in Canada. While estimates of incidence and impact of risk factors vary, clinical diagnosis of OBPI is reliable. Timely referral to a multidisciplinary centre is critical. While not all OBPI cases will require operative nerve repair, peripheral nerve specialists best assess injury,(206) and impairment allowing for timely operative and nonoperative therapy.(18) Guardians(10,20,21) and Canadian OBPI surgeons indicate preference for early referral.(22,23,195) The optimal window for operative reconstruction is three months of age for the most severe injuries, with the latest surgical indications at nine months.(22)

From our systematic review of primary management (Chapter 3), only three studies provided timing and criteria for referral from primary care including: no recovery at six months,(149) impaired deltoid and biceps at 2 to 3 months,(159) and absence of

active elbow extension at one month or absence of active elbow flexion with EMG absence of biceps motor unit potentials at one month.(18) However, referrals in Canada are generated by primary care without expertise in peripheral nerve injury, and without experience interpreting EMG to indicate prognosis. Even if surgical candidates are reliably identified using the algorithm, the remainder of infants still likely benefit from therapist referral. Specialized paediatric therapists and EMG technicians are generally employed at academic multidisciplinary centres in Canada. Referral to therapists is achieved through the physician in the multidisciplinary team.

4.6.4 Limitations

This study has limitations. The Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) and Hospital Morbidity Database (HMDB) only includes infants born in hospital. Discharge diagnoses are generated by primary care and may not be accurate. Given the previous literature and our systematic review of primary management (Chapter 3), incidence is likely underestimated. Quebec is not subject to mandatory reporting and identification of OBPI cases was inconsistent.

For risk factor analysis, risk factors were generated from a previous national epidemiological study(3) and studies from our systematic review including a primary outcome of OBPI incidence or risk. A systematic review of risk factors was not completed. Among risk factors identified, we were limited to those coded in the administrative database. Maternal BMI, weight gained, and obesity were not available. Further, OBPI cases with total absence of risk factors could not be determined. Newborn

weight was limited to dichotomous variables, preventing a robust analysis. Only summary data was available; patient-level data was not available to analyze multiple risk factors within a patient or determine the number of newborns without any risk factors.

In analyzing referrals, data was generated from organizational or single-provider databases. Province and country of birth for each patient could not be verified. Further, a proportion of patients may have been assessed at multiple centres. Bias from each of these factors would lead to overestimation of referrals. Still, the proportion of OBPI referrals to multidisciplinary centres was 45% at best. Provincial data is difficult to interpret given no centre in the Territories, Saskatchewan, and the Maritimes in the timeframe studied. For referral indicators, only summary data were available from each centre for number by one month, three months and over three months. Finally, quality indicators were generated based on our review and the literature instead of a formal consensus process.

4.7 Conclusions

4.7.1 Implications for Practice

Risk factors agree with the existing literature. Dystocia is the predominant modifiable risk factor, both in prevention and management. OBPI is identified by primary care in at least 1.24 per 1000 live births prior to initial hospital discharge. This study demonstrates the need for timely referral. A maximum of 45% of these identified cases were referred to specialized multidisciplinary centres. Referral by one month allows for

optimized assessment, care, and education. Among referrals, timing was good in 28% (by one month), satisfactory in 38% (by three months), and late in 34% (later than three months).

4.7.2 Implications for Research

While shoulder dystocia and macrosomia are significant risk factors for OBPI, predicting fetal size prior to delivery remains difficult. OBPI incidence is stable over time, despite improvements in perinatal care; future study should continue to focus on modifiable risk factors. Data in large national administrative databases should be further analyzed to generate a predictive model. This study provides the first quality indicators of Canadian OBPI referral. The gap in referral to multidisciplinary care is established with quality indicators at clinically relevant time points. This practice gap should be addressed with knowledge tools to target knowledge, educated referral and practice variation. Interventions should guide the referral process for timing and centre.

Table 4-1: a) OBPI cases by year and province, b) Total newborn records by year and province, c) Annual incidence by year and province, d) Annual national incidence excluding Quebec

a) OBPI Cases

	2004	2005	2006	2007	2008	2009	2010	2011	TOTAL
Newfoundland and Labrador	8	12	6	5	8	6	9	8	62
Prince Edward Island	0	2	0	2	1	2	3	0	10
Nova Scotia	11	5	16	11	8	12	17	15	95
New Brunswick	12	13	11	9	7	9	7	9	77
Quebec	--	--	28	35	30	29	21	22	165
Ontario	192	168	179	162	181	200	174	138	1394
Manitoba	16	9	19	22	22	26	21	17	152
Saskatchewan	9	15	24	18	17	21	26	19	149
Alberta	57	57	55	55	50	65	54	55	448
British Columbia	61	47	51	48	67	49	46	35	404
Territories	2	1	2	2	1	2	1	1	12
TOTAL CANADA	**368**	**329**	**391**	**369**	**392**	**421**	**379**	**319**	**2968**

b) All Newborns

	2004	2005	2006	2007	2008	2009	2010	2011	TOTAL
Newfoundland and Labrador	4492	4490	4592	4571	4900	4935	4788	4447	37215
Prince Edward Island	1365	1278	1415	1404	1397	1419	1368	1418	11064
Nova Scotia	8520	8609	8512	9125	8982	9103	8801	8979	70631
New Brunswick	6830	6967	7065	7332	7468	7468	7380	7171	57681
Quebec	--	--	79951	82757	85539	85610	85304	85490	504651
Ontario	136923	138062	140093	143070	142236	142184	139729	141184	1123481
Manitoba	14115	14487	15018	15564	15858	16150	16087	16134	123413
Saskatchewan	11908	12221	12508	13670	13995	14456	14455	14497	107710
Alberta	40444	41705	45508	48784	49962	50740	49757	50097	376997
British Columbia	39829	40207	41327	43318	43661	43888	42751	42972	337953
Territories	1426	1444	1506	1547	1591	1596	1515	1575	12200
TOTAL CANADA	**265852**	**269470**	**357495**	**371142**	**375589**	**377549**	**371935**	**373964**	**2762996**

c) National Incidence per 1000 births

	2004	2005	2006	2007	2008	2009	2010	2011	TOTAL	Lower 95%CI	Upper 95%CI
Newfoundland and Labrador	1.78	2.67	1.31	1.09	1.63	1.22	1.88	1.80	1.67	1.25	2.08
Prince Edward Island	0.00	1.56	0.00	1.42	0.72	1.41	2.19	0.00	0.90	0.34	1.46
Nova Scotia	1.29	0.58	1.88	1.21	0.89	1.32	1.93	1.67	1.35	1.07	1.62
New Brunswick	1.76	1.87	1.56	1.23	0.94	1.21	0.95	1.26	1.33	1.04	1.63
Quebec	--	--	0.35	0.42	0.35	0.34	0.25	0.26	0.33	0.28	0.38
Ontario	1.40	1.22	1.28	1.13	1.27	1.41	1.25	0.98	1.24	1.18	1.31
Manitoba	1.13	0.62	1.27	1.41	1.39	1.61	1.31	1.05	1.23	1.04	1.43
Saskatchewan	0.76	1.23	1.92	1.32	1.21	1.45	1.80	1.31	1.38	1.16	1.61
Alberta	1.41	1.37	1.21	1.13	1.00	1.28	1.09	1.10	1.19	1.08	1.30
British Columbia	1.53	1.17	1.23	1.11	1.53	1.12	1.08	0.81	1.20	1.08	1.31
Territories	1.40	0.69	1.33	1.29	0.63	1.25	0.66	0.63	0.98	0.43	1.54
TOTAL CANADA	**1.38**	**1.22**	**1.09**	**0.99**	**1.04**	**1.12**	**1.02**	**0.85**	**1.07**	**1.04**	**1.11**

d) National Incidence per 1000 births, excluding Quebec

	2004	2005	2006	2007	2008	2009	2010	2011	TOTAL	Lower 95%CI	Upper 95%CI
CANADA	1.38	1.22	1.31	1.16	1.25	1.34	1.25	1.03	1.24	1.20	1.29

Table 4-2: Odds ratios for OBPI risk factors

Risk factors marked with (*) are determined using only Ontario data.

