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BMJ Open

Lumbar spine surgery across 15-years: trends, complications and reoperations in a time-series study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-028743
Article Type:	Research
Date Submitted by the Author:	01-Jan-2019
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Keywords:	Neurosurgery < SURGERY, Orthopaedic & trauma surgery < SURGERY, EPIDEMIOLOGY

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Manuscripts

Lumbar spine surgery across 15-years:

trends, complications and reoperations in a time-series study

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ABSTRACT

Studies from different Western countries have reported a rapid increase in spinal surgery rates, an increase that exceeds by far the growing incidence rates of spinal disorders in the general population. There are few studies covering all lumbar spine surgery and no previous studies from Norway.

Objectives

The purpose of this study was to investigate trends in all lumbar spine surgery in Norway over 15 years, including length of hospital stay, and rates of complications and reoperations.

Design

A time-series study over 15 year using hospital patient administrative data and sociodemographic data from the National Registry in Norway.

Setting and participants

Patients aged ≥ 18 years discharged from Norwegian public hospitals between 1999 and 2013.

Outcome measures

Annual rates of simple (microsurgical discectomy, decompression) and complex surgical procedures (fusion, disc prosthesis) in the lumbar spine.

Results

The rate of lumbar spine surgery increased by 54%, from 78 (95%CI [75-80]) to 120 [107-113] per 100,000, from 1999 to 2013. More men had simple surgery whereas more women had complex surgery. Among elderly people over 75 years, lumbar surgery increased by a factor of five during the 15-year period. The rates of complications were low, but increased from 0.7% in 1999 to 2.4% in 2013.

1 **Conclusions**

2 There was a substantial increase in lumbar spine surgery in Norway from 1999 to 2013,
3 similar to trends in other Western world countries. The rise in lumbar surgery among elderly
4 people represents a significant workload and challenge for health services, given our aging
5 population.

6 **Key Words**

7 neurosurgery, orthopaedic & trauma surgery, epidemiology

8 **Strengths and limitations of this study**

- 9 1. From 1999 to 2013 the annual rates of all lumbar spine surgery, including both simple
10 procedures like microdiscectomy and decompression and complex procedures like
11 fusion and disc prosthesis, in Norwegian public hospitals more than doubled.
- 12 2. The median length of hospital stay decreased from 7 days in 1999 to 4 days in 2013,
13 but patients who received complex surgery the median length of stay was nearly
14 double that of those who underwent a simple procedure (8 versus 4 days).
- 15 3. More men underwent simple surgical procedures, whereas more women underwent
16 complex surgical procedures over the 15 years.
- 17 4. Most surgeries were performed on patients aged 40–59, but a substantial shift
18 towards operations performed on the older age groups was apparent for both simple
19 and complex surgery.
- 20 5. The complication rates were low, and were significantly associated with younger and
21 middle-aged groups, receiving complex surgery, and having an extended hospital
22 stay.

23 **INTRODUCTION**

24 Low back pain is the leading cause of years lost to disability worldwide, and this burden is
25 increasing as our population ages [1]. Low back pain was responsible for 60.1 million
26 disability-adjusted life years in 2015, an increase of 54% since 1990, with the largest increase
27 seen in low- and middle-income countries [1]. The economic burden is extensive, mostly due
28 to sickness absence costs, but also due to the high cost of diagnostic tests and, in particular,
29 spinal surgery [1]. The use of spinal surgery has increased considerably in many Western
30

1
2
3 1 countries over the past 20 years [2-11]. This increase cannot be explained by higher
4
5 2 incidence or prevalence rates of spinal disorders [2-7], and there are marked variations in
6
7 3 spinal surgery rates between and within countries [7, 11].

8
9 4 National administrative databases provide important information regarding health
10
11 5 services, which is crucial for planning and allocating healthcare resources. Many previous
12
13 6 studies on the rates of all types of lumbar surgery come from the USA [2, 4, 7, 9]. There are
14
15 7 also studies from Germany [6], United Kingdom [10], Sweden [3], and Denmark [5], but none
16
17 8 from Norway. Moreover, none of the published studies provide an overview of *all* types of
18
19 9 spinal surgery including simple surgical procedures such as microsurgical discectomy and/or
20
21 10 decompression, and complex surgical procedures like fusions and disc prosthesis. An
22
23 11 overview of all spinal surgery, including complication and reoperation rates, will provide
24
25 12 important information for the evaluation of current public health services, as well as the
26
27 13 planning of future services.

28
29 14 Hence, the primary aim of this study was to investigate the longitudinal trends in
30
31 15 hospital discharges of *all* surgical procedures for lumbar spine disorders in Norway from
32
33 16 1999 to the end of 2013. Further, length of hospital stay, and rates of complications and
34
35 17 reoperations over the 15-year period were investigated.

36 37 19 **MATERIAL AND METHODS**

38 39 20 ***Design***

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41
42 21 This was a retrospective observational study comprising all discharges from Norwegian
43
44 22 public hospitals over a 15-year period (1999–2013). Norway (population of 4.46 million in
45
46 23 1999 and 5.05 million in 2013) [12] has a national healthcare system divided into four health
47
48 24 regions (South-East, West, Middle, and North). Private surgery, primarily day surgery,
49
50 25 became available after 2007. It is estimated that currently approximately 7% of all elective
51
52 26 spinal surgeries take place in the private sector [13].

53 54 27 ***Data source***

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57 28 Hospital patient administrative data were retrieved from a national database located at the
58
59 29 Norwegian Knowledge Centre for the Health Services. The database was initially established
60

1
2
3 1 as a part of the project “*Post-hospitalization survival rates in Norway as indicators of hospital*
4 2 *quality*”. A detailed description of the methods employed in data collection is published
5 3 elsewhere [14]. Patient administrative data for the period 1999–2009 were extracted
6 4 directly from all Norwegian public hospitals, and, for the period 2010–2013, from the
7 5 Norwegian Patient Registry (NPR). Norwegian hospitals were mandated to submit data to
8 6 the NPR since 2010. Each hospitalization record contains a personal identifier, codes for
9 7 diagnoses, medical procedures, and date and time of admission and discharge. Data from
10 8 the National Registry provided by Statistics Norway made it possible to link the NPR data to
11 9 patients’ age, sex, and municipality of residence. Each entry in the database represents a
12 10 single hospitalization record including diagnoses based on ICD-10 and surgical procedure
13 11 codes based on the NOMESCO Classification of Surgical Procedures (NCSP) [15].

12 ***Patient and Public Involvement***

13 13 Due to the use of administrative data in this study patients or public were not involved in
14 14 this project.

16 ***Selection of sample and classification of outcome***

17 17 Inclusion criteria were: age ≥ 18 years and a lumbar spine diagnosis code (ICD-codes from
18 18 M40 to M54). Exclusion criteria were: diagnoses related to the cervical, thoracic, or an
19 19 unspecified region of the spine, as well as diagnoses indicating cancer, trauma, spinal
20 20 fractures, pregnancy, spinal infections, and inflammatory diseases.

21 21 For identifying discharges with *simple* surgical procedures defined as discectomy
22 22 and/or decompression, the following NCSP ABC codes were used [15]: ABC07, ABC16,
23 23 ABC26, ABC28, ABC36, ABC40, ABC56, ABC66, and ABC99. The *complex* surgical procedures
24 24 included procedure codes for fusion surgery (NAG and NAN), disc prosthesis (NAB and NAC),
25 25 and revision surgery (NAT and NAU) [15]. Further, NAE, NAF, NAH, NAM, NAT, and NAU
26 26 procedure codes were included if coexisting with NCSP codes indicating a complex
27 27 procedure. This is similar to the classification used in the Norwegian Registry for Spine
28 28 Surgery (NORspine) [16]. A list of all included procedure codes can be delivered by
29 29 contacting the corresponding author.

1
2
3 1 *Complications* were identified by the following ICD-10 codes occurring within 30 days
4
5 2 after a discharge: postoperative hematoma (T81.0), post-procedural shock (T81.1),
6
7 3 unintentional puncture/laceration (T81.2), disruption of wound/wound dehiscence (T81.3),
8
9 4 infection following a procedure (T81.4), foreign body accidentally left in body following
10
11 5 procedure (T81.5), acute reaction to foreign body accidentally left during a procedure
12
13 6 (T81.6), vascular complications following a procedure (T81.7), unspecified or other
14
15 7 complications of procedure, either upon initial surgical admission or upon readmission
16
17 8 (T81.8-9), and complications during anesthesia (T88.4-5). NAW (reoperation) and AW
18
19 9 (reoperations of the nervous system) procedure codes that occurred within 30 days after the
20
21 10 initial surgery were also classified as *complications*. NAW and AW procedure codes occurring
22
23 11 later than 30 days after an initial procedure were classified as *reoperations*.

