

BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email info.bmjopen@bmj.com

BMJ Open

Trends in long-term opioid prescriptions for musculoskeletal conditions in Australian general practice: a national longitudinal study using MedicineInsight, 2012-2018

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-045418
Article Type:	Original research
Date Submitted by the Author:	01-Oct-2020
Complete List of Authors:	Black-Tiong, Sean; The University of Adelaide Faculty of Health and Medical Sciences, Discipline of General Practice, Adelaide Medical School Gonzalez-Chica, David; The University of Adelaide Faculty of Health and Medical Sciences, Discipline of General Practice, Adelaide Medical School; The University of Adelaide, Adelaide Rural Clinical School Stocks, Nigel; The University of Adelaide Faculty of Health Sciences, Discipline of General Practice
Keywords:	Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, PAIN MANAGEMENT, EPIDEMIOLOGY, Back pain < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE, PUBLIC HEALTH

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3 **1 Trends in long-term opioid prescriptions for musculoskeletal conditions in Australian**
4 **2 general practice: a national longitudinal study using MedicineInsight, 2012-2018**

5
6
7 3 Short Title: Trends in long-term opioid prescribing in Australia
8
9

10 4
11
12 5
13
14 6 Sean Black-Tiong¹

15
16 7 sean.black-tiong@adelaide.edu.au
17

18 8 David Alejandro Gonzalez-Chica^{1,2}

19
20 9 david.gonzalez@adelaide.edu.au
21

22 10 Nigel Stocks¹

23
24 11 nigel.stocks@adelaide.edu.au
25
26 12

27
28 13 ¹ Discipline of General Practice, Adelaide Medical School, The University of Adelaide,
29 14 Adelaide, SA, Australia

30 15 ² Adelaide Rural Clinical School, The University of Adelaide, Adelaide, SA, Australia
31
32
33 16

34 17 Corresponding author:

35
36 18 David Alejandro Gonzalez-Chica

37
38 19 Discipline of General Practice, The University of Adelaide, Helen Mayo North building, 109
39 20 Frome Road, Level 1, Room 113. Adelaide, 5005, South Australia, Australia.

40
41 21 E-mail: david.gonzalez@adelaide.edu.au
42

43 22 Phone: +61 8 8313 1631
44
45 23
46
47 24
48
49 25
50
51 26
52
53

54 27 Word count: 3,396
55
56 28
57
58
59
60

1 ABSTRACT

2 **Objective:** Describe trends and patterns in long-term opioid prescriptions among adults with
3 musculoskeletal conditions (MSK).

4 **Design:** Interrupted time-series analysis based on an open cohort study

5 **Setting:** A representative sample of 402 Australian general practices contributing data to the
6 MedicineInsight database.

7 **Participants:** 811,174 patients aged 18+ years with a diagnosis of MSK and three or more
8 consultations in any two consecutive years between 2012 and 2018. Males represented 44.5%
9 of the sample, 28.4% had 65+ years and 1.9% were Aboriginal or Torres Strait Islanders.

10 **Primary and secondary outcome measures:** Annual prevalence and cumulative incidence
11 (%) of long-term opioid prescribing (3+ prescriptions in 90 days) among patients with a MSK.
12 Average duration of these episodes in each year between 2012 and 2018.

13 **Results:** The prevalence of long-term opioid prescribing increased from 5.5% in 2012 to 9.1%
14 in 2018 [annual change OR=1.09 IC95% 1.08-1.09], but a slightly lower incidence was
15 observed in 2018 [3.0% vs 3.6-3.8% in other years; annual change OR=0.99 IC95% 0.98-0.99].
16 The incidence was between 37%-52% higher among practices located in rural Australia or
17 lower socioeconomic areas. Individual risk factors included increasing age (3.4 times higher
18 among those aged 80+ years than the 18-34-year group in 2012, increasing to 4.8% in 2018),
19 identifying as Aboriginal or Torres Strait Islander (1.7-1.9 higher incidence than their peers),
20 or living in disadvantaged areas (36%-57% more likely than among those living in wealthiest
21 areas). Long-term opioid prescriptions lasted in average 287-301 days between 2012-2016,
22 reducing to 229 days in 2017 and 140 days in 2018. A longer duration was observed in practices
23 from more disadvantaged areas and females in all years, except in 2018.