	Odds Ratio	95% Confidence Interval	
Birth injury to Humerus	115.018	86.737	152.521
Shoulder Dystocia	59.849	55.49	64.549
Fracture of Clavicle	30.959	26.35	36.374
Macrosomia >4500g	12.602	11.305	14.048
Birth Asphyxia*	8.637	5.808	12.845
Heavy for Dates*	7.224	6.198	8.421
Pre-existing Diabetes	5.754	4.711	7.028
Forceps Traction	5.43	4.869	6.056
Episiotomy*	4.359	3.957	4.802
Vacuum Traction	3.483	3.188	3.806
Fetal Asphyxia*	3.46	2.292	5.226
Impaired Glucose Tolerance	2.805	1.59	4.95
Gestational Diabetes	2.277	2.026	2.56
Breech Delivery	2.245	1.412	3.571
Intracranial hemorrhage*	1.253	0.562	2.795
Twin or Multiple Births*	0.446	0.253	0.786
Caesarean Section	0.152	0.129	0.179

Table 4-3: OBPI referrals to Canadian multidisciplinary centres

Province	Center(s)	OBPI Cases	Referrals (proportion of provincial referrals)
Martimes (NL, PE, NS, NB)	Dalhousie	244	*Not available** (0%)
Quebec**	U de Montreal	165	253 (153%)
Ontario	U of Toronto	1394	411 (29%)
	McMaster		139 (10%)
	U of Ottawa***		26 (2%)
	Western		*Awaiting*
	Total ON		**576 (41%)**
Manitoba	U of Manitoba	152	51 (34%)
Saskatchewan	*None*	149	*No center* (0%)
Alberta	U of Alberta	448	103 (23%)
	U of Calgary		85 (19%)
	Total AB		**188 (42%)**
British Columbia	U of British Columbia	404	120 (30%)
Territories (YT, NT, NU)	*None*	12	*No center* (0%)
TOTAL CANADA	**All**	**2968**	**1188 (40%)**

*Surgeon began practice after timeframe
**Cases estimated for 2004 and 2005
***Surgeon began practice in 2008

Table 4-4: Timing of OBPI referral by centre

Center	Referrals	By 1 month (% of refs)	By 3 months* (% of refs)
Dalhousie	*Not available***	*0 (0%)*	*0 (0%)*
U de Montreal	253	9 (4%)	125 (49%)
U of Toronto	411	171 (42%)	297 (72%)
McMaster	139	46 (33%)	93 (67%)
U of Ottawa***	*26*	*5 (19%)*	*10 (38%)*
Western	*Awaiting*	*0 (0%)*	*0 (0%)*
Total ON	**576**	**222 (39%)**	**400 (69%)**
U of Manitoba	51	*Awaiting*	38 (75%)
U of Alberta	103	48 (47%)	84 (82%)
U of Calgary	85	35 (41%)	60 (71%)
Total AB	**188**	**83 (44%)**	**144 (77%)**
U of British Columbia	120	23 (19%)	79 (66%)
TOTAL CANADA	**1188**	**337 (28%)**	**786 (66%)**
*Referrals by 3 months include 1 month data **Surgeon began practice after timeframe ***Surgeon began practice in 2008			

CHAPTER 5: OBSTETRICAL BRACHIAL PLEXUS INJURY: A CLINICAL PRACTICE GUIDELINE

5.1 Abstract

5.1.1 Introduction

The objective of this study is to develop an evidence-based clinical practice guideline for the primary management of OBPI. Four gaps in OBPI care exist: 1) The historic poor use of evidence, 2) Timing of referral to multidisciplinary care, 3) Indications and timing of operative nerve repair, and 4) Distribution of expertise in Canada.

5.1.2 Methods

The consensus group consisted of 12 physicians representing all ten Canadian OBPI centres. Canadian incidence and risk factors were reviewed with a prospective national newborn database, 2004-2012. Data were correlated with consultations at Canadian centres to determine referral patterns. A systematic review of primary management was completed. Based on this evidence, draft recommendations were crafted and distributed to the consensus group. A modified Delphi approach to consensus was used; agreement was defined by RAND criteria.

5.1.3 Results

Incidence was 1.24/1000 births. Risk factors reflected the known literature. Systematic review included 99 articles. Low quality evidence suggests nerve repair reduces

functional impairment in OBPI. Recommendations are: 1) Physically examine newborns for OBPI if upper extremity movement is asymmetric or delivery was complicated by shoulder dystocia, humeral fracture or clavicular fracture; 2) Refer all newborns with OBPI to a multidisciplinary centre by 1 month of age; 3) With referral, provide complete pregnancy and birth history, and physical exam findings (including Horner's syndrome) at birth; 4) Teams at multidisciplinary centres should include: i. A dedicated therapist with experience in the assessment and treatment of OBPI, ii. A peripheral nerve surgeon with experience in microsurgical repair of OBPI; 5) Nonoperative therapy delivered outside of a multidisciplinary centre should be advised by a multidisciplinary team; 6) Offer microsurgical nerve repair: i. For injuries clinically consistent with root avulsion injury, ii. For all other injuries meeting centre-defined operative criteria applied beginning at 3 months of age, 7) For objective outcome assessment, a common data set includes: i. Clinical distribution using Narakas classification at initial multidisciplinary centre assessment, ii. Limb length, Active Movement Scale and Brachial Plexus Outcome Measure when applicable at 1 month, 3 months, 6months, 12 months, 24 months, then annually for the duration of follow-up.

5.1.4 Discussion

Implementation and dissemination of recommendations will guide primary management of OBPI.

5.2 Rationale

OBPI treatment advanced in the 1980s with the application of microsurgical nerve repair to the paediatric population.(30) At present, assessment(22) and rehabilitation therapy(31) are provided at specialized multidisciplinary centres.(19,145,214,218) For infants with residual deficits, numerous operative algorithms,(22,23,25,28,32,33) repair techniques,(14,34–41) and evaluation methods(42) are available. Authors have expressed the need for guidelines addressing primary management of OBPI(20,43) based on the following challenges and gaps in its management: evidence in the literature is weak,(16,17) timing of referral by primary care(18) and surgical indications vary,(23) and expertise is concentrated at academic centres in major cities (Chapter 4).

Considering these gaps, OBPI is a suitable topic for guideline development.(46) A guideline can address critical aspects(46) of a prevalent injury. Further, the guideline may reconcile a divergence of opinion(46) between primary care and specialized healthcare personnel, and provide a more coherent and consistent approach for guardians. Guidelines can address the clinical environment and optimize care by improving knowledge among clinicians, improving educated referral, influencing care processes at tertiary care centres, minimizing practice variation, informing policy, and establishing criteria for evaluation/quality review.(45)

The process of guideline development itself can foster collaboration and cohesion among national specialists.(44) A unified approach improves transparency,(46) with greater likelihood of delivering a consistent messaging to primary care providers and guardians. Engaging opinion leaders may influence implementation with primary care

providers, and health policy in local clinical settings. Lastly, guideline development is often the first stage in a creating a program of research to address previously known and newly identified gaps.(45)

The impetus for this project was from McMaster University's OBPI Clinic. The centre has published a treatment algorithm for the primary surgical management of OBPI.(23) Gaps in management are discussed, summarized as: 1) The historic poor use of evidence, 2) Timing of referral to multidisciplinary care, 3) Indications and timing of operative nerve repair, and 4) Distribution of expertise in Canada.

A clinical practice guideline can help to address each of these gaps. There is a clear opportunity to improve the quality of OBPI care.(219) Management differs between primary care providers and multidisciplinary centres in Canada, and as a result may not be optimized. Timing of referral and surgery are critical in peripheral nerve injuries; the optimal window for operative reconstruction is under three months of age in total plexus and avulsion injury patterns. The evidence base is not optimized,(219) and does not provide direction to support decisions of the clinical community. A synthesis of primary management represents new evidence; applying it to the development of guideline recommendations, a series of more actionable messages would result.(219) Finally, system performance is not optimized;(219) referral quality indicators demonstrate space for improvement.(220)

5.3 Objectives

5.3.1 Objectives

1. To develop an evidence-based clinical practice guideline for the primary management of OBPI.

5.3.2 Questions

To achieve the guideline's goals, the following research questions were used to guide the collection of evidence and data.

5.3.2.1 Primary

1. Among infants with OBPI, what is effect of primary operative management on physical function versus nonoperative management during the first two years of life?

5.3.2.2 Secondary

2. Among infants with identified OBPI, what is the timing of referral to a specialized centre to optimize nonoperative and operative management?

3. Among children undergoing follow-up for OBPI with nonoperative or operative therapy, which outcomes should be collected in a common dataset for multicenter research?

5.3.3 Target Patient Population

Patients with OBPI identified by primary care providers, being considered for referral to a multidisciplinary centre, being considered for management at a multidisciplinary centre, and being followed at a multidisciplinary centre.

5.3.4 Intended Users

Intended users include primary care providers delivering care to infants in the first year of life, and peripheral nerve surgeons, therapists, and other healthcare providers treating residual OBPI impairment.

5.3.5 Interventions to Consider

Guideline development considered facets of primary OBPI management. This included: identification by primary care physicians, referral to multidisciplinary centres, and nonoperative and operative primary management therapy at these centres.

Guideline development excluded prevention, diagnostic investigations (eg. electromyography/nerve conduction studies, computed tomography, magnetic resonance imaging, etc.) and secondary therapy (eg. Botulinum toxin, muscle transfer, osteotomy, etc.).

5.4 Methods

The development of this guideline followed Cancer Care Ontario's Program in Evidence-Based Care framework, the Guideline Development Cycle.(219,221)

5.4.2 Working Group

A working group was established prior to commencement of any portion of the project. The working group consisted of two plastic surgeons with expertise in management of OBPI (one the head of a multidisciplinary OBPI), and a health services researcher with expertise in the science and practice of clinical practice guidelines (Appendix 2).

The working group defined the scope of the project, including review methodology and guideline recommendations. The group's composition was opportunistic; it combined a trainee in both health research methodology and plastic surgery with local supervisors who are experts in peripheral nerve reconstruction and guideline development respectively.