24 12 **Background characteristics**

25
26
27 13 Patient age, gender, length of hospital stay, and number of operations were included. Age
28
29 14 was categorized as 18–39 years, 40–59 years, 60–75 years, or >75 years.

30 15 **Statistical analyses**

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35 16 Annual surgical incidence rates were calculated per 100,000 inhabitants based on the size of
36
37 17 the total Norwegian population on Jan 1st of each analyzed year, retrieved from Statistics
38
39 18 Norway [12]. Surgical incidence rates across age groups, gender, and type of surgery
40
41 19 (simple/complex) were compared with χ^2 - and z-tests. Length of hospital stay over the time
42
43 20 period and in relation to background characteristics was compared using a non-parametric
44
45 21 Kruskal-Wallis test. Possible associations between complications and background
46
47 22 characteristics were analyzed using a multivariate logistic regression. All tests were two-
48
49 23 sided and p-values <0.05 were considered statistically significant. Data analyses were
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51 24 performed using SPSS version 25.0 (IBM, Armonk, NY, USA) and STATA version MP15.

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53 25

54 26 **RESULTS**

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57 27 A total of 67,855 discharges for 57,081 individual patients were identified. A total of 56,764
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59 28 (83.7%) discharges were for simple surgical procedures and 11,091 (16.3%) discharges were

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2
3 1 for complex surgical procedures. Most of the complex surgical procedures were fusion
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5 2 surgeries (94%). Further, 48,495 individual patients (71.5%) had only one discharge due to
6
7 3 spinal surgery. The mean age of the patients was 52.3 (SD 15.9), and 51.4% were men.

8
9 4 Background characteristics of all included discharges are presented in Table 1.

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11 5 The median length of hospital stay for all patients undergoing spinal surgery
12
13 6 decreased from 7.1 [IQR 6.0] days in 1999 to 3.8 [IQR 4.1] in 2013 (Table 1). For those
14
15 7 undergoing a complex procedure the median length was nearly double that of those who
16
17 8 underwent a simple procedure [8.2 (IQR) days versus 4.3 (IQR)]. In the simple surgery group,
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19 9 the length of hospital stay was reduced from a median of 6.2 [IQR 5.0] days in 1999 to 3.1
20
21 10 [IQR 3.1] in 2013, and in the complex surgery group there was a reduction from a median of
22
23 11 11.0 [IQR 6.1] in 1999 to 7.0 [IQR 4.0] in 2013.

24
25
26 12 **Insert Table 1 here**

27
28 13 The annual surgical rate including both simple and complex procedures increased
29
30 14 from 77.8 (95%CI [75.2-80.4]) per 100,000 in 1999 to 119.9 (95%CI [107.0-112.8] in 2013
31
32 15 (Fig1). The rate of simple procedures increased by 138% (from 64.3 to 88.9 per 100,000
33
34 16 inhabitants for 1999 and 2013, respectively), and the rate of complex procedures increased
35
36 17 by 154% (from 13.6 to 21.0 per 100,000). During the 15-year study period, significantly more
37
38 18 males underwent simple surgical procedures, whereas more females underwent complex
39
40 19 surgical procedures (Fig2).

41
42
43 20 **Insert Fig1 and Fig2 here**

44
45 21 Most surgeries were performed on patients aged 40–59 (Fig3). A substantial shift
46
47 22 towards operations performed on the older age groups is apparent for both simple and
48
49 23 complex surgery. Among those aged 75 years and above, the rate of simple surgery
50
51 24 increased by more than a factor of five by 2013, reaching 167.8 [154.3-181.3]. A similar shift
52
53 25 was also apparent for the complex procedures. In 1999 only 7.8 [30.3-42.9] operated
54
55 26 patients per 100,000 inhabitants were in the oldest age group, whereas in 2013 this rate had
56
57 27 increased to 36.6 [30.3-42.9]. In the younger age groups, the complex surgery rate remained
58
59 28 stable over the 15-year period.

60
29 **Insert Fig3 here**

1
2
3 1 The occurrence of complications was generally low. During the 15-year period a total
4 of 977 (1.4%, 95% [CI 1.38 – 1.56]) discharges were coded with diagnoses or procedures
5 2
6 3 indicating complications. Of these, 42% occurred during the index stay and 68% underwent
7 4
8 5 reoperation within 30 days. Over the 15-year period, the complication rate more than
9 6
10 7 tripled, from 0.7% in 1999 to 2.4% in 2013. The multivariate analysis showed that
11 8
12 9 complications were significantly associated with younger and middle-aged groups, receiving
13 10
14 11 complex surgery, and having an extended hospital stay (Table 2). There was no statistically
15 12
16 13 significant interaction between type of surgery (simple vs complex) and length of hospital
17 14
18 15 stay (p=0.296), or between age groups and type of surgery (p=0.678).

19 10 A total of 10,015 (14.8%, 95% CI [14.5 – 15.0]) discharges were reoperations; 517
20 11 (0.8%, 95%CI [[0.8 – 0.9]) occurred between 30 and 90 days after the index discharge, 2611
21 12 (3.8%, 95%CI [3.7 – 4.0]) between 91 days and 12 months, and 2429 (3.6%, 95%CI [3.5 – 3.7])
22 13
23 14 between the first and second year. There was a large decrease in the proportion of patients
24 15
25 16 who received reoperations during the 15-year period: from 21.6% in 1999 to 2.3% in 2013.

26 15 **Insert Table 2 here**

27 16

28 17 **DISCUSSION**

29 18 This national study identified a significant increase in lumbar spine surgery in Norway from
30 19 1999 to 2013. This increase was most marked in the use of simple surgical procedures like
31 20 microsurgical discectomy and/or decompression surgery, in particular among elderly
32 21 patients above 75 years of age. The increase in complex surgery, for the most part fusion
33 22 surgery, was also most prevalent in the oldest age group.

34 23 The main strength of the current study is that it covers all spinal surgery procedures
35 24 carried out in public hospitals in Norway during a 15-year period, except for surgery due to
36 25 red flag diagnosis (like cancer, spinal infections, inflammatory diseases) or trauma. A
37 26 potential weakness is the risk of misclassification of diagnoses or procedures [23]. The lack
38 27 of accuracy of diagnosis in such registries has been reported and a systematic review on this
39 28 field has showed that procedure coding might be more accurate than coding based upon
40 29 diagnosis [24]. Therefore, in order to reduce misclassification in the current study, we used
41 30 the surgical procedure coding in combination with diagnoses when classifying the types of

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2
3 1 surgery provided. Further, we argue that the risk of misclassification is minor in this study as
4
5 2 we assessed two large and different types of spinal surgery (simple versus complex spinal
6
7 3 surgery procedures). As expected, the two groups differ with respect to length of hospital
8
9 4 stay, complications, and reoperations. We considered classifying spinal surgery into simple
10
11 5 and complex procedures, useful when reporting trends in spinal surgery within a large and
12
13 6 heterogeneous dataset such as hospital administrative data used in this study. Finally,
14
15 7 another weakness is that the present material did not include surgery conducted in private
16
17 8 clinics/hospitals. Private for-profit hospitals in Norway perform currently approximately 7%
18
19 9 of the total number of elective surgical procedures [13], usually as day surgeries. This might
20
21 10 have contributed to the increase in complications in public hospitals after private surgery
22
23 11 became common in 2007. Private surgery would leave the public hospitals to deal with the
24
25 12 more complex cases and procedures during this portion of the study period (2007–2013). A
26
27 13 previous study comparing surgery due to disc herniation in public and private hospitals in
28
29 14 Norway, showed that patients operated by simple procedures due to lumbar disc herniation
30
31 15 in public hospitals were older, and had more comorbidity and other risk factors associated
32
33 16 with unfavorable outcomes compared to those operated in the private clinics [25].

34 17 There are very few published papers that provide an overview of *all* types of spinal
35
36 18 surgery for degenerative disorders over an extended time period. There is one study by
37
38 19 Davis [17], that presents trends in both cervical and lumbar spine surgery in the USA from
39
40 20 1979 to 1990. It states that hospitalization rates for all types of lumbar spinal surgery
41
42 21 (including fusion, disc and exploration/decompression) increased markedly among both
43
44 22 sexes. In line with Davis et al, our results demonstrate that more men than women receive
45
46 23 lumbar spine surgery. Several studies on different types of spinal surgery, such as disc
47
48 24 herniation and spinal fusion surgery, have been published [2-11]. In general, the findings in
49
50 25 the present paper are in accordance with the other studies from Scandinavian countries [3,
51
52 26 5] and Germany [6], which show increased rates for lumbar disc herniation and spinal
53
54 27 stenosis surgery. The increase reported in most of the western-European countries is not as
55
56 28 large as that found in the United States [2, 4, 7, 9, 11] and United Kingdom [10].
57
58 29 Furthermore, these results also fit with the overall national healthcare expenditure across
59
60 30 countries; in Norway it is 10.4% of the GDP, which is similar to other western-European
31
32 countries such as Germany and Sweden, as compared to 17.1% in the United States [18].