24 **Conclusions:** The continued rise in the prevalence of long-term opioid prescribing is of
25 concern, despite a recent reduction in the incidence and duration of opioid management.

26 **Keywords:** Narcotic Analgesics, Electronic Health Records, Musculoskeletal Diseases,
27 Chronic Pain, Incidence

1 ARTICLE SUMMARY

2 Strengths and limitations of this study

- 3 • A national sample including 135,358 instances of long-term opioid prescriptions (3+ opioid
4 prescriptions in 90 days) and 811,174 adult patients with musculoskeletal conditions from
5 Australian general practice over seven years.
- 6 • Patients and practices from all Australian states, with different socioeconomic and
7 demographic profiles, and from urban and rural regions are included in the study.
- 8 • The study explores the incidence and duration of long-term opioid prescriptions over time
9 and their association with sociodemographic characteristics.
- 10 • Individuals attending multiple clinics for prescriptions are not tracked by MedicineInsight,
11 which may underestimate the real frequency. Moreover, the findings reflect prescribing
12 patterns rather than medication use, and the available data does not allow the investigation
13 of the place/professional that initiated these prescriptions.

1 INTRODUCTION

2 Musculoskeletal conditions (MSK) represent a public health problem worldwide due to their
3 increasing prevalence and contribution to the global burden of disability.^{1 2} In Australia, MSK
4 affect approximately 30% of adults (6.1 million individuals), but its prevalence is even higher
5 in lower socioeconomic groups and the elderly.³⁻⁵ In terms of health costs, MSK account for
6 9% of the total Australian health-care expenditure, representing the fourth most expensive
7 group of diseases in the country.⁶

8 MSK are among the ten most frequent problems managed by general practitioners (GPs).⁴ The
9 principal symptom associated with MSK and the main reason for visiting a GP is chronic pain.³⁻
10 ⁵ As a consequence, MSK represent the leading cause of disability due to the impact of chronic
11 pain on the quality of life.^{1 3 5-7}

12 Countries such as Australia, the United States, Canada, Belgium and the United Kingdom
13 recognise MSK and chronic pain management as a public health priority and have developed
14 national policies aiming to improve prevention and management.^{1 8} The strategies and actions
15 include models of care orientated toward high-value care options for MSK pain management,
16 as well as regular monitoring of their prevalence, patterns of medication use/prescription, and
17 side effects related to the use of these medications.^{1 2 8}

18 The management of chronic pain among patients with MSK can be challenging.⁸⁻¹⁴ Current
19 guidelines recommend non-pharmacological interventions as the primary initial approach for
20 managing MSK pain. At the same time, non-steroidal anti-inflammatory drugs (NSAIDs)
21 represent the first-line pharmacological therapy.^{8 12 15} The use of opioids for pain management
22 is discouraged due to the increased risk of severe side effects, especially in elderly patients or
23 among long-term users.⁸⁻¹⁵ Harmful effects associated with opioid use include sedation, falls,
24 respiratory depression, and death, as well as an increased risk of dependence and diversion.
25 Moreover, long-term use of opioids can potentiate chronic pain mechanisms, reducing the
26 effect of these drugs at standard doses.^{8 13 15}

27 Despite their recognised harmful effects, opioid use has increased in the last decades, especially
28 among high-income countries such as the United States, Canada, the United Kingdom,
29 Germany, Norway, Australia and New Zealand.¹⁶⁻²⁰ However, some of these countries have
30 reported an apparent plateau of opioid use among patients with MSK in recent years.^{14 21-26} In
31 Australia, a systematic review showed a significant rise in opioid use up to 2017, mainly driven