5.4.3 Guideline Consensus Group

Guideline implementation was considered in design of the guideline consensus group,(44) and followed the positional approach.(222) The positional approach identifies personnel with influence over local health policy and resources.(223) By choosing individuals fitting this phenotype, the goal was to enhance communication, dissemination and implementation of the final results with primary care providers, and administration in individual clinical settings. To this end, lead physicians at each Canadian OBPI multidisciplinary centre of excellence were invited to be members of the guideline consensus group. The lead physicians were selected to improve ownership among the

consensus group,(46) and alter culture by forming a network for future research.(44) The working group's clinical expert (JRB) personally contacted each surgeon to participate.

Twelve physicians agreed to participate in guideline development, all surgeons. The result created a Canadian network of OBPI opinion leaders. Each physician individually is a local expert in OBPI in his/her centre, and each contributes to the clinical management, research, and postgraduate resident training in paediatric peripheral nerve injury.

To introduce the project, members of the consensus group members were invited to a group meeting at the 2013 Annual Meeting of the Canadian Society of Plastic Surgeons in Calgary, Alberta. In guideline development, their tasks included: providing feedback on the systematic review of primary management (Chapter 3), approving quality indicators for referral timing analysis (Chapter 4),(46) collecting and providing volume and timing of referrals at their centres (Chapter 4), participating in the formal consensus process to craft, refine, and agree upon recommendations for the clinical practice guideline (Chapter 5), and establish a common data set for future OBPI research.

5.4.4 Sources of Evidence

Four sources of evidence and information were used to inform the recommendations: identification of existing guidelines for the management of OBPI, systematic review and meta-analysis of primary management of OBPI (Chapter 3), epidemiological review of Canadian incidence, risk factors and referral patterns (Chapter

4), systematic review of evaluation methods for OBPI,(42) and environmental scan of referral algorithms and clinical pathways.

5.4.4.1 Identification of existing guidelines

Recognized databases were searched for existing clinical practice guidelines. OBPI is referred to by many terms,(224) with specific variation in the leading (eg. neonatal or paediatric instead of obstetrical) and end (eg. palsy instead of injury) terms. For sensitivity, only the term "brachial plexus" was used in searches. The following databases were searched on November 1, 2012, and updated as of February 15, 2014:

- National Guideline Clearinghouse (Results = 20)
- CMA Infobase (2)
- NICE - National Institute of Clinical Excellence (7)
- NICE Evidence (37)
- SIGN - Scottish Intercollegiate Guidelines Network (0)
- GIN - Guidelines International Network (0)
- BMJ Clinical Evidence (2)
- Agency for Healthcare Research and Quality (42)
- American Society of Plastic Surgeons (0)
- Society of Obstetricians and Gynaecologists of Canada (0)
- Royal Australian and New Zealand College of Obstetricians and Gynaecologists (2)
- RCOG Guidelines (0)
- NHMRC National Health and Medical Research Council (0)
- NHMRC Clinical Practice Guidelines Portal (0)
- National Library of Medicine - Health Services/Technology Assessment Text (23)

Results of the guideline search are discussed in this section since this step dictated the need for a full literature review. In total, 135 results were reviewed by a single reviewer (CJC). One result was relevant, Van Aerde et al., a "position statement and practice point" from the Canadian Paediatric Society.(225) Van Aerde et al.'s conclusions for primary management were based on a descriptive review of the literature.(195) Recommendations do not address the first question by the working group, the specific

role and timing of operative therapy, and did not utilize a current, optimized synthesis of the OBPI literature in development.(219) Further, Van Aerde et al.'s recommendations do not adequately address the objectives stated by the working group,(219) following the previous operative management algorithm.(23) Given these factors, an update of the evidentiary base for primary OBPI management, and the formulation of new recommendations were indicated by the working group.

5.4.4.2 Systematic review and meta-analysis of primary management

A systematic review investigating primary nerve repair compared to nonoperative management for physical function in OBPI was performed, see **Chapter 3: Primary management of obstetrical brachial plexus injury (OBPI): a systematic review and meta-analysis**.

5.4.4.3 Review of Canadian epidemiology

An identified gap is delayed referral of identified OBPI cases to multidisciplinary care.(23) To avoid bias and increase precision in estimates, the consensus group members recommended a formal analysis of Canadian epidemiology. A review of Canadian incidence, risk factors, and multidisciplinary referral volume and timing was performed, see **Chapter 4: Obstetrical brachial plexus injury: Incidence, risk factors and referral patterns in Canada**.

5.4.4.4 Systematic review of outcome assessment

To inform the selection of outcome measures for multicentre research, a focused search for systematic reviews investigating OBPI outcome measures was performed by a single reviewer (CJC). Only records meeting each of the following criteria were included:

- Systematic review
- Published in peer-reviewed journals as full reports
- Reviewed outcome measures
- Included OBPI patients
- English language only
- Published in the last five years (since 2009)

The same sensitive electronic search strategy from the systematic review was used (Appendix 1), executed February 15, 2014: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 2009 to Present, Ovid MEDLINE Daily Update February 15, 2014, EMBASE 2009 to 2014 Week 6 and reviews in the Cochrane Library 2014, Issue 1 (Appendix 1).

A single reviewer (CJC) screened titles and abstracts. Screening was highly sensitive; any potentially relevant references were included in full-text review. Articles were retrieved and evaluated by the same reviewer. Systematic reviews were assessed for quality using the AMSTAR tool.(226)

5.4.4.5 Environmental scan

Given the poor, scare evidence, an environmental scan was also indicated. A search was performed to provide an estimate of referral processes in other jurisdictions, and inform recommendations.(219) Relevant professional organizations were searched for applicable documents (Section 5.4.4.1). An untargeted web search using Google's

search engine was completed November 1, 2012 and updated February 15, 2014. The following terms were queried:

- "brachial plexus"
- referral
- guidelines

A single reviewer (CJC) browsed links in an unstructured manner. Multidisciplinary clinic websites were reviewed for referral process from primary care, timing and specific criteria.

5.4.7 Recommendation Development

5.4.7.1 Preliminary guideline recommendation topic list

The working group lead (CJC) generated a topic list for recommendations,(227) with consideration of opportunities for quality improvement as defined in Eden et al.(227,228) The topic list was discussed and edited with the working group clinical expert (JRB).

5.4.7.2 Initial formulation of recommendations

Evidence was assigned to each topic by the working group lead (CJC). For primary management, functional impairment was considered the most important outcome measure, balanced against adverse events. For referral to a multidisciplinary centre, guardian preference was considered.(10,20,21) The working group identified a guardian and surgeon preference to establish a conservative timing for referral. Referring a proportion of children earlier than necessary to maximize education, therapy, and

operative planning is preferred versus late or missed referral in a proportion with impairment. For outcome measures, validated and disease-specific outcome measures were considered important. Quality of evidence, bias, and uncertainty were considered in all outcomes.(229)

Recommendations were based on best available evidence. Guideline recommendations focused exclusively on the clinical perspective. The clinical setting of each Canadian multidisciplinary centre differs with provincial health care systems, and catchment area. While implementation will ultimately necessitate consideration of resources, this will need to be tailored to each jurisdiction(229)

The working group lead (CJC) drafted recommendations. Wording was deliberate to be actionable, concise, informative, evidence-based, and patient-oriented.(229) Recommendations were discussed and edited with the working group clinical (JRB) and methodological (MCB) experts.

5.4.8 Formal Consensus

A formal consensus process was selected given the limited and poor quality literature.(219,230) To improve ownership(46) of the recommendations among the specialists and to create a unified and transparent(230) message to primary care providers and guardians,(46) physicians at each Canadian multidisciplinary centre participated in the consensus process.

An electronic modified Delphi approach(231) was selected for its transparent, explicit and structured methodology.(219,232,233) The process(219) is outlined in Figure

5-1. Recommendations drafted by the working group were distributed to the guideline consensus group members in an electronic survey. Key evidence summaries were included with each recommendation: the systematic review of primary management, analysis of Canadian epidemiology, and systematic review of evaluation methods. Each consensus group member rated his/her agreement using a nine-point Likert scale(234) ranging from "strongly agree" to "strongly disagree" (Figure 5-2). The opportunity to provide written feedback was available for each recommendation. Weekly email reminders were sent to nonresponders.

The numerical threshold for consensus to "support" and "reject" recommendations were defined a priori following RAND criteria. The working group lead (CJC) collected and analyzed responses confidentially; numerical agreement scores were analyzed and written feedback was reviewed and categorized by themes. The working group modified recommendations not meeting criteria for support or rejection based on the consensus group's feedback. Modified recommendations were again distributed to the consensus group for rating and review.

Numerical ratings for each recommendation were classified into consensus to "support" and "reject", with those in between being "uncertain". This was determined as per the RAND/UCLA Appropriateness Method User's Manual,(234) by calculating each recommendation's median score and dispersion. Consensus was defined based on a group size of 12 OBPI physicians.(234) A median of 7-9 with 3 or fewer ratings outside of the 7-9 range was defined as consensus to support the recommendation. A median of 1-3 and 3 or fewer ratings outside of the 1-3 range was defined as consensus to reject the

recommendation. Further, 4 or more members rating in both the 1-3 and 7-9 ranges was defined as consensus to reject the recommendation. Other combinations were defined as uncertain, indicating the need for modification.