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2
3 1 The increase in public lumbar spine surgery in Norway is difficult to understand,
4
5 2 because only minor increases in the incidence and severity of low back pain have been
6
7 3 reported in the Norwegian population [19]. However, parts of the increase may be explained
8
9 4 by the growing number of elderly patients and the increase of hospital surgeons in general
10
11 5 [20]. In addition, there has been a substantial rise in the use of radiographic examinations
12
13 6 such as MRI, which might have led to more surgery [21]. The large variations in spinal
14
15 7 surgery rates may also be explained by a lack of uniform and consensus-based criteria for
16
17 8 surgery, financial incentives for surgical interventions, and new technology [7-10, 22].

18 9 The mean complication rate during the study period was low, but it increased to 2.4%
19
20 10 at the end of the period. This increase may be explained by the increase in reoperations
21
22 11 within 30 days at the end of the 15-year period. Hence, there seems to be a trend towards a
23
24 12 shorter timeframe for reoperations by the end of this 15-year time period, a trend which is
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26 13 also reported in the Swedish study of lumbar disc herniation surgery between 1987 and
27
28 14 1999 [3]. Our finding that older patients were less likely to experience complications and
29
30 15 receive reoperations compared with the younger and middle-aged groups is hard to explain.
31
32 16 It may be that surgeons are more hesitant to reoperate older people, and are more selective
33
34 17 with respect to other potential risk factors for complications after surgery.

35 18 **CONCLUSION**

36
37 19 There was a substantial increase in spinal surgery in Norway from 1999 to 2013. The rise in
38
39 20 number of surgeries, in particular among elderly people, represents a significant workload
40
41 21 for hospitals in Norway, and a challenge to the public healthcare system in terms of meeting
42
43 22 the increased burden associated with low back pain in an aging population.

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17 8 **Contributors;** MG, JH and JAZ designed the study. MG and MCS analysed the data, and JAZ, OF, LG,
18 and TKS contributed in discussion of analyses and results presentation. MG wrote the manuscript
19 with all authors contributing in reading, commenting and approving the final manuscript.
20
21

22
23 11 **The original protocol for the study** can be delivered upon request to the corresponding author.
24
25

26 12 **Funding statement:** This work was supported by the South-Eastern Norway Regional Health
27 Authority, grant number 2013030.
28
29

30 14 **Competing interests:** There are no competing interests to be reported in this study.
31
32

33 15 **Any checklist and flow diagram for the appropriate reporting statement:** not relevant
34
35

36 16 **Patient consent:** not required
37
38

39 17 **Ethics approval:** The study was approved by the Norwegian Data Inspectorate (2014/14413) and the
40 Norwegian Regional Ethics Committee (2013/1662, REC south-east D).
41
42

43 19 **Data sharing statement:** It is not possible to participate in data sharing due to ethical reasons and
44 strict data protection regulation in Norway.
45
46

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48 21 **Figure legends:**
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51 22 Fig 1. Annual surgery rates per 100,000 population of simple and complex lumbar surgical procedures
52 in Norway from 1999 to 2013.
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55 24 Fig 2. Annual incidence per 100,000 population of simple and complex lumbar surgery in Norway
56 from 1999 to 2013, according to gender.
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3 1 Fig 3. Annual incidence per 100,000 inhabitants of simple (upper figure) and complex (lower figure)
4 2 surgery in Norway from 1999 to 2013, according to age groups.

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For peer review only

Table 1. Characteristics of 67,855 lumbar spine operations in 57,081 patients in Norway, 1999 to 2013

	No. of operations (%)	Length of stay, median days [range, IQR]
Age (years)		
18-39	16396 (24.2)	4.2 [724, 4.4]
40-59	28237 (41.7)	6.3 [618, 4.7]
60-75	16160 (23.9)	5.9 [250, 5.8]
> 75	6910 (10.2)	7.2 [226, 6.7]
Missing	152	
Gender		
Male	34902 (51.4)	4.7 [239, 4.4]
Female	32801 (48.3)	6.0 [724, 5.8]
Missing	152	
Year of operation		
1999	3460 (5.1)	7.1 [149.9, 6.0]
2000	3996 (5.9)	7.0 [420, 6.0]
2001	4200 (6.2)	7.0 [138, 6.0]
2002	3865 (5.7)	6.2 [202, 6.0]
2003	4557 (6.7)	6.1 [238, 5.4]
2004	4396 (6.5)	6.1 [250, 5.8]
2005	4572 (6.7)	6.0 [724, 5.3]
2006	4422 (6.5)	5.8 [138, 5.5]
2007	4255 (6.3)	5.1 [618, 5.0]
2008	4164 (6.1)	4.9 [179, 4.3]

2009	4449 (6.6)	4.2 [142, 4.9]
2010	5130 (7.6)	4.1 [183, 4.8]
2011	5241 (7.7)	4.0 [210, 4.2]
2012	5597 (8.2)	4.1 [165, 4.2]
2013	5551 (8.2)	3.8 [219, 4.1]
Missing	0	0
Type of surgery		
Simple	56764 (83.7)	4.3 [724, 4.3]
Complex	11091 (16.3)	8.2 [420, 5.7]
No. of operations		
One	57029 (84.0)	5.1 [724, 5.0]
Two	8623 (12.7)	5.2 [618, 5.1]
Three	1602 (2.4)	6.2 [205, 6.0]
≥ Four	467 (0.7)	6.9 [115, 4.4]
Missing	134	134

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Table 2. Multivariate logistic regression model analysis of factors associated with complications (including reoperation within 30 days) due to lumbar spine surgery in Norway from 1999 to 2013 (N=67,855)

	Complications (n=977)	OR	Lower 95% CI	Upper 95% CI
Age (years)				
18-39	250	Ref		
40-59	460	0.97	0.83	1.13
60-75	198	0.61	0.50	0.74
> 75	69	0.51	0.39	0.67
Missing	152			
Gender				
Male	510	Ref		
Female	467	0.90	0.79	1.02
Missing	152			
Length of stay (cont.)		1.02	1.01	1.02
Type of surgery				
Simple	659	Ref		
Complex	318	2.34	2.04	2.69
Year of operation				
1999	24	Ref		
2000	29	0.98	0.57	1.71
2001	29	1.03	0.60	1.77
2002	33	1.31	0.77	2.22

Trends in lumbar spine surgery

2003	44	1.52	0.92	2.50
2004	41	1.46	0.88	2.43
2005	67	2.23	1.39	3.57
2006	60	2.25	1.40	3.63
2007	58	2.25	1.39	3.64
2008	56	2.29	1.42	3.71
2009	80	3.12	1.97	4.94
2010	89	3.03	1.93	4.78
2011	93	3.03	1.93	4.77
2012	140	4.31	2.79	4.67
2013	134	4.16	2.68	6.44
Missing	134			

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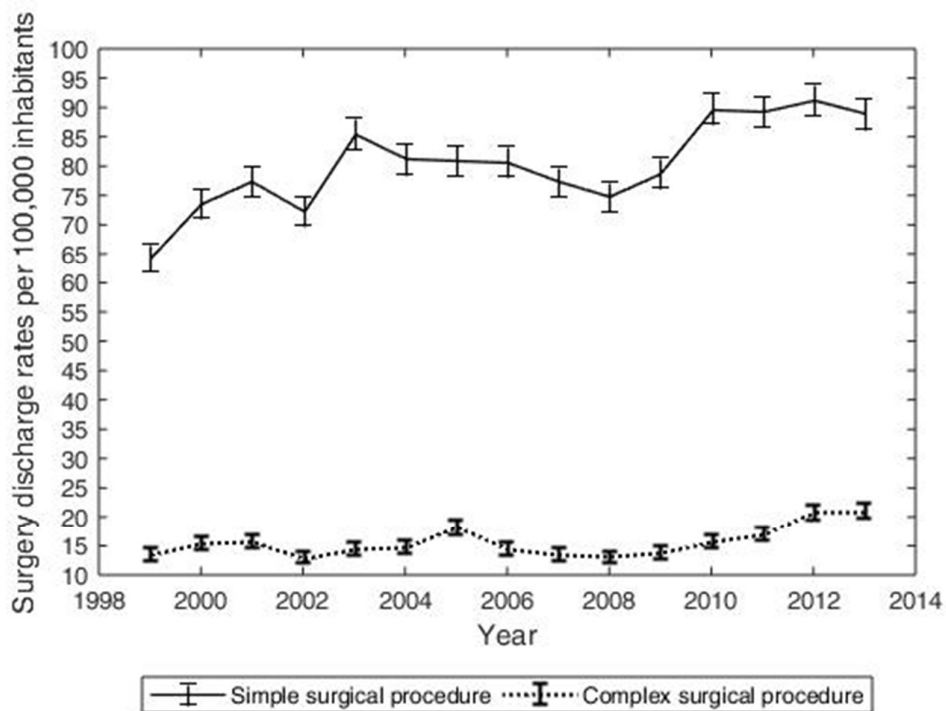


Fig 1. Annual surgery rates per 100,000 population of simple and complex lumbar surgical procedures in Norway from 1999 to 2013.

