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DOI: 10.1136/bmjopen-2015-010571

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Document Version Publisher's PDF, also known as Version of record


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Natural course of pain and disability following primary lumbar discectomy: protocol for a systematic review and meta-analysis

A Rushton,1 N Heneghan,1 M W Heijmans,2,3 J B Staal,4 P Goodwin5

ABSTRACT

Introduction: Knowledge about the natural clinical course is needed to improve understanding of recovery postsurgery as outcome is poor for some patients. Knowledge of the natural clinical course of symptoms and disability will inform optimal timing and the nature of rehabilitation intervention. The objective of this study is to provide first evidence synthesis investigating the natural clinical course of disability and pain in patients aged >16 years post primary lumbar discectomy.

Methods and analysis: A systematic review and data synthesis will be conducted. Prospective cohorts that include a well-defined inception cohort (point of surgery) of adult participants who have undergone primary lumbar discectomy/microdiscectomy will be included. Outcomes will include measurements reported on 1 or more outcomes of disability and pain, with a baseline presurgery measurement. Following development of the search strategy, 2 reviewers will independently search information sources, assess identified studies for inclusion, extract data and assess risk of bias. A third reviewer will mediate on any disagreement at each stage. The search will employ sensitive topic-based strategies designed for each database from inception to 31 January 2016. There will be no language or geographical restrictions. Risk of bias will be assessed using a modified QUality In Prognostic Studies (QUIPS) tool. Data will be extracted for time points where follow-up was at least 80%. Means and 95% CIs will be plotted over time for pain and disability. All results will be reported in the context of study quality.

Ethics and dissemination: This review will provide the first rigorous summary of the course of pain and disability across all published prospective cohorts. The findings will inform our understanding of when to offer and how to optimise rehabilitation following surgery. Results will be published in an open access journal. The study raises no ethical issues.

PROSPERO registration number: CRD42015020806.

BACKGROUND

Rationale

Eighty per cent of the population is affected by low back pain at some point within their lifetime1, contributing to estimates of £10.7 billion annually for lost productivity and sickness/disability benefit.2 The largest single component of expenditure (31%) is management of low back pain is surgery.2 A common surgical procedure is lumbar discectomy to excise prolapsed intervertebral disc material when causing severe leg pain. In the UK National Health Service, primary lumbar discectomy operations have increased from 7043 (2001/2002 financial year) to 8478 in the 2013/2014 financial year.3 Paralleling this increase, the mean hospital stay has reduced from 6.6 days (1999–2000) to 2.3 days (2013/2014).3 International data provide annual estimates of 12 000 operations in the Netherlands4 and 287 122 in the USA.5

Although lumbar discectomy success rates are reported as high (46–75% at 6–8 weeks, and 78–95% at 1–2 years postsurgery), ongoing problems are an issue for a substantial number of patients. The evidence suggests 30–70% of patients continue to experience pain,7 and that 3–12% required further surgery.8 Approximately, 14% of patients required revision surgery in the UK in 2013/2014 (1164 operations).9 Ongoing
problems are a key issue for this patient population from a quality of life perspective, particularly owing to the mean age for surgery of 45 years being of working age.

Rehabilitation for this population is also problematic, with documented variability of surgeon and physiotherapist advice and management post operatively.9–10 Whether patients receive rehabilitation is dependent on where they live and local practices. If they do receive rehabilitation, the content and number of sessions varies considerably.10

Our recent systematic review (16 trials) evaluating effectiveness of all physiotherapy interventions post-primary single level lumbar discectomy11 and an updated Cochrane systematic review (22 trials) of rehabilitation programmes (including physiotherapy) postlumbar disc surgery6 identified variability of timing of interventions and outcomes as a key issue. Statistical pooling was limited, but meta-analyses suggested a short-term positive effect of physiotherapy on pain, function and disability starting 4–6 weeks postsurgery, and a potential benefit from more intensive exercise interventions. However, the influence of the natural course of pain and disability following the operation on outcomes is unclear, and this identifies a wider issue that a clear understanding of the natural course is required to inform effective management. In addition, very different definitions of recovery are used in the literature making it difficult to obtain pooled estimates of recovery rates. Postoperative rehabilitation could possibly be harmful for patients if outcomes of the natural clinical course are better than outcomes of rehabilitation interventions. Additionally, a clear trend in recovery could indicate optimal timing for rehabilitation.

To enhance our understanding and inform future research, detail of the natural clinical course of pain and disability following lumbar discectomy is required. This knowledge is important as future research needs to evaluate how intervention outcomes relate to the natural course. To date, there has been no systematic review collating these data in this population.

**Objective**

To investigate the natural clinical course of pain and disability,12 with a baseline presurgery measurement.