Qualifying statements were added to recommendations based on consensus group feedback. This allowed for necessary clarification and contextualization to be provided even in cases when consensus was obtained according the a priori criteria. Qualifying statements provide detail for the more pithy recommendation wording. The final document was distributed to members of the consensus group for information and for any final feedback.

The modified Delphi approach accommodated the geographic distribution of consensus group.(235) Further, it permitted individual feedback, anonymous from the remainder of the consensus group. Among the current group of Canadian OBPI specialists, many were fellowship and/or residency trained under another Canadian specialist. This approach prevented the consensus process from being dominated by a minority of senior or vocal participants.(236)

5.5 Results

5.5.1 Sources of Evidence

5.5.1.1 Identification of existing guidelines

Results of the search for existing guidelines was discussed in Section 5.4.4.1. The failure to identify an existing guideline motivated the subsequent original research.

5.5.1.2 Review of primary management

A systematic review investigating primary nerve repair compared to nonoperative management for physical function in OBPI is reported, see **Chapter 3: Primary management of obstetrical brachial plexus injury (OBPI): a systematic review and meta-analysis**.

5.5.1.3 Review of Canadian epidemiology

An analysis of Canadian epidemiology and multidisciplinary referral is reported, see **Chapter 4: Obstetrical brachial plexus injury: Incidence, risk factors and referral patterns in Canada**.

5.5.1.4 Review of outcome assessment

The search strategy resulted in 397 unique citations: MEDLINE (67), EMBASE (298), Cochrane Library (82). Nine articles were selected for full text review.(42,109,214,237–242) Six were excluded for not analyzing outcome measures.(214,237,239–242) Three articles were eligible.(42,109,238) AMSTAR criteria for each article are summarized in Table 5-1. Overall, few outcome assessment tools are validated and reliable in OBPI. Each review emphasized the need for robust evaluation addressing each domain of The World Health Organization's International Classification of Function, Disability and Health (ICF);(243) a global classification of health, characterizing function and disability. Using the ICF allows for a structured and

universally consistent health assessment. The overall ICF classification in youth is divided into domains: Body Functions and Structures, Activity and Participation and Environmental Factors. ICF Core Sets aim to assess specific diseases with the minimum necessary categories. No OBPI Core Set is established for OBPI, though one in development.(244) No existing single tool addresses all domains.

Ho et al.(109) reviewed outcomes for development of the Brachial Plexus Outcome Measure (BPOM). They included 46 articles, classifying with respect to ICF, and determining essential upper limb movements. They found existing outcomes primarily address ICF domains of body functions and structures. Fewer address activity, and participation. For those that do, activity or participation deficits specific to OBPI impairment are not identified. The BPOM was rationalized to provide disease-specific activity and participation outcome measure for OBPI with internal consistency and construct validity reported. The BPOM complements the AMS. In contrast to other tools, it is practical to administer and score, is OBPI specific, and evaluates the complete upper extremity.

Bialocerkowski et al.(238) analyzed 33 outcome measures for psychometric properties. Outcomes were again classified by ICF; 22 evaluate body function, 10 activities and participation, and 1 quality of life. Twelve addressed psychometric properties. Many measures were not analyzed for disease-specific reliability and validity. The review concluded outcomes with the most robust psychometric properties were the Active Movement Scale,(111) the Assisting Hand Assessment,(245) the Pediatric Evaluation of Disability Index (PEDI),(108) and the Pediatric Outcomes Data Collection

Instrument (PODCI).(246) Ho et al.(109) addressed the AHA, PEDI, and PODCI as not qualitatively assessing disease-specific outcome or helping discriminate intervention selection for joint levels. Further, using the AHA requires impractical video scoring, and the PEDI only detects activity limitations in OBPI hand impairment.(109) Bialocerkowski et al.(238) noted the BPOM is new, and has only undergone preliminary psychometric evaluation.

Chang et al.(42) identified 126 evaluation methods; "*65 physical assessment methods, 6 different classification methods, 41 reported functional outcome evaluations, and 14 methods for diagnostic evaluation*". Evaluation methods were again interpreted by ICF classification. Narakas classification(112,182) was appreciably the most common classification system used, though reliability and validity have not been formally established, and it addresses only the ICF body function and structures domain. Assessment tools similarly favoured body function and structures. Only the Active Movement Scale (AMS), Toronto Scale Score (TSS), Mallet Scale, AHA, and PODCI were reported as validated for OBPI. The review suggested assessment addressing all ICF domains, though agreement is lacking in evaluating activity and participation.

The working group evaluated the results of review of outcome assessment. In addition to the identified ICF domains, the clinical expert (JRB) proposed an indication of upper extremity growth as a physiologic measure: limb length and circumference.(7) Limb length(247) and circumference(248) discrepancies are established OBPI sequelae. Growth discrepancy is limited with nerve repair, and correlates with impairment.(249) Measurements are reliable, and discrepancies are detected as early as one month in severe

lesions.(7) Further, impaired muscle growth is established in animal models;(250,251) discrepancies are worsened with more severe lesions and improved with repair in a critical developmental window.

Timing of outcome assessment was not discussed in reviews. From our systematic review of primary management, outcomes were measured until at least two years of age for nonoperative management, or two years following operative management (Chapter 3).

5.5.1.5 Environmental scan

Environmental scan identified seven documents advising referral for identified OBPI to specialty care.(252–258) Specialty care included therapists and/or surgeons with identified OBPI expertise. Each document was a clinical pathway or care algorithm.

For five documents,(252–256) referral timing could be differentiated between "severe" (ie. total plexus) injury and "other" OBPI (ie. upper plexus).(252,255) In one case(253) only "severe" referral was advised because the pathway was targeted at therapists already treating nonoperative cases. For severe injury, referral was suggested: immediately,(253) urgently,(255) at 2-4 weeks,(252) at 6 weeks,(254) and at 8 weeks.(256) For other OBPI (ie. upper plexus), referral was suggested: as soon as fracture is ruled out,(256) at 6 weeks,(254) and at 2 months. In the two documents where OBPI severity could not be stratified, referral was advised at 1-2 weeks (in NICU if possible)(257) and within 1 month.(258) One document advised immediate paediatric referral for suspected OBPI in newborns delivered at home.(256)

5.5.2 Recommendation Domains

The preliminary topic list included:

- Identification of OBPI by primary care
- Timing of referral to a multidisciplinary centre
- Information to communicate between primary care (diagnosis), multidisciplinary care (specialized therapy) and primary care (follow-up)
- Personnel at multidisciplinary centres
- Timing of operative therapy
- Common dataset elements for national multicenter research

5.5.3 Formal Consensus

The working group drafted seven recommendations addressing the topic list; three recommendations were composed of two subparts. Draft recommendations were distributed in an electronic questionnaire to the consensus group. All members responded; time range 1-25 days. Responses and feedback are summarized in Table 5-2. Based on a priori criteria, consensus was established with the first round of review. The consensus group supported all recommendations. The median score was greater or equal to 7 for all recommendations with 0 or 1 scores outside the 7-9 range (Table 5-2). Ten members of the consensus group completed the optional post-questionnaire feedback, rating their experience with the original research on the same nine-point Likert scale (Figure 5-2):(234)

- I read the original research completely: **Mean 7.0, Range 3-9**
- The original research is objective: **Mean 7.5, Range 6-9**
- The original research is informative: **Mean 7.5, Range 7-9**
- The original research influenced my agreement ratings: **Mean 5.8, Range 3-8**

The working group drafted qualifying statements based on consensus group feedback. Recommendations and qualifying statements were electronically distributed to the consensus group; no member disapproved or provided additional feedback.

5.5.4 Review

The working group reviewed the final recommendations and evidentiary base. No other internal or external review process was specified a priori. Given that recommendations were established by a formal consensus process of key stakeholders in Canada, external review is not appropriate and would be redundant.(219)

5.5.4 Next Steps

The consensus group has established a network, "the Canadian OBPI Working Group". As a first step in addressing gaps in management, the focus of this guideline was primary management and referral. This was seen as critical first step as the team of surgeons across Canada had not previously collaborated. The next version will extend the practice guideline to include recommendations, and evidence relevant to all providers involved in OBPI care: therapists, primary care providers, and secondary specialists. The multidisciplinary revision is expected in two years.

5.6 Recommendations

5.6.1 Recommendation 1

Physically examine newborns for OBPI if upper extremity movement is asymmetric or delivery was complicated by shoulder dystocia, humeral fracture or clavicular fracture.

5.6.1.1 Qualifying Statements

A primary care physician with experience in newborn assessment should perform a focused physical examination on newborns with an identified deficit or risk factor.