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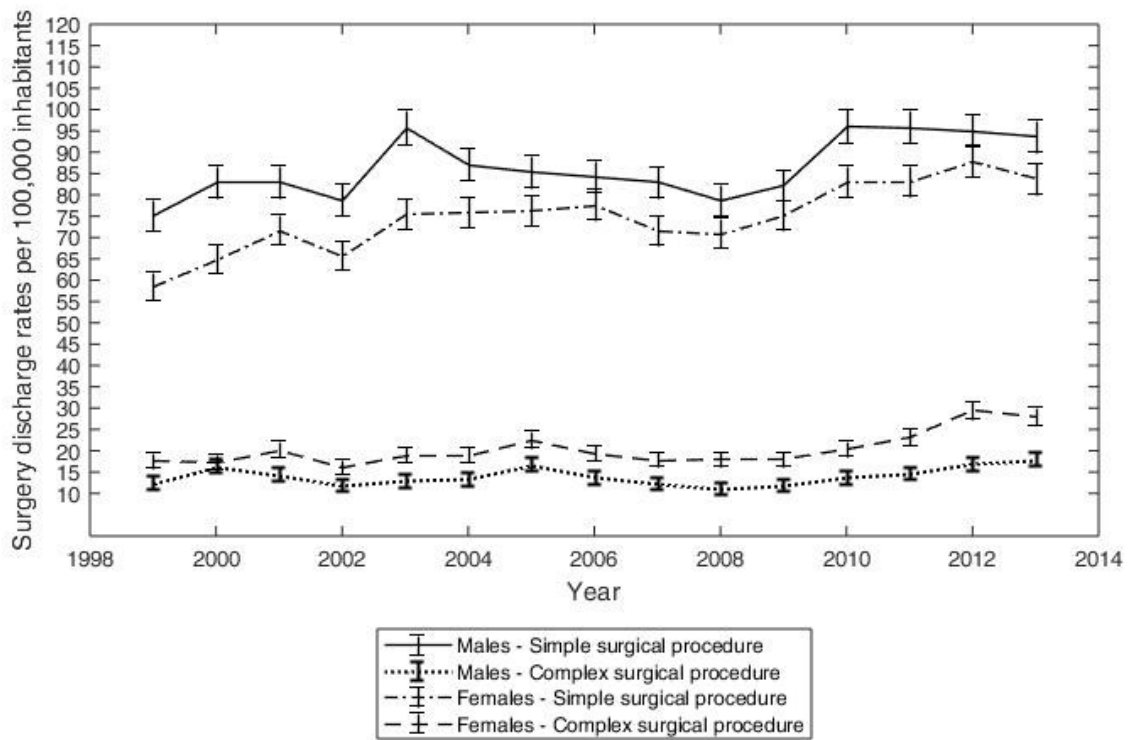


Fig 2. Annual incidence per 100,000 population of simple and complex lumbar surgery in Norway from 1999 to 2013, according to gender.

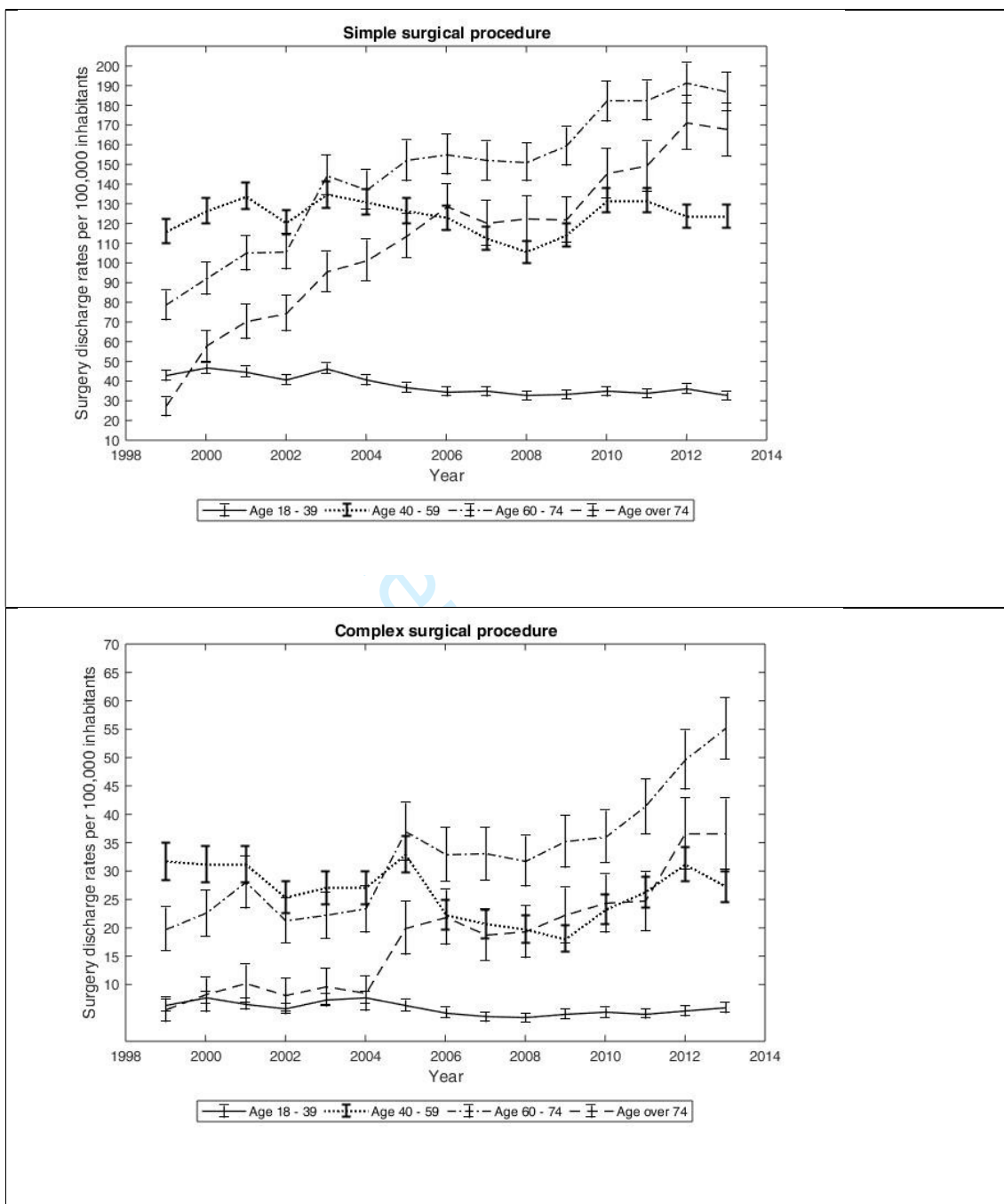


Fig 3. Annual incidence per 100,000 inhabitants of simple (upper figure) and complex (lower figure) surgery in Norway from 1999 to 2013, according to age groups.

BMJ Open

Lumbar spine surgery across 15-years: trends, complications and reoperations in a longitudinal observational study from Norway

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-028743.R1
Article Type:	Research
Date Submitted by the Author:	06-Jun-2019
Complete List of Authors:	Grotle, Margreth; Hogskolen i Oslo og Akershus, Department of Physiotherapy; Oslo universitetssykehus Ullevål, Research and Communication Unit for Musculoskeletal Health Småstuen, Milada; Oslo Metropolitan University, Department of Nursing and Health Promotion Fjeld, Olaf; Oslo universitetssykehus Ullevål, Research and Communication Unit for Musculoskeletal Disorders Grøvre, Lars; Sykehuset Ostfold HF, Helgeland, Jon; Nasjonalt folkehelseinstitutt, Division of Health Services Storheim, Kjersti; Research and Communication Unit for Musculoskeletal Health (FORMI); Faculty of Health Sciences, Oslo Metropolitan University Solberg, Tore; University Hospital of North Norway, Neurosurgery; North Norway Health Authority, The Norwegian Registry for Spine Surgery Zwart, John-Anker; Oslo University Hospital, Department of Neurology and FORMI; University of Oslo, Faculty of Medicine
Primary Subject Heading:	Surgery
Secondary Subject Heading:	Surgery, Health services research
Keywords:	Neurosurgery < SURGERY, Orthopaedic & trauma surgery < SURGERY, EPIDEMIOLOGY

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4 1 **Lumbar spine surgery across 15-years:**
5 2 **trends, complications and reoperations in a longitudinal observational study**
6 3
7 4 **from Norway**

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17
18 8 **ABSTRACT**

19 9 Studies from different Western countries have reported a rapid increase in spinal surgery
21 10 rates, an increase that exceeds by far the growing incidence rates of spinal disorders in the
22 11 general population. There are few studies covering all lumbar spine surgery and no previous
23 12 studies from Norway.