1
2
3
4
5 1 by oxycodone.²⁷ Nonetheless, most data regarding opioid use in Australia analysed data from
6
7 2 the Pharmaceutical Benefits Scheme (PBS) database.²⁷ PBS data represent an efficient and
8
9 3 cost-effective way to monitor dispensed medicines and trends over time²⁸. However, studies
10
11 4 based on dispensed medications tend to underestimate opioid use²⁹, the investigation of patterns
12
13 5 is usually restricted to age and sex distribution, and the use of aggregated data cannot
14
15 6 distinguish between incident users, prevalent users or long-term users.²⁷ Understanding the
16
17 7 determinants and patterns of long-term opioid prescription/use is fundamental to inform
18
19 8 stakeholders and propose targeted interventions aiming to reduce their use for MSK
20
21 9 management.^{9-11 18 27} In Australia, only a few studies have examined opioid prescribing and its
22
23 10 association with sociodemographic characteristics at the local level but not across states or
24
25 11 including urban and rural areas.^{30 31}

26
27 12 In this sense, MedicineInsight is a national longitudinal database established in 2011 by NPS
28
29 13 MedicineWise to collect comprehensive, de-identified patient data from GP electronic medical
30
31 14 records (EMR) across Australia.³² Data from MedicineInsight has previously used to assess
32
33 15 trends and patterns of preventive activities, medication prescriptions and laboratory requests
34
35 16 for acute and chronic conditions managed in Australian general practice.^{5 32-37} This study aims
36
37 17 to utilise MedicineInsight data to estimate the prevalence and cumulative incidence of long-
38
39 18 term opioid prescription among adult patients with MSK. Furthermore, it describes trends in
40
41 19 opioid prescriptions between 2012-2018 and investigates associations with patient and practice
42
43 20 characteristics.

44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 21 22 **METHODS**

23 *Study design*

24 This is an interrupted time-series study analysing data from MedicineInsight, a large general
25
26 24 practice database including patients from 662 general practices (8.2% of all general practices
27
28 25 in Australia) and over 2,700 GPs across Australia.³² Although practices participating in
29
30 26 MedicineInsight were recruited using a non-random process, all Australian states and regions
31
32 27 are represented, and the database includes practices vary in size and type of services offered.
33
34 28 Patients in the database have been found to be comparable with the general population as
35
36 29 measured by sociodemographic variables and clinical conditions.^{5 32} The information extracted
37
38 30

1
2
3
4 1 from MedicineInsight for the present study include EMR dating between 1 January 2011 and
5 2 31 December 2018.

6
7
8 3 Patients within a practice have a unique identifying number which allows all the EMR held in
9 4 the database for an individual to be linked and tracked over time. Patients' EMR are collected
10 5 monthly, de-identified and securely transferred to NPS MedicineWise's data warehouse.
11 6 Routinely collected information includes: demographics (gender, aboriginality, year of birth,
12 7 patient postcode and area of residence), clinical information (diagnoses, reasons for
13 8 consultation, immunisations), prescribed medications (generic and brand names, doses, active
14 9 ingredient and number of repeats reasons for prescription, known allergies, drug reactions),
15 10 pathology test results, clinical measurements (temperature, blood pressure, weight, height,
16 11 waist circumference), and smoking status.³²

12 *Participants*

13 To improve data quality, only practices established for at least two years before the end of the
14 14 analysis period, with recorded data (i.e., diagnosis, reason for encounter, or reason for
15 15 prescription) in at least 10% of clinical encounters, an average of 30 or more prescriptions per
16 16 week and a consistent number of consultations over time (i.e. ratio between the highest and
17 17 lowest number of annual total consultations lower than five, no gaps of more than six weeks in
18 18 the previous two years in practice data) were included.