5.6.1.2 Key Evidence

- From our review of Canadian epidemiology, OBPI was identified in 1.24 per 1000 newborns. From our systematic review of primary management, pooled incidence in demographic samples was 2.1 per 1000 births (95% CI 1.6-2.6).
- From our review of Canadian epidemiology, risk factors with the highest odds ratios were "birth injury to humerus" OR=115.0 (95% CI 86.7-152.5), "shoulder dystocia" OR=59.8 (95% CI 55.5-64.5) and "fracture of clavicle" OR=31.0 (95% CI 26.4-36.4).
- Foad et al.(3) utilized a sample of all United States paediatric discharges, including 17,334 OBPI. Shoulder dystocia had a 100 times greater risk for injury. Forty-six percent of OBPI cases had one or more identified risk factors.
- In Canada's healthcare system, referrals to specialty physicians (ie. OBPI multidisciplinary centres) are generated by other physicians. A primary care physician with experience in newborn assessment should examine children with asymmetric upper extremity movements to detect OBPI, comorbidities and possible alternate diagnosis for appropriate management, including referral.

5.6.2 Recommendation 2

Refer all newborns with OBPI to a multidisciplinary centre by 1 month of age.

5.6.2.1 Qualifying Statements

A proportion of newborns will completely recover within days of birth and do not necessitate referral to a multidisciplinary centre. Newborns with complete recovery as assessed by primary care providers experienced in the assessment of musculoskeletal and neurological deficits do not necessitate referral.

5.6.2.2 Key Evidence

- The selection of one month was informed by environmental scan (Section 5.5.1.5), practice patterns,(22,23) Malessy et al.'s assessment algorithm,(18) and the previous Canadian position statement.(195)
- Prior to the review of Canadian epidemiology, the consensus group approved one month as a quality indicator of "good" referral timing.
- Early referral to a multidisciplinary centre permits guardian education,(21) early treatment by specialized therapists,(8,22) serial assessment for recovery, and appropriate operative assessment.(18)
- Guardians prefer early referral to a multidisciplinary centre.(10,20,21)

- Neuropraxic injuries recover rapidly, and infants are substantially to completely recovered by one month.(22,23,25,195) From our review, 35% of patients (95% CI 23-48%) are in this group.
- Primary care providers may underestimate residual impairment in OBPI. From our review of primary management, nonoperative management of OBPI in demographic populations results in functional impairment in 18% (95% CI 14-23%). Only three reports assess outcomes with physical scales; the remainder rely on subjective assessment. This reflects traditional reports of OBPI from primary care, reporting transient injury without sequelae.(19,61,62) In contrast, full recovery occurs in 73% (95% CI 64-81) of patients from demographic samples. "Full recovery" itself is likely overestimated.(6) Interpreted inversely, the author-defined incidence of any residual impairment is 27% (19-36%). This proportion demonstrates at least 19-36% of OBPI cases have an uncharacterized, unidentified residual impairment.
- A systematic review by Pondaag et al.(6) concluded OBPI prognosis is worse than identified in the literature and predicted in practice.

5.6.3 Recommendation 3

With referral, provide complete pregnancy and birth history, and physical exam findings (including Horner's syndrome) at birth.

5.6.3.1 Qualifying Statements

Clinical records should indicate risk factors, severity of injury, and course of recovery. While clinical records are important, they are not necessary; do not delay referral to a multidisciplinary centre to obtain records.

5.6.3.2 Key Evidence

- No study identified analyzed the impact of referral information or communication on outcome.
- Given the absence of a gold-standard baseline investigation,(5) serial examination over time is required to determine severity of OBPI. Clinical records may provide an estimate of initial severity and progression of recovery.
- Discussion of risk factors contributes to guardian education,(21) especially for future pregnancies.(144)
- Clinical root level involvement (eg. presence of hand paralysis) and Horner's syndrome are discerning characteristics in Narakas classification(112) for baseline injury classification (see Recommendation 7).

5.6.4 Recommendation 4

Teams at multidisciplinary centres should include:

i. A dedicated therapist with experience in the assessment and treatment of OBPI

ii. A peripheral nerve surgeon with experience in microsurgical repair of OBPI

5.6.4.1 Qualifying Statements

Teams at multidisciplinary centres are responsible for the assessment, treatment, rehabilitation and education of children with OBPI and their parents/guardians. Teams should include the personnel necessary to deliver the highest level of treatment available in Canada. The recommendation does not pertain to healthcare providers involved in diagnostic investigations or secondary treatment. A therapist is a physio- or occupational therapist, or equivalent. Ideally the therapist will have pediatric experience and/or be mentored to develop skills to manage OBPI patients. A peripheral nerve surgeon is a plastic, neuro- or orthopedic surgeon, or equivalent. The peripheral nerve surgeon will have the training, experience and infrastructure to perform microsurgical nerve reconstruction procedures on pediatric patients.

5.6.4.2 Key Evidence

- No study identified analyzed the impact of multidisciplinary teams or their included disciplines on OBPI outcomes.
- Our review of primary management pooled all nonoperative management, including natural history; outcomes did not analyze specific nonoperative therapy interventions or protocols. Descriptions of nonoperative management protocols were poor. The only reliable factor was involvement of a therapist in management. Among 65 studies with patients treated by specialists, the care team was multidisciplinary in 43.

- Two previous systematic reviews(55,79) addressed nonoperative interventions excluding natural history. Each review highlighted the importance of therapists delivering nonoperative treatment,(24,55) and suggested all infants be assessed by a specialized therapist,(79) for management and parent/guardian education.(10) Nonoperative treatments and therapy protocols were only descriptively reviewed in these prior reviews; details of interventions were poor prohibiting replication,(55) and insufficient evidence exists to support specific treatment recommendations beyond therapist referral itself.(55,79)
- Primary care providers likely underestimate residual impairment in OBPI (see Recommendation 2).
- A peripheral nerve surgeon should have the experience and resources to perform microsurgical nerve repair for OBPI (see Recommendation 6).

5.6.5 Recommendation 5

Nonoperative therapy delivered outside of a multidisciplinary centre should be advised by a multidisciplinary team.

5.6.5.1 Qualifying Statements

None

5.6.5.2 Key Evidence

- No study identified analyzed the impact of nonoperative therapy delivered, or supervised by a specialized multidisciplinary centre versus in the community.
- Community providers may not have the expertise to recognize and characterize residual impairment. Ongoing communication between multidisciplinary and community providers may identify patient issues throughout the child's growth and development, and expedite specialized assessment.
- Primary care providers likely underestimate residual impairment in OBPI (see Recommendation 2).

5.6.6 Recommendation 6

Offer microsurgical nerve repair:

i. For injuries clinically consistent with root avulsion injury.

ii. For all other injuries meeting centre-defined operative criteria applied beginning at 3 months of age.

5.6.6.1 Qualifying Statements

Total plexus injuries with clinical evidence consistent with T1 root avulsion (eg. Horner's syndrome) should be offered nerve repair as soon as the injury pattern is apparent and the child is fit for the procedure.

5.6.6.2 Key Evidence

- Primary operative management of OBPI is associated with lower risk of functional impairment versus nonoperative management of similar patients.
- From our review of primary management, pooled analysis of 222 patients from nine cohort studies shows nerve repair reduces impairment; RR 0.58, 95% CI 0.43-0.79, $p<0.001$. This outcome may underestimate the effectiveness of primary nerve repair. Results are consistent in analysis of case series, RR 0.39, 95% CI 0.33-0.45.
- Avulsion injuries are the most severe; these injuries are worse than the severity represented by our pooled analysis. The nerve root is physically separated from the motor cell body within the spinal cord. No motor spontaneous recovery is expected.(8)
- Mortality and major adverse events are not common risks of modern microsurgical nerve repair. Adverse events were reported in 19 series of operative management in our review. No deaths were reported. Major events occurred in 1.5% of cases.

5.6.7 Recommendation 7

For objective outcome collection, a common data set includes:

i. Clinical distribution using Narakas classification at initial multidisciplinary centre assessment.

ii. Limb length (Bain, 2012), Active Movement Scale (AMS) (Curtis, 2002) and Brachial Plexus Outcome Measure (BPOM) when age applicable (Ho,

2012) at 1 month, 3 months, 6 months, 12 months and 24 months of age, then annually for the duration of follow-up.

5.6.7.1 Qualifying Statements

The common data set provides consistent baseline stratification and outcome measurement, facilitating multicentre research. Data set outcomes are not operative indications. Alternatively to Narakas classification, injury distribution can be classified by involved nerve roots and evidence of Horner's syndrome. For consistency, each outcome should be measured as defined in the primary literature (eg. limb length to nearest 0.5cm).

5.6.7.2 Key Evidence

- For injury baseline classification, Narakas classification(112,182) is by far the most common classification system used, though reliability and validity are not formally established, and modifications have been suggested.(182)
- Three systematic reviews(42,109,238) suggested assessing OBPI using the ICF domains. An ICF Core Set is currently lacking.(244)
- Active Movement Scale(111) is validated in OBPI with robust psychometric properties. It measures ICF Body Functions and Structure.
- The Brachial Plexus Outcome Measure(109) is a disease-specific functional assessment tool with excellent construct validity. It complements the AMS. Psychometric evaluation and analysis of evaluative validity are pending. In contrast to other tools, it is practical to administer and score, and evaluates the

complete upper extremity. It measures ICF Activity and Participation in the context of a child's own environment.