24 13 **Objectives**

25 14 The purpose of this study was to investigate trends in all lumbar spine surgery in Norway
26 15 over 15 years, including length of hospital stay, and rates of complications and reoperations.

27 16 **Design**

28 17 A longitudinal observational study over 15 year using hospital patient administrative data
29 18 and sociodemographic data from the National Registry in Norway.

30 19 **Setting and participants**

31 20 Patients aged ≥ 18 years discharged from Norwegian public hospitals between 1999 and
32 21 2013.

33 22 **Outcome measures**

34 23 Annual rates of simple (microsurgical discectomy, decompression) and complex surgical
35 24 procedures (fusion, disc prosthesis) in the lumbar spine.

36 25 **Results**

37 26 The rate of lumbar spine surgery increased by 54%, from 78 (95%CI [75-80]) to 120 [107-113]
38 27 per 100,000, from 1999 to 2013. More men had simple surgery whereas more women had
39 28 complex surgery. Among elderly people over 75 years, lumbar surgery increased by a factor

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3 1 of five during the 15-year period. The rates of complications were low, but increased from
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5 2 0.7% in 1999 to 2.4% in 2013.
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8 **Conclusions**

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10 4 There was a substantial increase in lumbar spine surgery in Norway from 1999 to 2013,
11
12 5 similar to trends in other Western world countries. The rise in lumbar surgery among elderly
13
14 6 people represents a significant workload and challenge for health services, given our aging
15
16 7 population.
17

18 **Key Words**

19
20 9 neurosurgery, orthopaedic & trauma surgery, epidemiology
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22

23 **Strengths and limitations of this study**

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25
26 11 1. This study covers all lumbar spine surgery in Norwegian public hospitals across 15
27
28 12 years, and all annual rates during the time period were adjusted for age and gender.
29
30 13 2. In order to minimize the risk of misclassification, surgical procedure codings were
31
32 14 used in combination with diagnoses to group all surgery into two main categories;
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34 15 simple surgery such as microdiscectomy and decompression, and complex surgery
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36 16 such as fusion and disc prosthesis .
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38 17 3. This study did not include data from private clinics, which currently cover
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40 18 approximately 7% of the elective surgery in Norway.
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42 19 4. Cases for non-lumbar indications, cancer, trauma, infection, pregnancy and
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44 20 inflammation were excluded.
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46 21 5. The design and material of this study did not allow us to adjust for all potential
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48 22 confounding factors, that might have influenced the multivariate analyses of
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50 23 complications due to surgery .
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1 INTRODUCTION

2 Low back pain is the leading cause of years lost to disability worldwide, and this burden is
3 increasing as our population ages [1]. Low back pain was responsible for 60.1 million
4 disability-adjusted life years in 2015, an increase of 54% since 1990, with the largest increase
5 seen in low- and middle-income countries [1]. The economic burden is extensive, mostly due
6 to sickness absence costs, but also due to the high cost of diagnostic tests and, in particular,
7 spinal surgery [1]. The use of spinal surgery has increased considerably in many Western
8 countries over the past 20 years [2-11]. This increase cannot be explained by higher
9 incidence or prevalence rates of spinal disorders [2-7], and there are marked variations in
10 spinal surgery rates between and within countries [7, 11].

11 National administrative databases provide important information regarding health
12 services, which is crucial for planning and allocating healthcare resources. Many previous
13 studies on the rates of all types of lumbar surgery come from the USA [2, 4, 7, 9]. There are
14 also studies from Germany [6], United Kingdom [10], Sweden [3], and Denmark [5], but none
15 from Norway. Moreover, none of the published studies provide an overview of *all* types of
16 lumbar spinal surgery including simple surgical procedures such as microsurgical discectomy
17 and/or decompression, and complex procedures such as fusions and disc prosthesis. An
18 overview of all spinal surgery, including complication and reoperation rates, will provide
19 important information for the evaluation of current public health services, as well as the
20 planning of future services.

21 Hence, the primary aim of this study was to investigate the longitudinal trends in
22 hospital discharges of *all* surgical procedures for lumbar spine disorders in Norway from
23 1999 to the end of 2013. Further, length of hospital stay, and rates of complications and
24 reoperations over the 15-year period were investigated.

26 MATERIAL AND METHODS

27 *Design*

28 This was a retrospective, longitudinal, observational study comprising all discharges from
29 Norwegian public hospitals over a 15-year period (1999–2013). Norway (population of 4.46
30 million in 1999 and 5.05 million in 2013) [12] has a national healthcare system divided into

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3 1 four health regions (South-East, West, Middle, and North). Private surgery, primarily day
4 surgery, became available after 2007. It is estimated that currently approximately 7% of all
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7 3 elective spinal surgeries take place in the private sector [13].
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10 4 **Data source**

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13 5 Hospital patient administrative data was retrieved from a national database located at the
14 Norwegian Knowledge Centre for the Health Services. The database was initially established
15 6 as a part of the project “*Post-hospitalization survival rates in Norway as indicators of hospital*
16 7 *quality*”. A detailed description of the methods employed in data collection is published
17 8 elsewhere [14]. Patient administrative data for the period 1999–2009 were extracted
18 9 directly from all Norwegian public hospitals, and, for the period 2010–2013, from the
19 10 Norwegian Patient Registry (NPR). Norwegian hospitals were mandated to submit data to
20 11 the NPR since 2010. Each hospitalization record contains a personal identifier, codes for
21 12 diagnoses, medical procedures, and date and time of admission and discharge. Data from
22 13 the National Registry provided by Statistics Norway made it possible to link the NPR data to
23 14 patients’ age, sex, and municipality of residence. Each entry in the database represents a
24 15 single hospitalization record including diagnoses based on ICD-10 and surgical procedure
25 16 codes based on the NOMESCO Classification of Surgical Procedures (NCSP) [15]. The
26 17 NOMESCO Classification has been used in Norway, Sweden, Denmark, Finland, Iceland and
27 18 Estonia since 1999. The NSCP algorithm used in this study has been validated by the
28 19 Norwegian registry for spine surgery (NORspine) [16] and the Norwegian patient registry
29 20 under the Norwegian Directorate of Health [17].
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45 22 **Patient and Public Involvement**

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48 23 Due to the use of administrative data in this study patients or public were not involved in
49 24 this project.
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52 25 53 26 **Selection of sample and classification of outcome**

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56 27 Inclusion criteria were: age ≥ 18 years and a lumbar spine diagnosis code (ICD-codes from
57 28 M40 to M54). Exclusion criteria were: diagnoses related to the cervical, thoracic, or an
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3 1 unspecified region of the spine, as well as diagnoses indicating cancer, trauma, spinal
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5 2 fractures, pregnancy, spinal infections, and inflammatory diseases.
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8 3 For identifying discharges with *simple* surgical procedures defined as discectomy and/or
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10 4 decompression, the following NCSP ABC codes were used [15]: ABC07, ABC16, ABC26,
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12 5 ABC28, ABC36, ABC40, ABC56, ABC66, and ABC99. The *complex* surgical procedures included
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14 6 procedure codes for fusion surgery (NAG and NAN), disc prosthesis (NAB and NAC), and
15
16 7 revision surgery (NAT and NAU) [15]. Further, NAE, NAF, NAH, NAM, NAT, and NAU
17
18 8 procedure codes were included if coexisting with NCSP codes indicating a complex
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20 9 procedure. This is similar to the algorithm used in the NORspine [16] and the Norwegian
21
22 10 patient registry [17]. A list of all included procedure codes can be delivered by contacting the
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24 11 corresponding author.

25
26 12 *Complications* were identified by the following ICD-10 codes occurring within 30 days
27
28 13 after a discharge: postoperative hematoma (T81.0), post-procedural shock (T81.1),
29
30 14 unintentional puncture/laceration (T81.2), disruption of wound/wound dehiscence (T81.3),
31
32 15 infection following a procedure (T81.4), foreign body accidentally left in body following
33
34 16 procedure (T81.5), acute reaction to foreign body accidentally left during a procedure
35
36 17 (T81.6), vascular complications following a procedure (T81.7), unspecified or other
37
38 18 complications of procedure, either upon initial surgical admission or upon readmission
39
40 19 (T81.8-9), and complications during anesthesia (T88.4-5). NAW (reoperation) and AW
41
42 20 (reoperations of the nervous system) procedure codes that occurred within 30 days after the
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44 21 initial surgery were also classified as *complications*. NAW and AW procedure codes occurring
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46 22 later than 30 days after an initial procedure were classified as *reoperations*.