19 The sample included all regular patients (i.e. individuals with three or more consultations in
20 20 any two consecutive years) aged 18 years or older (Figure 1). The sample was further restricted
21 21 to patients with at least one recorded visit in the 12 months preceding the initial opioid
22 22 prescription and follow-up time ended six months after the last medical encounter, in order to
23 23 differentiate between past and current patients on opioids.²¹ Therefore, despite data in
24 24 MedicineInsight was available since 2011, the analyses were restricted to the period 2012-
25 25 2018. Patients were also excluded if they had a record of cancer or neuropathic pain up to 12
26 26 months before or six months after the start date of the initial long-term opioid prescription
27 27 episode. Therefore, we used data from 811,174 regular adult patients with MSK attending 402
28 28 general practices across Australia.

29 *[FIGURE 1 HERE]*

30 *Musculoskeletal conditions*

1 Data regarding MSK conditions were extracted from the database using previously published
2 algorithms.⁵ The diagnosis, reason for encounter and reason for prescription fields were used
3 to identify patients with a potentially painful MSK condition, as these are typical fields used
4 by GPs to record morbidity in Australian general practice.³² Most general practices use coding
5 systems (i.e. 'Docle', 'Pyefinch' or the International Classification of Primary Care 2), and
6 these were mapped to the Systematized Nomenclature of Medicine - Clinical Terms
7 (SNOMED-CT).^{5 32 38} The list of MSK conditions included i) osteoarthritis, ii) osteoarthrosis,
8 iii) spondylarthritis, iv) fibromyalgia, v) polymyalgia rheumatica, vi) rheumatoid arthritis, vii)
9 psoriatic arthritis, viii) myofascial pain, ix) chronic fatigue syndrome, x) gout, xi) Paget
10 disease, xii) osteoporosis, xiii) tenosynovitis, xiv) chronic back pain and xv) other conditions
11 recorded as 'chronic musculoskeletal pain'. Synonyms and misspellings of these terms were
12 also used, considering that GPs can also use free-text in the completion of the diagnosis. The
13 data extraction algorithms used in this study are available from the authors by request.

14 *Prescription data*

15 Data regarding opioid prescriptions (i.e. codeine, tramadol, tapentadol, oxycodone, morphine,
16 fentanyl, buprenorphine, hydromorphone) were extracted from the prescription dataset using
17 generic and brand names.³⁹ Using recommendations from the literature,^{21 40} a new 'episode of
18 opioid prescription' was defined as a prescription provided to the patient where no opioid was
19 prescribed within six months from the 'end of the last episode'. The 'end date' of an 'episode
20 of opioid prescription' was considered as being 28 days after the last prescription was provided
21 (i.e. in Australia, opioids can be prescribed for up to 28 days without repeats).^{8 39} An episode
22 of 'long-term opioid prescription' was defined as patients receiving i) three or more scripts
23 (including the initiating script) within 90 days of the initial script or ii) a total of 10 or more
24 consecutive scripts with an interval lower than 180 between 'episodes of opioid prescription',
25 even though the first three were not provided within 90 days. An episode of 'long-term opioid
26 prescription' ended when the patient had not received a prescription for opioids for six or more
27 months.^{8 39} A total of 135,358 instances of long-term opioid prescriptions were identified over
28 the period (Figure 1), with 88% of them matching a consultation when the GP recorded a MSK
29 as the reason for diagnosis, reason for encounter and/or reason for prescription (i.e. excluding
30 cancer or neuropathic pain) within a period lasting from 30 days before the initial opioid
31 prescription, or up to 120 days after it.^{8 39}

32 *Data analysis*

1
2
3
4
5 1 The prevalence of long-term opioid prescriptions was estimated as the percentage of regular
6 2 patients with MSK attending the practice that year that were on opioids (i.e. long-term opioid
7 3 prescription), either because these prescriptions started in that year or previous years. The
8 4 cumulative incidence of long-term opioid prescription was estimated as the percentage of
9 5 regular patients with MSK in any year between 2012 and 2018 starting opioids that year (i.e.
10 6 patients “at risk” not on opioids). The average annual change in the prevalence or incidence of
11 7 long term opioid prescription was investigated using logistic regression, and the results
12 8 expressed as odds ratios (OR) with their respective 95% confidence intervals (95% CI).