- Physiologically, limb length and circumference(7) are reliable, and discrepancies are detected as early as one month in severe lesions. Growth discrepancy is limited with nerve repair, and correlates with impairment.(249)
- Timing of outcome assessment was not discussed in reviews. From our systematic review of primary management, outcomes were measured until at least two years of age for nonoperative management, or two years following operative management.

5.7 Discussion

This is the first formal clinical practice guideline for the primary management of OBPI. Recommendations include primary operative and nonoperative management, referral to multidisciplinary centres, and outcome assessment for children with OBPI in Canada. This guideline can contribute to improving knowledge among providers, improving educated referral, minimizing practice variation, influencing care processes at multidisciplinary centres, informing policy and establishing criteria for evaluation/quality review.

5.7.1 Historic Perspective

The approach to OBPI management was transformed in the 1980s(30,112) with microsurgery in the paediatric population.(27,60) The original literature was composed of case series and small cohort studies investigating novel nerve repair techniques and operative indications.(30,48,70,136) However, a divergence of opinion(46) remained between paediatric primary care providers and specialized healthcare personnel. Prognosis for spontaneous recovery was overestimated by primary care.(6)

Currently, the major points of contention among OBPI surgeons include operative timing, indications and procedure.(8,71) Research has addressed these topics without evidence to definitively support the broader and simpler questions in OBPI management; are nerve repair and nonoperative therapy effective?(55,80) Evidence is lacking to guide nonoperative interventions and therapy protocols.(55,79) No previous synthesis addressed the comparative studies of operative versus nonoperative management.

Clinical and research factors contribute to the difference of opinion(46) between primary care and specialists. This leads to variable and suboptimal referral patterns. Nerve injuries are variable; prognosis and indicated treatment differ significantly with severity. In neuropraxic injuries, complete recovery is expected spontaneously;(23) in neurotmesis, the axon and connective tissue are completely disrupted and no recovery potential exists without nerve repair.(8) No gold standard investigation exists to differentiate injury severity, and clinical interpretation is complex.(18) Primary care providers for newborns lack the familiarity and expertise to educate guardians and monitor recovery for OBPI.(19,20) Combined with the dearth of conclusive evidence,

historic attitudes remain in primary care; “permanent sequelae are rare”,(19,61,62) and operative repair is “unwarranted”.(63)

5.7.2 Recommendation Context

Timing of referral to a multidisciplinary centre is patient/guardian important,(20) providing early coordinated assessment by specialized physicians and therapists. Recommendations 1-3 address primary care awareness of OBPI, and inform clinically relevant referral. The one month time point is conservative; a proportion of OBPI is neuropraxic and may resolve spontaneously by this time (35%, 95% CI 23-48%). However, our own review of primary management (Chapter 3), and other reviews(6) indicated recovery is overestimated and residual impairment is not recognized. While an identified algorithm endorsed early referral of severe injuries and potential surgical candidates,(18) it relied on performance and interpretation of specialized EMG beyond primary care expertise. It is feasible a referral system could be overseen by multidisciplinary centres with expertise to interpret clinical history and the diagnostic investigations completed at satellite centres; timing of consultation with physicians and therapists could then be triaged appropriately. No such system has been developed, but it could address the geographic distribution of OBPI specialists in Canada.

Nonoperative and operative therapies are patient and surgeon-important, limiting functional impairment. Recommendations 4-6 reflect the personnel and management to provide best evidence-based OBPI care. Evidence is lacking to recommend specific nonoperative intervention or therapy protocols. Our review demonstrated the superiority

of nerve repair meeting author-defined criteria beginning at three months of age versus nonoperative management. Recommendations do not differentiate OBPI severity beyond avulsion, or identify the best surgical algorithm and nerve repair procedure.(8,71) Algorithms for nerve repair typically include multiple indications for repair based on serial examination findings and assessment tool scores.(22,23) Further evidence is required to guide specifics of nonoperative and operative protocols.

To inform specific therapy recommendations, multicentre study is required to achieve sufficient sample size given the range of OBPI patterns and nerve repair options available.(16) In its design and execution, this guideline has formed a network of opinion leaders with representatives from every Canadian multidisciplinary centre.(44) These centres have been involved in the care of 1188 OBPI cases in an eight-year span (Chapter 4), with two centres not active throughout the time period. Moving forward, an engaged network of opinion leaders and consistent outcome assessment will facilitate comparison of the multiple interventions and algorithms already practiced at Canadian centres.(23,24,29,40,259)

5.7.1 Strengths

This guideline has a number of strengths in its design and execution. Methodology was rigorous and specified a priori, following an established framework.(219) A positional approach(222) was used to establish consensus group, composed of the lead physicians at each of Canada's ten multidisciplinary OBPI centres. The group was established prior to completion of the evidentiary base to inform design, and share

ownership.(46) Implementation and dissemination began in guideline design;(44) opinion leaders were chosen for their influence on local health policy and resources, and communication with their catchments of primary care providers.(223)

The poor evidence base was identified as a gap in OBPI care; a systematic review of primary management and review of Canadian epidemiology were designed and executed to synthesize the literature and establish the burden of OBPI in Canada. Further, a thorough review of guideline databases and environmental scan were completed to inform recommendations with poor evidence base. Clear connections were established between the evidence identified and recommendations. Recommendations themselves address broad, system-level questions in the management of common birth morbidity. They provide clinically relevant guidance to an identified divergence of opinion between primary care and specialists.(46) Further, a baseline for system performance is established with quality indicators for referral.

A formal consensus process was selected given the limited and poor quality evidence base.(219,230) The electronic modified Delphi approach(231) is transparent and structured.(219,232,233) The process accommodated the geographic distribution of consensus group.(235) Anonymity prevented the consensus process from being dominated by a minority of senior participants.(236)

5.7.2 Limitations

This guideline has limitations. In selecting the consensus group, a positional approach identified lead physicians at each Canadian multidisciplinary centre. These

physicians were all surgeons; all members of the group represented a single discipline. Conflicts of interest are not formally declared. Guidelines produced by a single discipline are more likely biased.(227) Future updates to this guideline will be multidisciplinary, involving therapists, primary care physicians and other specialists involved with secondary OBPI management. Further, one individual was included in both the working group as a clinical expert, and the consensus group as the lead OBPI physician at McMaster University. This had minimal bias on final recommendations; if his responses were all changed to "disagree" (1 on the 9-point scale) all recommendations would still meet criteria for support.

In generating recommendations, an estimation of cost was not available in the literature. Recommendations were based on best clinical evidence. Further, the working group did not formally solicit patient/guardian preferences. Recommendations instead relied on patient preferences for referral, education and management from in the literature.(18,20,21,142)

Finally, in the recommendations themselves, statement 7b included three outcome measures. Each outcome should have been listed individually, to elicit individual consensus ratings and feedback. This did not impact final recommendations; only one member disagreed with this composite recommendation. Finally, the three outcome measures endorsed by the consensus group are authored by members of the consensus group,(7,109,111) and one in the working group.(7) The AMS and BPOM were endorsed in previous reviews(42,238) and were selected for being disease-specific and validated with complementary ICF domains. Limb growth was consistently reported in the

clinical,(247–249) and basic science literature.(250,251) The report by Bain et al.(7) was selected for its reliable measurement description.

Figure 5-1: Summary of the modified Delphi approach, from (219)