47 ***Background characteristics***

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50 24 Patient age, gender, length of hospital stay, and number of operations were included. Age
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52 25 was categorized as 18–39 years, 40–59 years, 60–75 years, or >75 years.

53 54 55 26 ***Statistical analyses***

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58 27 Annual surgical incidence rates were calculated per 100,000 inhabitants based on the size of
59
60 28 the total Norwegian population on Jan 1st of each analyzed year, retrieved from Statistics

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3 1 Norway [12]. Surgical incidence rates across age groups, gender, and type of surgery
4 (simple/complex) were compared with χ^2 - and z-tests. Length of hospital stay over the time
5 2 period and in relation to background characteristics was compared using a non-parametric
6 3 Kruskal-Wallis test. Possible associations between complications and background
7 4 characteristics were analyzed using a multivariate logistic regression. All tests were two-
8 5 sided and p-values <0.05 were considered statistically significant. Data analyses were
9 6 performed using SPSS version 25.0 (IBM, Armonk, NY, USA) and STATA version MP15.
10 7
11 8

9 RESULTS

10 A total of 67,855 discharges for 57,081 individual patients were identified. A total of 56,764
11 (83.7%) discharges were for simple surgical procedures and 11,091 (16.3%) discharges were
12 for complex surgical procedures. Most of the complex surgical procedures were fusion
13 surgeries (94.0%). Further, 48,495 individual patients (71.5%) had only one discharge due to
14 spinal surgery. The mean age of the patients was 52.3 (SD 15.9), and 51.4% were men.
15 Background characteristics of all included discharges are presented in Table 1.

16 The median length of hospital stay for all patients undergoing spinal surgery
17 decreased from 7.1 [Inter quartil range (IQR) 6.0] days in 1999 to 3.8 [IQR 4.1] in 2013 (Table
18 1). For those undergoing a complex procedure the median length was nearly double that of
19 those who underwent a simple procedure [8.2 (IQR 4.3) days versus 4.3 (IQR 5.7)]. In the
20 simple surgery group, the length of hospital stay was reduced from a median of 6.2 [IQR 5.0]
21 days in 1999 to 3.1 [IQR 3.1] in 2013, and in the complex surgery group there was a
22 reduction from a median of 11.0 [IQR 6.1] in 1999 to 7.0 [IQR 4.0] in 2013.

24 Insert Table 1 here

25 The annual surgical rate including both simple and complex procedures increased
26 from 77.8 [95%CI (75.2-80.4)] per 100,000 in 1999 to 119.9 [95%CI (107.0-112.8)] in 2013
27 (Fig1). The rate of simple procedures increased by 138% (from 64.3 to 88.9 per 100,000
28 inhabitants for 1999 and 2013, respectively), and the rate of complex procedures increased
29 by 154% (from 13.6 to 21.0 per 100,000). During the 15-year study period, significantly more
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3 1 males underwent simple surgical procedures, whereas more females underwent complex
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5 2 surgical procedures (Fig2).
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8 3 **Insert Fig1 and Fig2 here**
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11 4 Most surgeries were performed on patients aged 40–59 (Fig3). A substantial shift
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13 5 towards operations performed on the older age groups is apparent for both simple and
14
15 6 complex surgery. Among those aged 75 years and above, the rate of simple surgery
16
17 7 increased by more than a factor of five by 2013, reaching 167.8 [154.3-181.3]. A similar shift
18
19 8 was also apparent for the complex procedures. In 1999 only 7.8 [30.3-42.9] operated
20
21 9 patients per 100,000 inhabitants were in the oldest age group, whereas in 2013 this rate had
22
23 10 increased to 36.6 [30.3-42.9]. In the younger age groups, the complex surgery rate remained
24
25 11 stable over the 15-year period.
26

27 12 **Insert Fig3 here**
28

29 13 The occurrence of complications was generally low. During the 15-year period a total
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31 14 of 977 [1.4%, 95% (CI 1.38 – 1.56)] discharges were coded with diagnoses or procedures
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33 15 indicating complications. Of these, 42% occurred during the index stay and 68% underwent
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35 16 reoperation within 30 days. During the 15-year period, there was an increase in reoperations
36
37 17 within 30 days, leading to a large increase in the complication rate, from 0.7% in 1999 to
38
39 18 2.4% in 2013. The multivariate analysis showed that complications were significantly
40
41 19 associated with younger and middle-aged groups, receiving complex surgery, and having an
42
43 20 extended hospital stay (Table 2). There was no statistically significant interaction between
44
45 21 type of surgery (simple vs complex) and length of hospital stay ($p=0.296$), or between age
46
47 22 groups and type of surgery ($p=0.678$).

48
49 23 A total of 10,015 [14.8%, 95% CI (14.5 – 15.0)] discharges were reoperations; 517
50
51 24 [0.8%, 95%CI (0.8 – 0.9)] occurred between 30 and 90 days after the index discharge, 2611
52
53 25 [3.8%, 95%CI (3.7 – 4.0)] between 91 days and 12 months, and 2429 [3.6%, 95%CI (3.5 – 3.7)]
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55 26 between the first and second year. There was a large decrease in the proportion of patients
56
57 27 who received reoperations during the 15-year period: from 21.6% in 1999 to 2.3% in 2013.

58 28 **Insert Table 2 here**
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1 DISCUSSION

2 This national study identified a significant increase in lumbar spine surgery in Norway from
3 1999 to 2013. This increase was most marked in the use of simple surgical procedures like
4 microsurgical discectomy and/or decompression surgery, in particular among elderly
5 patients above 75 years of age. The increase in complex surgery, for the most part fusion
6 surgery, was also most prevalent in the oldest age group.

7 The main strength of the current study is that it covers all spinal surgery procedures
8 carried out in public hospitals in Norway during a 15-year period, except for surgery due to
9 red flag diagnoses (cancer, spinal infections, inflammatory diseases, etc) or trauma. A
10 potential weakness is the risk of misclassification of diagnoses or procedures [18]. The lack
11 of accuracy of diagnosis in such registries has been reported and a systematic review on this
12 field has showed that procedure coding might be more accurate than coding based upon
13 diagnosis [19]. In order to reduce misclassification in the current study, we used the surgical
14 procedure coding in combination with diagnoses when classifying the types of surgery
15 provided. Further, we argue that the risk of misclassification is minor in this study as we
16 assessed two large and different types of spinal surgery (simple versus complex spinal
17 surgery procedures). As expected, the two groups differ with respect to length of hospital
18 stay, complications, and reoperations. We considered classifying spinal surgery into simple
19 and complex procedures useful when reporting trends in spinal surgery within a large and
20 heterogeneous dataset such as hospital administrative data used in this study. Finally, the
21 present material did not include surgery conducted in private clinics/hospitals. Private for-
22 profit hospitals in Norway perform currently approximately 7% of the total number of
23 elective surgical procedures [13], usually as day surgeries. This might have contributed to the
24 increase in complications in public hospitals after private surgery became common in 2007.
25 Private surgery would leave the public hospitals to deal with the more complex cases and
26 procedures during this portion of the study period (2007–2013). A previous study comparing
27 surgery due to disc herniation in public and private hospitals in Norway, showed that
28 patients operated by simple procedures due to lumbar disc herniation in public hospitals
29 were older, and had more comorbidity and other risk factors associated with unfavorable
30 outcomes compared to those operated in the private clinics [20].

1
2
3 1 There are very few published papers that provide an overview of *all* types of spinal
4 2 surgery for lumbar degenerative disorders over an extended time period. Davis [21]
5 3 reported that hospitalization rates for all types of lumbar surgery (including fusion and
6 4 decompression) increased markedly in the USA from 1979 to 1990 . In line with Davis, our
7 5 results demonstrate that more men than women received lumbar spine surgery. Several
8 6 studies on the rates of different types of spinal surgery, such as disc herniation and spinal
9 7 fusion surgery, have been published [2-11, 22]. In general, the findings in the present paper
10 8 are in accordance with the other studies from Scandinavian countries [3, 5] and Germany
11 9 [6], which show increased rates for lumbar disc herniation and spinal stenosis surgery. The
12 10 increase reported in most of the western-European countries is not as large as that found in
13 11 the United States [2, 4, 7, 9, 11] and United Kingdom [10]. Furthermore, these results also fit
14 12 with the overall national healthcare expenditure across countries; in Norway it is 10.4% of
15 13 the GDP, which is similar to other western-European countries such as Germany and
16 14 Sweden, as compared to 17.1% in the United States [23].