13
14
15
16
17
18
19 9 The association between sociodemographic characteristics and the incidence of long-term
20 10 opioid prescription was also explored using logistic regression, and the variables were included
21 11 in the models considering two hierarchical levels. The first level included practice
22 12 characteristics: state, rurality (i.e. major cities, inner regional, or outer regional/remote
23 13 Australia) and the practice’s Index of Relative Socioeconomic Advantage and Disadvantage
24 14 [IRSAD, as provided by MedicineInsight (based on the postcode of the practice) and divided
25 15 in quintiles]. IRSAD is a relative indicator of economic and social advantage/disadvantage of
26 16 people and households within an area generated by the Australian Bureau of Statistics and
27 17 based on a range of census variables.⁴¹ Higher IRSAD scores indicate that the practice is
28 18 located in a more advantaged area. The second level included patient characteristics: gender
29 19 (males/females), age in groups (18-34, 35-49, 50-64, 65-79, 80+ years), aboriginality
30 20 (Aboriginal or Torres Strait Islander: No, Yes, not recorded), and the patient’s IRSAD (divided
31 21 in quintiles).

32
33
34
35
36
37
38
39
40
41
42 22 Results of the logistic regression models were expressed as marginal predicted probabilities
43 23 (i.e. adjusted cumulative incidence) instead of odds ratio to facilitate interpretation of the
44 24 results, as many medical doctors, researchers and health policymakers are not familiar with
45 25 these measures of association.⁴² Wald tests for heterogeneity or trend were used to estimate the
46 26 p-values due to the use of clustered data (i.e. practice defined as the cluster).

47
48
49
50
51 27 Quantile regression models were used to investigate the variables associated with the median
52 28 duration (in days) of the long-term opioid prescription among incident cases, considering the
53 29 same levels of adjustment as above.

54
55
56
57 30 All analyses were performed using the statistical software STATA 15.0 (StataCorp, Texas,
58 31 USA) and conditioned to the patient’s probability of being in the sample to minimise selection
59
60

1 bias (i.e. the likelihood of receiving medical treatments or diagnosis increase with the number
2 of visits to the practice).⁴³

3 *Ethics approval*

4 The Human Research Ethics Committee of the University of Adelaide exempted this study of
5 an ethical review as only non-identifiable data was used. Access to the data for this study was
6 approved by the MedicineInsight Data Governance Committee (project 2016–004 and 2019-
7 029).

8 *Patient and public involvement*

9 Patients or the public were involved in the design, or conduct, or reporting, or dissemination
10 plans of our research. The provision of information for the study underwent a formal approval
11 process guided by the MedicineInsight independent external Data Governance Committee that
12 includes GPs, consumer advocates, privacy experts and researchers. Moreover, two of the
13 authors are active GPs regularly attending patients affected by MSK, which also supported the
14 design of the study.

15 **RESULTS**

16 The sample consisted of 811,174 unique regular adult patients with MSK attending one of the
17 MedicineInsight practices between 2012 and 2018 (Figure 1). The total number of regular
18 patients with MSK per year is shown in Figure 2. The sample ranged between 160,834 and
19 299,431 over the period.

20 The overall ‘prevalence’ of long-term opioid prescribing (i.e. patients with MSK on opioids,
21 either because they started that year or in previous years) increased from 5.5% in 2012 to 9.1%
22 in 2018 [annual change OR=1.09 IC95% 1.08-1.09; p-value for trend <0.001]. Figure 2 shows
23 the increase was related to a higher proportion of patients starting opioids in previous years,
24 rather than a rise in incident cases (i.e. those who started opioids in that year).

25 *[FIGURE 2 HERE]*

26 Table 1 shows males represented 44.5% of the sample, 28.4% had 65+ years, and 1.9% were
27 Aboriginal or Torres Strait Islanders. Individuals from different socioeconomic settings were
28 all represented in the study, and 40.0% were for regional or remote areas. The cumulative
29 incidence of long-term opioid prescription (i.e. excluding those who were already on opioids)

1
2
3
4
5 1 among regular patients with a MSK ranged between 3.6% and 3.8% between 2012-2016,
6
7 2 dropping to 3.0% in 2018 [3.0%; annual change OR=0.99 IC95% 0.98-0.99; p-value for trend
8
9 3 0.002].