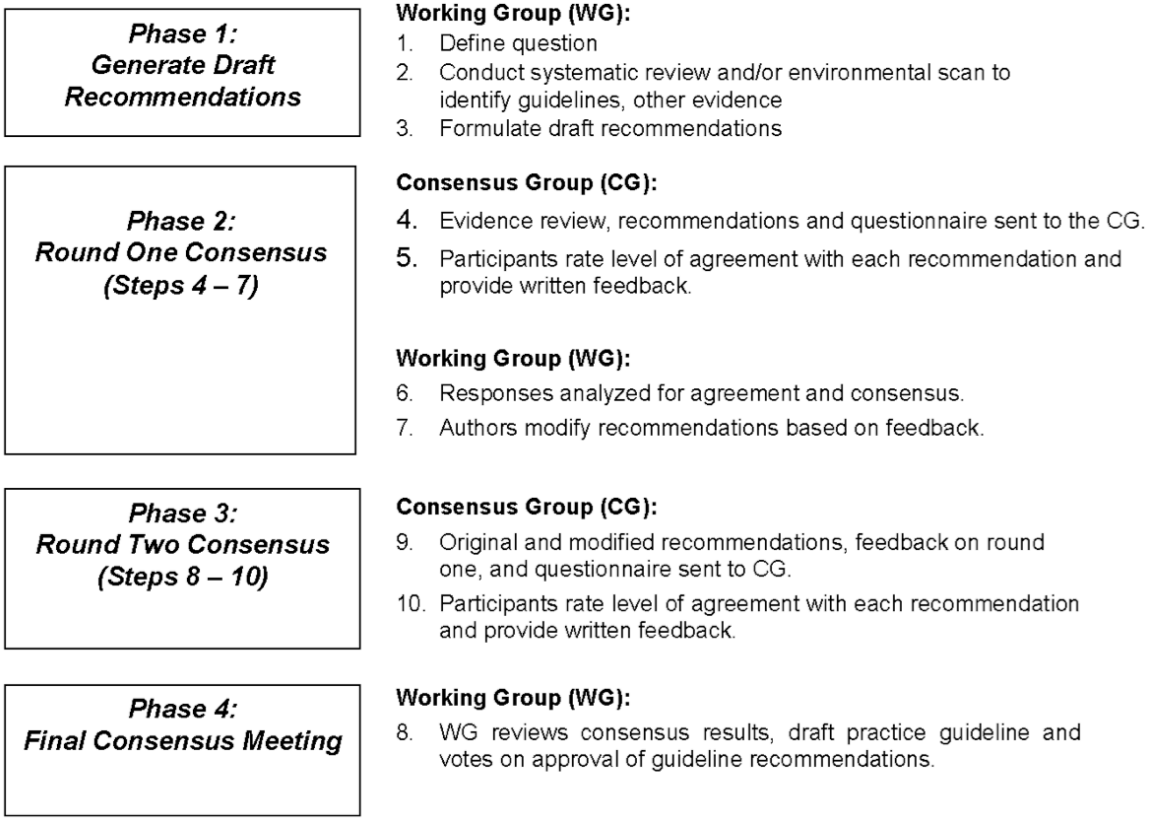


Figure 5-2: Sample recommendation agreement rating, nine-point

Table 5-1: AMSTAR criteria for systematic review of OBPI outcomes

	AMSTAR CRITERIA										
	"A priori" design	Duplicate selection and data extraction	Comprehensive lit search	Status of publication	List of studies	Included Characteristics	Scientific quality	Scientific quality in conclusions	Methods to combine studies	Publication bias assessed	Conflict of interest included
Ho 2012	Can't Answer	No	Yes	No	Can't Answer	No	Yes	Yes	Yes	No	No
Bialocerkowski 2013	Can't Answer	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No
Chang 2013	Can't Answer	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes

Table 5-2: Summary of consensus group responses to draft recommendations

	Responses (n=12)									Median	Feedback
	1	2	3	4	5	6	7	8	9		
Rec 1					1			1	10	9	Not **all** children born in hospital and/or with physicians, primary care to examine and as **gatekeeper** for referral
Rec 2							2	2	8	9	Small proportion of cases recover before discharge
Rec 3			1				5		6	8	Clinical records are **important and useful** but not **necessary**
Rec 4a							1	2	9	9	Provide definition of therapist
Rec 4b								1	11	9	Provide definition of surgeon
Rec 5							5	2	5	8	Communication **and/or** follow-up
Rec 6a								4	8	9	Clarify total plexus + T1 avulsion
Rec 6b							2	3	7	9	None
Rec 7a			1				7	1	3	7	Root levels an alternative to formal Narakas
Rec 7b			1				4	2	5	8	Outcomes are **not** a substitute for operative indications, limb length to nearest 0.5cm as in original report

CHAPTER 6: CONCLUSIONS

6.1 Overview

This chapter summarizes the findings of each component of this thesis, and discusses this thesis as a whole. Future direction for the newly established Canadian OBPI Working Group is suggested.

6.2 Systematic Review of Primary Management

Chapter 3 described a systematic review and meta-analysis of primary management of OBPI. In guideline development, this was performed to address the gap in the use of evidence in OBPI, and inform guideline recommendations pertaining to nonoperative and operative management.

It is the first systematic review to have directly analyzed nonoperative versus operative OBPI management. The review used a rigorous methodology to synthesize all available evidence from randomized controlled trials, observational studies and case series (n>9). Each step of study selection, quality assessment and data abstraction was performed in duplicate. Data were pooled to prevent confounding. Similar patients receiving operative and nonoperative management were compared. Objective definitions of functional impairment were applied as defined by the original assessment scale literature. Analysis accounted for study methodology and individual outcome quality. The

primary outcome was functional impairment; secondary outcomes included full recovery and adverse events.

Among cohort studies directly comparing nerve repair and nonoperative management in similar patients, nerve repair significantly reduces functional impairment RR 0.58, 95%CI 0.43-0.79, $p<0.001$. Results are similar with indirect comparison of operative care series with nonoperative care series, RR 0.39, 95%CI 0.33-0.45%. The inflated estimate of effect in case series comparison is due to higher inherent bias in lower quality study methodology. Death and major morbidity are not prevalent risk factors of modern microsurgical nerve repair. Proportion of residual impairment in demographic samples of nonoperative management is 27% (95% CI 19-36%). At least this proportion of children does not completely recover. Residual impairment with nonoperative management is underreported and uncharacterized in the primary care literature. There is no evidence to support specific nonoperative therapy protocols.

6.3 Review of Canadian Epidemiology

Chapter 4 described the review of OBPI epidemiology and burden of disease in Canada. It establishes national incidence, risk factors, and patterns and timing of referral to multidisciplinary centres. In guideline development, this was performed to quantify the identified gap in referral timing to multidisciplinary centres. The review measured volume and timing of referrals to multidisciplinary centres, estimated Canadian health

care burden, and generated initial quality indicators for referral timing. Ultimately, findings informed referral process recommendations.

It is the first Canadian study to analyze OBPI epidemiology. Identification of OBPI cases and risk factors used a national discharge database composed of administrative and clinical data. Identified cases were correlated with consultations at all Canadian multidisciplinary centres for the same time period to determine referral patterns. Timely referral was defined as "good" by one month of age, "satisfactory" by three months of age, and "poor" thereafter.

OBPI incidence was at least 1.24 per 1000 births (95% CI 1.20-1.29) and stable over the last eight years. Risk factors were consistent with a large fetus, difficult labour and comorbid birth trauma; the strongest are birth injury to humerus, shoulder dystocia and clavicle fracture. At best, 45% of OBPI cases were referred to multidisciplinary care. Among these referrals, 28% were by one month and 66% by three months (including one month referrals). No centre assesses the majority of its consultations by one month. Moving forward, these findings represent baseline quality data.

6.4 Clinical Practice Guideline

Chapter 5 described the development of a clinical practice guideline for the primary management of OBPI. The process addressed primary nonoperative and operative management, timing of referral to multidisciplinary centres, and a common dataset for future research. The guideline is intended for all health care providers treating

OBPI. Development included establishing a guideline consensus group composed of lead physicians at every Canadian OBPI multidisciplinary centre. These physicians were identified as opinion leaders in OBPI care, who will ultimately impact guideline implementation and dissemination through their influence with primary care providers and local health policy. This group of opinion leaders formed a new OBPI network. Our review of primary management and epidemiological review were completed in response to identified limitations in the evidentiary base. A formal consensus process was used given the poor quality and incomplete literature, geographic separation of group members, and need for individual anonymous feedback. Consensus was obtained during the first round of review on seven recommendations.

6.5 Implications

This is the first formal guideline for the management of OBPI. It represents the progression from the previous Canadian position statement(225) and surgical algorithms.(23,24) Considering OBPI from the knowledge-to-action cycle paradigm, this project addressed the cusp of knowledge creation and the action cycle (Figure 2-1).

The lack of a high quality synthesis was addressed with our systematic review and meta-analysis of operative versus nonoperative management. Beyond supporting the effectiveness of nerve repair, it demonstrated an historic misconception in OBPI spontaneous recovery; residual impairment is underestimated by primary care. These two concepts are critical to establish for optimal OBPI care; impairment does not simply

resolve spontaneously in a large proportion of cases, and effective and safe interventions are available.

The two critical clinical gaps in primary management were characterized and addressed. First was the perceived gap in referral timing to multidisciplinary centres. This is likely due to the historic misconceptions of OBPI recovery by primary care addressed in our systematic review. This gap was characterized in our review of Canadian epidemiology. The study estimated the burden of OBPI in Canada and provided a baseline measure of quality for referral timing. At least half of OBPI cases were not referred to multidisciplinary care. Among those that were referred, timing was not optimal for approximately three-quarters of cases. While existing evidence cannot support a specific therapy protocol, timing is critical and guardian preference for early referral was identified. Paediatric peripheral nerve management is highly specialized, with resources concentrated at multidisciplinary centres. The consensus group's rating supported a conservative approach to referral, where centres assess a proportion of children making excellent recovery versus missed or delayed referral presenting with sequelae.

The second clinical gap included indications and timing of nerve repair. The lack of consensus in operative management likely contributes to variability in referral timing. It is logical that primary care providers will not consistently refer patients when operative management is uncertain. Our systematic review of primary management is the first synthesis to support nerve repair in patients beginning at three months. While the evidence did not support one surgical algorithm, it is sufficient to support surgical

principles of early nerve repair in patients failing to recover. Further, it supported early referral necessary for operative planning.

The last gap identified was distribution of expertise in Canada. This is reflected in the lack of collaboration among Canadian OBPI multidisciplinary centres. A cohesive message was not available to inform primary care providers and guardians. The social element of this guideline's development, its interventional aspect, created the Canadian OBPI Working Group. This guideline has addressed only the broad gaps in OBPI management; further aspects of care require investigation.