**METHODS/DESIGN**

**Methodology**

This protocol following method guidelines by the Cochrane Back and Neck Group,14 Cochrane Handbook15 and PRISMA-P16 will inform the conduct of a systematic review. The protocol is registered with PROSPERO: CRD42015020806.17

**Amendments**

It was initially planned to investigate the natural history of a wider range of outcomes. However, the scoping search identified a greater number of prospective studies than anticipated. The protocol was revised, on 26 May 2015, to reflect a focus on disability and pain outcomes, and revised on 20 January 2016 to further develop search terms/databases, amend search dates and plans for data synthesis; and another author was recruited to provide statistical guidance.

**Eligibility criteria**

**Participants**

Adult patients who have undergone first-time lumbar discectomy/microdiscectomy/automated percutaneous discectomy, with no complications (eg, general anaesthetic, cardiopulmonary and thromboembolic) and surgical including cauda equina),18 and aged >16 years. Studies including participants undergoing revision surgery will be excluded if data cannot be obtained for the first-time surgery participants only. All clinical settings and providers were included. Any reported treatments postsurgery will be recorded carefully and evaluated as part of the risk of bias assessment.

**Outcome measures**

Measurements reported on one or more outcomes of pain and disability,12 with a baseline presurgery measurement.

**Studies**

Inception prospective cohort studies that included a well-defined inception cohort (episode inception, ie, point of surgery) of participants. The prospective cohort is the preferred design to enable control of unwarranted influences, and enables a stronger case for cause and effect relationships to be postulated.

**Information sources**

The search will employ sensitive topic-based strategies designed for each database from inception to 31 January 2016. There will be no language or geographical restrictions.

**Databases:**

- CINAHL (via EBSCOhost 1981–);
- EMBASE (via EBSCOhost 1974–);
- PubMed;
- MEDLINE (via OVIDSP 1946–);
- ZETOC (1993–);
- Scopus (1996–);
- TRIP (non-Premium version);
- Science Citation Index and Social Science Citation Index (journal search terms: Spine, neurology, orthopaedics);
- An additional search of the Cochrane Back and Neck Group website (http://back.cochrane.org/our-reviews), Cochrane Database of Systematic Reviews, and MEDLINE will identify any relevant
systematic reviews to enable checking of their reference lists.

Unpublished research:
- British National Bibliography for Report Literature (search terms: spine, disc, disectomy, surgery, sciatica);
- Ethos (search terms: spine, disc, disectomy, surgery, sciatica);
- OpenGrey (see Boolean search, box 1).

**Search strategy**

The search strategy will include (1) the study population terms suggested by the Cochrane Back and Neck Group, and (2) a strategy for searching MEDLINE for prognosis studies.

Study population terms:
- Population: Leg pain and/or low back pain
  - ‘leg pain’ OR ‘back pain’ OR exp backache OR ‘low-back pain’ OR sciatica OR ‘sciatic neuropathy’ OR lumbago OR ‘back disorders’ OR dorsalgia).
  - AND
- Target condition: Prolapsed intervertebral disc
  - (‘disc adj degeneration’ OR ‘disc adj prolapse’ OR ‘disc adj herniation’ OR ‘intervertebral disc$’ OR radiculopathies[mesh] OR ‘nerve root compression’[mesh]).
  - AND
- Intervention: lumbar disectomy
  - (discectom* OR diskectom* OR microdisc* OR microdisc OR microdisk* OR micro-disk* OR nucleotomy [mesh] OR nucleotomies[mesh]).
  - AND
- Methodology: prospective cohort studies
  - (inception OR survival OR ‘life tables’ OR ‘log rank’ OR prospective OR cohort OR ‘follow-up’ OR ‘follow-up study’).

Examples of searches that will be used include: MEDLINE OvidSP advanced search (box 2), OpenGrey and EBSCOhost Boolean search (box 1) and SCOPUS search (table 1). Syntax (truncation, wildcards and quotation marks) and operators will be amended according to the specific databases.

Reference list searches of all relevant publications will take place online where accessible. The reference lists of articles not available online will be searched manually.

No filters will be applied, so where feasible, duplicates will be removed. Authors of grey literature will be contacted when conference abstracts and proceedings are found.

**Study records**

**Data management**

Records will be managed through EndNote; specific software for managing bibliographies.