10
11 4 The same table also shows the sociodemographic factors associated with the cumulative
12
13 5 incidence of long-term opioid prescribing. In any investigated year, the cumulative incidence
14
15 6 was 37%-52% higher among individuals attending practices located in rural Australia or areas
16
17 7 with a very low IRSAD, compared to those attending practices located in major cities or areas
18
19 8 with a higher IRSAD. Individual risk factors associated with a higher incidence of long-term
20
21 9 opioid prescribing included increasing age (3.4 times higher among those aged 80+ years than
22
23 10 the 18-34-year group in 2012, increasing to 4.8% in 2018), identifying as an Aboriginal or
24
25 11 Torres Strait Islander (1.7-1.9 higher incidence than their peers), or living in areas with a lower
26
27 12 IRSAD (36%-57% more likely than among those living in wealthiest areas). Neither the state
28
29 13 where the practice was located nor the patient's gender was associated with this outcome.

30
31
32
33
34
35
36
37
38
39
40
41
42 [TABLE 1 HERE]

43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408
409
410
411
412
413
414
415
416
417
418
419
420
421
422
423
424
425
426
427
428
429
430
431
432
433
434
435
436
437
438
439
440
441
442
443
444
445
446
447
448
449
450
451
452
453
454
455
456
457
458
459
460
461
462
463
464
465
466
467
468
469
470
471
472
473
474
475
476
477
478
479
480
481
482
483
484
485
486
487
488
489
490
491
492
493
494
495
496
497
498
499
500
501
502
503
504
505
506
507
508
509
510
511
512
513
514
515
516
517
518
519
520
521
522
523
524
525
526
527
528
529
530
531
532
533
534
535
536
537
538
539
540
541
542
543
544
545
546
547
548
549
550
551
552
553
554
555
556
557
558
559
560
561
562
563
564
565
566
567
568
569
570
571
572
573
574
575
576
577
578
579
580
581
582
583
584
585
586
587
588
589
590
591
592
593
594
595
596
597
598
599
600
601
602
603
604
605
606
607
608
609
610
611
612
613
614
615
616
617
618
619
620
621
622
623
624
625
626
627
628
629
630
631
632
633
634
635
636
637
638
639
640
641
642
643
644
645
646
647
648
649
650
651
652
653
654
655
656
657
658
659
660
661
662
663
664
665
666
667
668
669
670
671
672
673
674
675
676
677
678
679
680
681
682
683
684
685
686
687
688
689
690
691
692
693
694
695
696
697
698
699
700
701
702
703
704
705
706
707
708
709
710
711
712
713
714
715
716
717
718
719
720
721
722
723
724
725
726
727
728
729
730
731
732
733
734
735
736
737
738
739
740
741
742
743
744
745
746
747
748
749
750
751
752
753
754
755
756
757
758
759
760
761
762
763
764
765
766
767
768
769
770
771
772
773
774
775
776
777
778
779
780
781
782
783
784
785
786
787
788
789
790
791
792
793
794
795
796
797
798
799
800
801
802
803
804
805
806
807
808
809
810
811
812
813
814
815
816
817
818
819
820
821
822
823
824
825
826
827
828
829
830
831
832
833
834
835
836
837
838
839
840
841
842
843
844
845
846
847
848
849
850
851
852
853
854
855
856
857
858
859
860
861
862
863
864
865
866
867
868
869
870
871
872
873
874
875
876
877
878
879
880
881
882
883
884
885
886
887
888
889
890
891
892
893
894
895
896
897
898
899
900
901
902
903
904
905
906
907
908
909
910
911
912
913
914
915
916
917
918
919
920
921
922
923
924
925
926
927
928
929
930
931
932
933
934
935
936
937
938
939
940
941
942
943
944
945
946
947
948
949
950
951
952
953
954
955
956
957
958
959
960
961
962
963
964
965
966
967
968
969
970
971
972
973
974
975
976
977
978
979
980
981
982
983
984
985
986
987
988
989
990
991
992
993
994
995
996
997
998
999
1000