15 15 The increase in public lumbar spine surgery in Norway is difficult to understand,
16 16 because only minor increases in the incidence and severity of low back pain have been
17 17 reported in the Norwegian population [24]. However, parts of the increase may be explained
18 18 by the growing number of elderly patients and the increase of hospital surgeons in general
19 19 [25]. In addition, there has been a substantial rise in the use of radiographic examinations
20 20 such as MRI, which might have led to more surgery [26]. The large variations in spinal
21 21 surgery rates may also be explained by a lack of uniform and consensus-based criteria for
22 22 surgery, financial incentives for surgical interventions, and new technology [7-10, 27]. There
23 23 is a large need for high-quality scientific evidence as well as clinical consensus regarding an
24 24 optimal use of resource-demanding investigations and treatments connected to spinal
25 25 disorders. Many of the new technologies and more complex procedures have questionable
26 26 clinical or cost-benefit efficacy. Furthermore, we need stronger scientific evidence with
27 27 respect to the selection of patients to surgical treatment. Both in a clinical and societal
28 28 perspective, non-surgical management might be an appropriate option for patients who
29 29 wish to defer or avoid surgery [28]. The mean complication rate during the study period was
30 30 low, but it increased to 2.4% at the end of the period. This increase may be explained by the
31 31 increase in reoperations within 30 days at the end of the 15-year period. Hence, there seems
32 32 to be a trend towards a shorter timeframe for reoperations by the end of this 15-year time

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3 1 period, a trend which is also reported in the Swedish study of lumbar disc herniation surgery
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5 2 between 1987 and 1999 [3]. Our finding that older patients were less likely to experience
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7 3 complications and receive reoperations compared with the younger and middle-aged groups
8
9 4 is hard to explain. It may be that surgeons are more hesitant to re-operate older people, and
10
11 5 are more selective with respect to other potential risk factors for complications after
12
13 6 surgery.

14 15 7 **CONCLUSION**

16
17 8 There was a substantial increase in spinal surgery in Norway from 1999 to 2013. The rise in
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19 9 number of surgeries, in particular among elderly people, represents a significant workload
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21 10 for hospitals in Norway, and a challenge to the public healthcare system in terms of meeting
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23 11 the increased burden associated with low back pain in an aging population.

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55 27 **Contributors;** MG, JH and JAZ designed the study. MG and MCS analysed the data, and JAZ, OF, LG,
56
57 28 KS, and TKS contributed in discussion of analyses and results presentation. MG wrote the manuscript
58
59 29 with all authors contributing in reading, commenting and approving the final manuscript.
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1 **The original protocol for the study** can be delivered upon request to the corresponding author.

2 **Funding statement:** This work was supported by the South-Eastern Norway Regional Health
3 Authority, grant number 2013030.

4 **Competing interests:** There are no competing interests to be reported in this study.

5 **Any checklist and flow diagram for the appropriate reporting statement:** not relevant

6 **Patient consent:** not required

7 **Ethics approval:** The study was approved by the Norwegian Data Inspectorate (2014/14413) and the
8 Norwegian Regional Ethics Committee (2013/1662, REC south-east D).

9 **Data sharing statement:** It is not possible to participate in data sharing due to ethical reasons and
10 strict data protection regulation in Norway.

11 **Figure legends:**

12 Fig 1. Annual surgery rates per 100,000 population of simple and complex lumbar surgical procedures
13 in Norway from 1999 to 2013.

14 Fig 2. Annual incidence per 100,000 population of simple and complex lumbar surgery in Norway
15 from 1999 to 2013, according to gender.

16 Fig 3. Annual incidence per 100,000 inhabitants of simple (upper figure) and complex (lower figure)
17 surgery in Norway from 1999 to 2013, according to age groups.

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Table 1. Characteristics of 67,855 lumbar spine operations in 57,081 patients in Norway, 1999 to 2013

	No. of operations (%)	Length of stay, days, median [range, IQR]
Age (years)		
18-39	16396 (24.2)	4.2 [724, 4.4]
40-59	28237 (41.7)	6.3 [618, 4.7]
60-75	16160 (23.9)	5.9 [250, 5.8]
> 75	6910 (10.2)	7.2 [226, 6.7]
Missing	152	
Gender		
Male	34902 (51.4)	4.7 [239, 4.4]
Female	32801 (48.3)	6.0 [724, 5.8]
Missing	152	
Year of operation		
1999	3460 (5.1)	7.1 [149.9, 6.0]
2000	3996 (5.9)	7.0 [420, 6.0]
2001	4200 (6.2)	7.0 [138, 6.0]
2002	3865 (5.7)	6.2 [202, 6.0]
2003	4557 (6.7)	6.1 [238, 5.4]
2004	4396 (6.5)	6.1 [250, 5.8]
2005	4572 (6.7)	6.0 [724, 5.3]
2006	4422 (6.5)	5.8 [138, 5.5]
2007	4255 (6.3)	5.1 [618, 5.0]
2008	4164 (6.1)	4.9 [179, 4.3]

Trends in lumbar spine surgery

2009	4449 (6.6)	4.2 [142, 4.9]
2010	5130 (7.6)	4.1 [183, 4.8]
2011	5241 (7.7)	4.0 [210, 4.2]
2012	5597 (8.2)	4.1 [165, 4.2]
2013	5551 (8.2)	3.8 [219, 4.1]
Missing	0	0
Type of surgery		
Simple	56764 (83.7)	4.3 [724, 4.3]
Complex	11091 (16.3)	8.2 [420, 5.7]
No. of operations		
One	57029 (84.0)	5.1 [724, 5.0]
Two	8623 (12.7)	5.2 [618, 5.1]
Three	1602 (2.4)	6.2 [205, 6.0]
≥ Four	467 (0.7)	6.9 [115, 4.4]
Missing	134	134

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Table 2. Multivariate logistic regression model of factors associated with complications (including reoperation within 30 days) due to lumbar spine surgery in Norway from 1999 to 2013 (N=67,855)

	Complications (n=977)	OR	Lower 95% CI	Upper 95% CI
Age (years)				
18-39	250	Ref		
40-59	460	0.97	0.83	1.13
60-75	198	0.61	0.50	0.74
> 75	69	0.51	0.39	0.67
Missing	152			
Gender				
Male	510	Ref		
Female	467	0.90	0.79	1.02
Missing	152			
Length of stay (days)		1.02	1.01	1.02
Type of surgery				
Simple	659	Ref		
Complex	318	2.34	2.04	2.69
Year of operation				
1999	24	Ref		
2000	29	0.98	0.57	1.71
2001	29	1.03	0.60	1.77
2002	33	1.31	0.77	2.22

Trends in lumbar spine surgery

2003	44	1.52	0.92	2.50
2004	41	1.46	0.88	2.43
2005	67	2.23	1.39	3.57
2006	60	2.25	1.40	3.63
2007	58	2.25	1.39	3.64
2008	56	2.29	1.42	3.71
2009	80	3.12	1.97	4.94
2010	89	3.03	1.93	4.78
2011	93	3.03	1.93	4.77
2012	140	4.31	2.79	4.67
2013	134	4.16	2.68	6.44
Missing	134			

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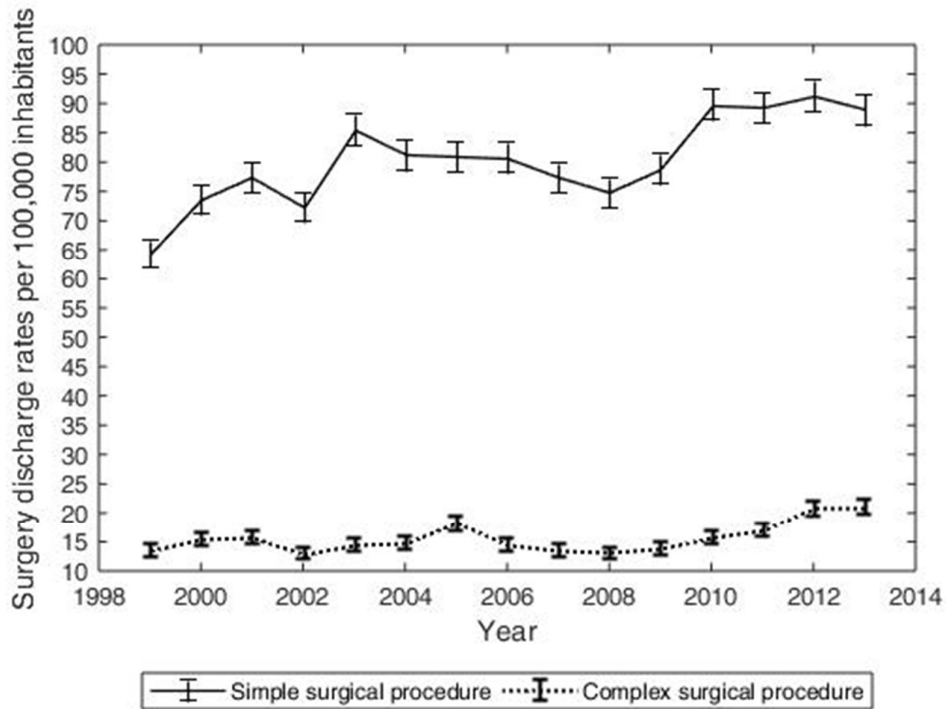


Fig 1. Annual surgery rates per 100,000 population of simple and complex lumbar surgical procedures in Norway from 1999 to 2013.