**Selection process**

Two reviewers (AR/PG) will search information sources independently and assess identified studies for inclusion, facilitated by grading each eligibility criterion as eligible/not eligible/might be eligible. The full text of a study will be reviewed and the study considered potentially relevant when it cannot be clearly excluded on the basis of its title and abstract alone following discussions between the two independent reviewers. Full text will be obtained for abstracts with insufficient information or in a situation of disagreement. A study will be included when both reviewers independently assess it as satisfying the inclusion criteria from the full text. A third reviewer (NH) will mediate in the event of disagreement following discussion. The process of decision-making for inclusion based on the eligibility criteria will be initially piloted on five articles to ensure that the criteria and interpretation of studies work effectively. The PRISMA flow diagram will document included and excluded studies, along with the reasons for exclusion.

**Data collection process**

Using a standardised form, two reviewers (AR/PG) will extract the data independently. A third reviewer (NH) will check the data for consistency and clarity. Any discrepancies in the data will be discussed and amended. The standardised form was iteratively developed and will be pilot tested on ≥5 papers by the two reviewers.

**Data items**

Data extracted for each cohort will include the summary data detailed in table 1.

**Outcomes and prioritisation**

Outcomes of interest were predefined as tools to measure pain and disability, as reflected in the domains from the WHO’s International Classification of Functioning, Disability and Health. Outcomes with established measurement properties (reliability, validity, responsiveness) and providing continuous data will be considered sufficiently similar to allow statistical pooling. Outcomes will be presented short term (≤3 months follow-up), medium term (>3, ≤12 months) and long term (>12 months). Short-term outcomes, reflecting the early postoperative period, and long-term outcomes are considered the time points of main interest.
### Box 2: Example of an advanced search strategy—MEDLINE OvidSP 1946 to 13 January 2016

#### Stages and detail of search strategy

1. "leg pain.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
2. "back pain.'mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
3. backache.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
4. 'low-back pain.'mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
5. sciatica.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
6. ‘sciatic neuropathy.’mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
7. lumbago.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
8. ‘back disorder$.’mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
9. dorsalgia.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11. (disc adj degeneration).m_titl.
12. exp spine/
13. (disc adj degeneration).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
14. (disc adj prolapse).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
15. (disc adj herniation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
16. ‘intervertebral disc$.’mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
17. radiculopathy.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
18. radiculopathies.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
19. 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. diskectomy.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
21. discectomy.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
22. microdisk$.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
23. micro-disc$.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
24. microdisk$.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
25. micro-disc$.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
26. (disc adj4 surgery).mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
27. nucleotomy.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
28. nucleotomies.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
29. 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
30. inception.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]
31. survival.mp. [mp/title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

Continued
Risk of bias in individual studies

Risk of bias for each included prospective cohort study will be independently assessed by the same initial reviewers. The third reviewer will again mediate in situations of disagreement. Cohen’s $\kappa$ will be used to assess agreement between reviewers. All tools and processes will be piloted a priori on $\geq$5 studies. Risk of bias will be assessed using a modified QUality In Prognostic Studies (QUIPS) tool. The QUIPS tool was designed to assess risk of bias in prognostic factor studies that ideally use a prospective cohort design. The wording of key issues in some sections required revision; and as the prognostic factors section was not relevant to this review it was subsequently removed. These modifications were also informed by Pengel et al who in their review of the prognosis of low back pain, including its natural course, collated six validity criteria from the existing literature. Through an iterative process the modified tool was developed and agreed. The definitive tool consists of eight components as detailed in table 1. A risk of bias, low, moderate or high, will be provided for each component in line with QUIPS; a narrative summary will be included in tabular form as illustrated by the example included in table 2. A critical evaluation of study risk of bias will be presented in the context of its impact on study results. This will be achieved through summarising the assessment of risk of bias items within each study, and across studies for each time point.

Data synthesis

If enough studies are included, a meta-analysis will be conducted using the disability and pain outcome data. Authors will be contacted to request either raw data, or additional summary statistics for those reported when data or details of variance are missing. Data will be extracted for time points where follow-up is at least 80%. Continuous outcome data will be presented in the original scale or converted to a 0–100 scale. When means or medians are not available, the midpoint of the range will be used. Means and 95% CIs will be plotted over time for pain and disability. When outcome data can be pooled across studies and follow-up time points (ie, short term, intermediate term and long term), n weighted pooled means will be used. If included studies have provided variance data, the variance weighted mean will be used in the meta-analyses. In the situation that several studies do not provide variance data, the n weighted mean will be used. Day 1 (ie, day of surgery) will be taken