6.6 Next Steps

The introduction described this thesis at the cusp of the knowledge creation and action cycle aspects of the KTA cycle. Considering the existing guideline, a high quality guideline itself is not sufficient for implementation.(104) The next step in the cycle, while beyond the scope of the thesis, involves implementation. While the recommendations are reviewed by national OBPI opinion leaders, and are more "usable" than the evidentiary base alone, consideration of context will improve implementation.(94) Adapting the OBPI guideline for each multidisciplinary centre's catchment with integration of primary care will improve recognition and adherence.

Components of this thesis provide the foundation to an integrative process to improve OBPI care in Canada by applying KT. Primary data and quality indicators, not previously utilized in OBPI research, can characterize gaps in care. Results of the

systematic review and guideline recommendations, both absent for OBPI, will direct clinical care and demonstrate gaps to address with a research enterprise. The social aspect of guideline creation provides a network to execute multicentre research, and unified information and education to primary care and guardians. Applying KT to OBPI in Canada provides an opportunity to improve the quality of care, health services, patient outcomes, and health policy.

Ultimately, implementation of the clinical practice guideline is critical; recommendations often fail to achieve potential benefits in care process, use of best evidence, and consistency in practice.(99–101) As a specialty, plastic surgery is beginning to measure guideline adherence at hospital and physician levels;(102) a review found inconsistency, with practices failing to meet recommendations following carpal tunnel release, screening mammography for breast augmentation, and deep vein thrombosis (DVT) prophylaxis in lower extremity reconstruction.(103)

There is little evidence to predict the success implementation interventions.(105) Integrated knowledge translation (IKT) interventions integrate relevant end-users and researchers from design to dissemination.(101) IKT is well suited to OBPI given the range of providers involved in OBPI care.(101) Collaboration between primary care providers, parents, specialists and resource managers is critical to optimize OBPI care.

Individually and within the scope of their expertise, each of Canada's OBPI centres has contributed high-level research recognized on the international level.(23,24,29,40,259) Our goal is to leverage the newly established network of opinion leaders, and their existing clinical care and research to advance a unified program of

research relevant to the entire multidisciplinary team involved in OBPI care. Two goals are multicentre trials and multidisciplinary guidelines.

By combining existing skills and established collaborators with knowledge translation expertise, we can create integrated and innovative OBPI strategies. Despite individual contributions, participants have not participated in multicentre studies, and do not have the capacity to address system-level issues alone. Our existing recommendations included outcome assessment to establish a common dataset for Canadian OBPI multidisciplinary centres. At the very least, existing variation in nonoperative therapy,(259) surgical algorithms,(23,24) and nerve reconstruction procedures(29,40) can be investigated with cohort studies. Fostering multicentre clinical trials can improve access to evidence-based therapies for all Canadians, and measure associated costs across our health care system.

Finally, the planned update to our guideline will include all relevant primary care and specialty disciplines. A multidisciplinary clinical practice guideline can serve to integrate a fragmented patient management system with current research and enhance implementation. OBPI involves the entire spectrum of healthcare services. Obstetricians modify risk factors of difficult deliveries. Patients are identified shortly following birth by primary care. Primary assessment, investigation and treatment at tertiary care centres involve specialized multidisciplinary teams including primary and secondary reconstructive surgeons, therapists, neurologists, radiologists, other physicians and child specialists. Patients encounter unique physical challenges throughout maturation. Only a multidisciplinary group can integrate public education and awareness, risk factor

modification, organized referral, assessment, therapy, and outcome assessment. Overall, our goal is to transform OBPI care with a model that recognizes the patient challenges from labour/delivery to full maturity, while achieving best care at every level of the healthcare system.

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APPENDIX 1: SEARCH CRITERIA

I. MEDLINE

1. brachial plexus.mp. or exp Brachial Plexus/
2. exp Brachial Plexus Neuropathies/
3. erb* palsy.mp.
4. erb* paralysis.mp.
5. Klumpke* palsy.mp.
6. Klumpke* paralysis.mp.
7. exp Paralysis, Obstetric/
8. exp Birth Injuries/
9. infant*.mp. or exp Infant/
10. neonat*.mp.
11. obstetric*.mp.
12. congenital.mp.
13. birth.mp.
14. perinatal.mp.
15. exp Child/ or child*.mp.
16. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
17. 1 or 2
18. 16 and 17
19. 3 or 4 or 5 or 6 or 7 or 18
20. limit 19 to (afrikaans or albanian or arabic or armenian or azerbaijani or belorussian or bengali or bosnian or bulgarian or burmese or catalan or chinese or croatian or czech or danish or dutch or esperanto or estonian or finnish or flemish or french or gaelic, scots or georgian or german or greek or hausa or hebrew or hindi or hungarian or icelandic or indonesian or interlingua or italian or japanese or kirghiz or korean or latin or latvian or lithuanian or macedonian or malay or marathi or masai or multilingual or norwegian or persian or polish or portuguese or pushto or rumanian or russian or serbian or slovak or slovene or spanish or swahili or swedish or tagalog or tamil or telugu or thai or turkish or ukrainian or urdu or vietnamese or welsh)
21. 19 not 20

II. EMBASE

1. brachial plexus.mp. or exp brachial plexus/
2. exp brachial plexus neuropathy/
3. exp brachial plexus injury/
4. erb* palsy.mp.
5. erb* paralysis.mp.
6. Klumpke* palsy.mp.

7. Klumpke* paralysis.mp.
8. exp birth injury/
9. infant*.mp.
10. infant/
11. child*.mp.
12. neonat*.mp.
13. congenital.mp. or exp congenital malformation/ or exp congenital disorder/
14. obstetric*.mp.
15. birth.mp.
16. perinatal.mp.
17. 1 or 2 or 3
18. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
19. 17 and 18
20. 4 or 5 or 6 or 7 or 19
21. limit 20 to (afrikaans or albanian or arabic or armenian or azerbaidzhani or basque or belorussian or bengali or bulgarian or burmese or bosnian or catalan or chinese or croatian or czech or danish or dutch or esperanto or estonian or finnish or french or gallegan or georgian or german or greek or hebrew or hindi or hungarian or icelandic or indonesian or irish gaelic or italian or japanese or korean or latvian or lithuanian or macedonian or malay or maori or mongolian or norwegian or persian or polish or polyglot or portuguese or pushto or romanian or russian or scottish gaelic or serbian or sinhalese or slovak or slovene or spanish or swedish or tagalog or thai or turkish or ukrainian or urdu or uzbek or vietnamese)
22. 20 not 21

III. CINAHL

S1. (MH "Brachial Plexus+") OR "brachial plexus" OR (MH "Brachial Plexus Neuropathies+")
S2. "erb* palsy"
S3. "erb* paralysis"
S4. "klumpke* palsy"
S5. "klumpke* paralysis"
S6. (MH "Infant+") OR "infant*"
S7. "neonat*"
S8. "obstetric*"
S9. "congenital"
S10. (MH "Birth Injuries+") OR "birth"
S11. "perinatal"
S12. (MH "Child+") OR "child"
S13. S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12
S14. S1 AND S13
S15. (MH "Brachial Plexus Birth Injuries")

S16. S2 OR S3 OR S4 OR S5 OR S14 OR S15

IV. Cochrane CENTRAL

#1. MeSH descriptor: [Brachial Plexus Neuropathies] explode all trees
#2. MeSH descriptor: [Brachial Plexus] explode all trees
#3. brachial plexus
#4. erb*
#5. klumpke*
#6. MeSH descriptor: [Infant] explode all trees
#7. infant
#8. obstetric*
#9. child*
#10. congenital
#11. perinatal
#12. MeSH descriptor: [Birth Injuries] explode all trees
#13. #1 or #2 or #3 or #4 or #5
#14. #6 or #7 or #8 or #9 or #10 or #11 or #12
#15. #13 and #14

APPENDIX 2: GUIDELINE PERSONNEL

I. Working Group

- **Dr. Christopher J. Coroneos** (lead author)
  MSc. candidate, Health Research Methodology, Department of Clinical Epidemiology & Biostatistics, McMaster University
  Resident, Division of Plastic Surgery, Department of Surgery, McMaster University
- **Dr. James R. Bain** (clinical expert)
  Professor and **Division Chair**, Division of Plastic Surgery, Department of Surgery, McMaster University
  Head, Obstetrical Brachial Plexus Injury Clinic, McMaster Children's Hospital
- **Dr. Melissa C. Brouwers** (methodological expert)
  Associate Member, Department of Clinical Epidemiology & Biostatistics, McMaster University
  Provincial Director, Program in Evidence-Based Care, Cancer Care Ontario

II. Consensus Group

Members of The Canadian OBPI Working Group

- **Dr. James Bain**, McMaster University
- **Dr. Michael Bezuhly**, Dalhousie University
- **Dr. Sean Bristol**, University of British Columbia
- **Dr. Howard Clarke**, University of Toronto
- **Dr. Robertson Harrop**, University of Calgary
- **Dr. Jennifer Lin**, Universite de Montreal
- **Dr. Jaret Olson**, University of Alberta
- **Dr. Douglas Ross**, Western University
- **Dr. Constantin Stanciu**, Universite de Montreal
- **Dr. Susan Thompson**, University of Manitoba
- **Dr. Cynthia Verchere**, University of British Columbia
- **Dr. Yvonne Ying**, University of Ottawa