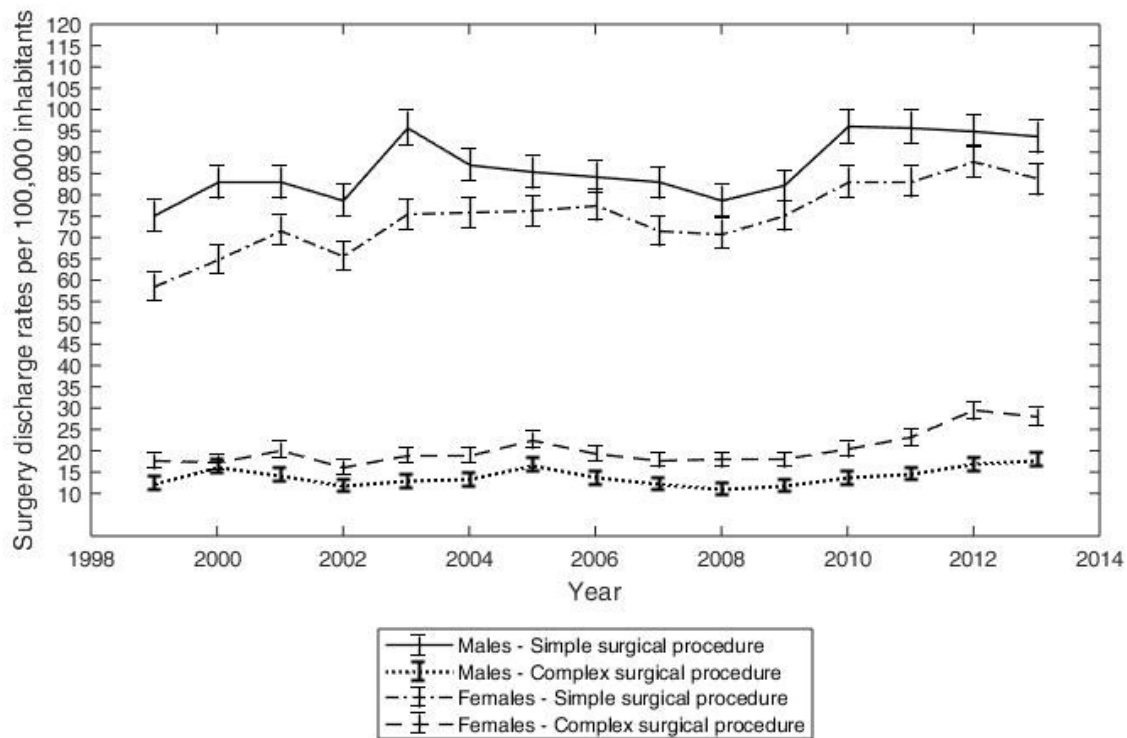


Fig 2. Annual incidence per 100,000 population of simple and complex lumbar surgery in Norway from 1999 to 2013, according to gender.

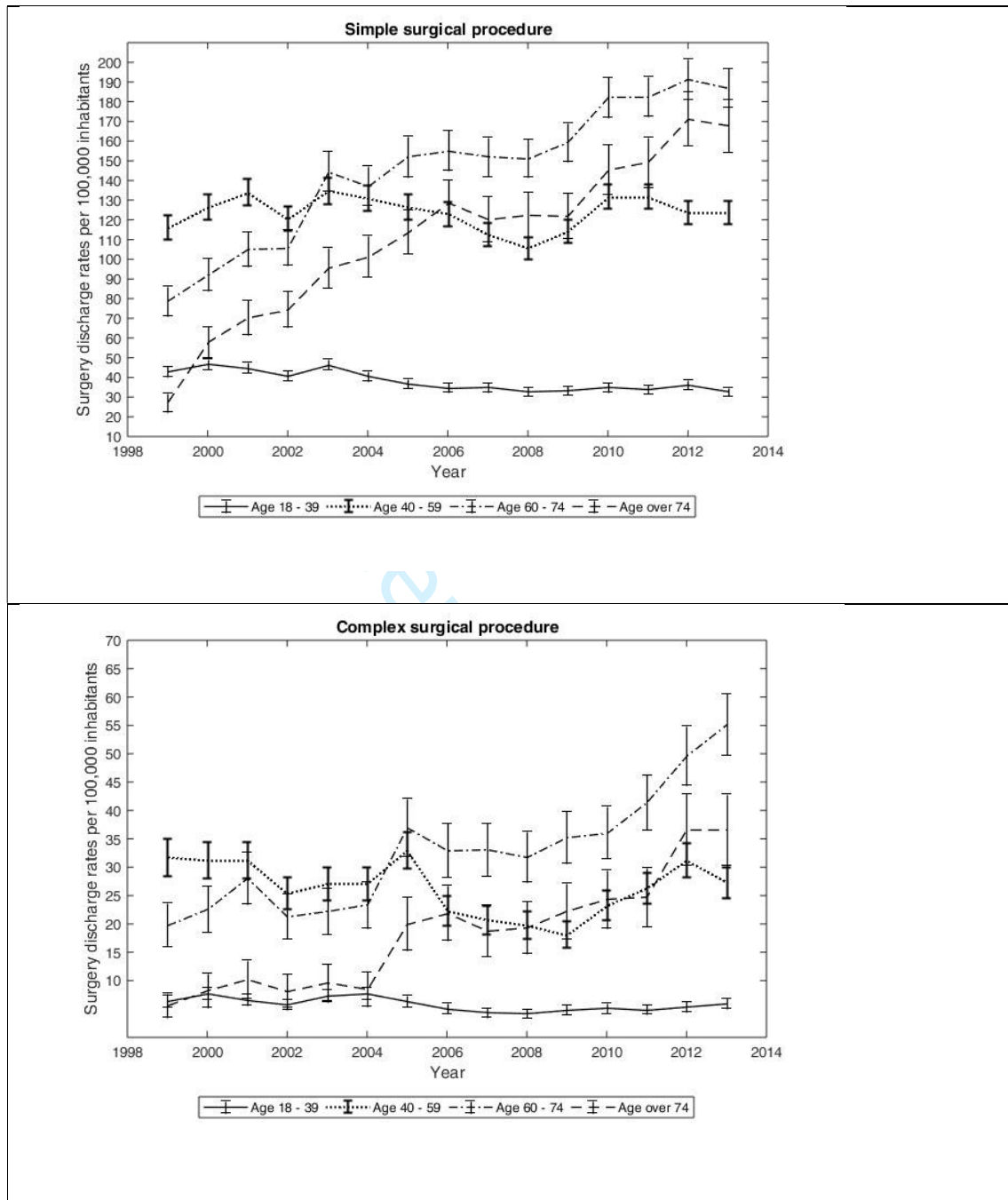


Fig 3. Annual incidence per 100,000 inhabitants of simple (upper figure) and complex (lower figure) surgery in Norway from 1999 to 2013, according to age groups.

STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

	Item No	Recommendation	
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	title abstract
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Introductions p. 3
Objectives	3	State specific objectives, including any prespecified hypotheses	"
Methods			
Study design	4	Present key elements of study design early in the paper	p. 4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	p. 4-5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (b) For matched studies, give matching criteria and number of exposed and unexposed	p. 4 p. 610-22 + p. 51.1-4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	p. 51.5-24
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	p. 46.10-22 + p. 51.5-24
Bias	9	Describe any efforts to address potential sources of bias	p. 61.1-10
Study size	10	Explain how the study size was arrived at	not relevant, all cases included
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	p. 61.1-10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	"
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	p. 61.12-15 not relevant "
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	p. 61.12-17 + Table 1 not relevant p. 6 + Table 1 + Fig 1+2
Outcome data	15*	Report numbers of outcome events or summary measures over time	
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	p. 71.13-26 + Table 2 not relevant

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Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	p. 8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	p. 8
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	p. 8-9
Generalisability	21	Discuss the generalisability (external validity) of the study results	p. 8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	p. 10

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at <http://www.strobe-statement.org>.