<table>
<thead>
<tr>
<th>Table 1 Data extraction variables</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Content</strong></td>
</tr>
<tr>
<td>Prospective study information</td>
</tr>
<tr>
<td>Year of publication</td>
</tr>
<tr>
<td>Surgical procedure</td>
</tr>
<tr>
<td>Mean duration of symptoms</td>
</tr>
<tr>
<td>Number of participants</td>
</tr>
<tr>
<td>Setting</td>
</tr>
<tr>
<td>Country</td>
</tr>
<tr>
<td>Intervention during follow-up phase</td>
</tr>
<tr>
<td>Pain outcome measure</td>
</tr>
<tr>
<td>Disability outcome measure</td>
</tr>
<tr>
<td>Baseline</td>
</tr>
<tr>
<td>Follow-up assessment points</td>
</tr>
<tr>
<td>Losses to follow-up</td>
</tr>
<tr>
<td>Results</td>
</tr>
</tbody>
</table>
Table 2  ROB assessment (adapted from QUIPS\textsuperscript{22} and Pengel \textit{et al}\textsuperscript{23})

<table>
<thead>
<tr>
<th>Study participation\textsuperscript{22}</th>
<th>Defined sample\textsuperscript{23}</th>
<th>Study attrition/complete follow-up\textsuperscript{22}</th>
<th>Outcome measurement\textsuperscript{22}</th>
<th>Statistical analysis and reporting\textsuperscript{22}</th>
<th>Blinded outcome\textsuperscript{23}</th>
<th>Overall statement of risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate ROB</td>
<td>Moderate ROB</td>
<td>Moderate ROB</td>
<td>Low ROB</td>
<td>Low ROB</td>
<td>Low ROB</td>
<td>Moderate 4</td>
</tr>
<tr>
<td>Some eligibility criteria, for example, prolapse &lt;6 mm may contribute to potential participants being excluded</td>
<td>Clear eligibility criteria based on detailed physical examination and radiology findings</td>
<td>No losses to follow-up at 6 months 8 (16%) patients lost to follow-up at 12 months</td>
<td>VAS 0–10 in cm Established measurement properties Measure standardised by independent assessor</td>
<td>Sufficient presentation of data No selective reporting of results</td>
<td>Independent assessor collected data</td>
<td></td>
</tr>
<tr>
<td>Example study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Suggests consecutive patients were considered</td>
<td></td>
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</tbody>
</table>

Note: prognostic factor section of QUIPS not relevant.
QUIPS, QUality In Prognostic Studies; ROB, risk of bias; VAS, visual analogue scale.
as the reference time. The influence of potential predictor variables will be explored where possible using metaregression analyses. Predictor variables of interest identified a priori include type of surgery, duration of symptoms prior to surgery, age at time of surgery, level of education, work satisfaction, coexistence of psychological complaints, evidence of passive avoidance coping function, level of preoperative pain and duration of sick leave (A Rushton, K Zoulas, A Powell, et al. Physical prognostic factors in lumbar discectomy surgery (PROSPERO 2015:CRD42015024168). In the case of significant findings, analyses per subgroup will be presented alongside the overall analyses.13

Metabiases
Assessment of any publication bias across studies will be included. This will involve an analysis of consistency between published protocols and study findings, a detailed search for unpublished studies, and consideration of competing interests from various research groups. Results will be reported narratively.

Confidence in cumulative evidence
The strength of the overall body of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method. A systematic review of cohort studies within the field of prognosis has previously been argued at the start as evidence of high quality.25 Iorio et al25 support that GRADE’s five domains of rating quality down (risk of bias and publication bias as detailed above, and imprecision, inconsistency and indirectness) and up (adaptation of two (large effect, dose–response gradient) of the three GRADE domains) apply equally to studies investigating prognosis. The GRADE domains of interest will be adapted for cohort studies as recommended by Iorio et al.25 This will enable a consistent method for evaluating confidence in estimates from the included studies in the review.

DISCUSSION
This systematic review will, through a rigorous methodology, identify and examine studies reporting the natural course of pain and disability over time following the first lumbar discectomy. No systematic review has previously addressed this objective although Parker et al., in a recent synthesis across all published cohorts, did evaluate the frequency of recurrent symptoms and reoperation following lumbar discectomy. They identified that ongoing leg/back pain was a problem for 3–34% patients in the short term (6–24 months, 39 cohorts, n=8156 patients), and for 5–36% patients in the long term (>24 months, 28 cohorts, n=6255). The incidence of recurrence (70 cohorts, n=18 085) of herniation ranged from 0% to 23%.26

Although risk of bias and overall level of evidence may limit analyses and confidence in this review’s conclusions, this best evidence synthesis will provide a better understanding of the natural course of patient recovery postsurgery.

Implications of results
This review will provide the first rigorous summary of the course of pain and disability across all published prospective cohorts of adult patients following first lumbar discectomy. The findings will inform our understanding of when to offer and how to optimise rehabilitation for pain and disability following surgery.

REFERENCES


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BMJ Open 2016 6:
doi: 10.1136/bmjopen-2015-010571

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