15 The average duration of the long-term opioid prescriptions among incident cases ranged from
16
17 287 to 301 days between 2012-2016, reducing to 229 days in 2017 and 140 days in 2018 (Table
18
19 2). The most consistent pattern observed over the investigated years was an increased duration
20
21 of prescribing among individuals attending practices located in lower socioeconomic areas (i.e.
22
23 up to 152 days longer than those attending practices located in the wealthiest areas) or females
24
25 (i.e. up to 77 days longer than in males). However, these differences were not evident in 2018.

26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42 [TABLE 2 HERE]

43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349 350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 471 472 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517 518 519 520 521 522 523 524 525 526 527 528 529 530 531 532 533 534 535 536 537 538 539 540 541 542 543 544 545 546 547 548 549 550 551 552 553 554 555 556 557 558 559 560 561 562 563 564 565 566 567 568 569 570 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600 601 602 603 604 605 606 607 608 609 610 611 612 613 614 615 616 617 618 619 620 621 622 623 624 625 626 627 628 629 630 631 632 633 634 635 636 637 638 639 640 641 642 643 644 645 646 647 648 649 650 651 652 653 654 655 656 657 658 659 660 661 662 663 664 665 666 667 668 669 670 671 672 673 674 675 676 677 678 679 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 695 696 697 698 699 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732 733 734 735 736 737 738 739 740 741 742 743 744 745 746 747 748 749 750 751 752 753 754 755 756 757 758 759 760 761 762 763 764 765 766 767 768 769 770 771 772 773 774 775 776 777 778 779 780 781 782 783 784 785 786 787 788 789 790 791 792 793 794 795 796 797 798 799 800 801 802 803 804 805 806 807 808 809 810 811 812 813 814 815 816 817 818 819 820 821 822 823 824 825 826 827 828 829 830 831 832 833 834 835 836 837 838 839 840 841 842 843 844 845 846 847 848 849 850 851 852 853 854 855 856 857 858 859 860 861 862 863 864 865 866 867 868 869 870 871 872 873 874 875 876 877 878 879 880 881 882 883 884 885 886 887 888 889 890 891 892 893 894 895 896 897 898 899 900 901 902 903 904 905 906 907 908 909 910 911 912 913 914 915 916 917 918 919 920 921 922 923 924 925 926 927 928 929 930 931 932 933 934 935 936 937 938 939 940 941 942 943 944 945 946 947 948 949 950 951 952 953 954 955 956 957 958 959 960 961 962 963 964 965 966 967 968 969 970 971 972 973 974 975 976 977 978 979 980 981 982 983 984 985 986 987 988 989 990 991 992 993 994 995 996 997 998 999 1000 22 **DISCUSSION**

23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
61
62
63
64
65
66
67
68
69
70
71
72
73
74
75
76
77
78
79
80
81
82
83
84
85
86
87
88
89
90
91
92
93
94
95
96
97
98
99
100
101
102
103
104
105
106
107
108
109
110
111
112
113
114
115
116
117
118
119
120
121
122
123
124
125
126
127
128
129
130
131
132
133
134
135
136
137
138
139
140
141
142
143
144
145
146
147
148
149
150
151
152
153
154
155
156
157
158
159
160
161
162
163
164
165
166
167
168
169
170
171
172
173
174
175
176
177
178
179
180
181
182
183
184
185
186
187
188
189
190
191
192
193
194
195
196
197
198
199
200
201
202
203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230
231
232
233
234
235
236
237
238
239
240
241
242
243
244
245
246
247
248
249
250
251
252
253
254
255
256
257
258
259
260
261
262
263
264
265
266
267
268
269
270
271
272
273
274
275
276
277
278
279
280
281
282
283
284
285
286
287
288
289
290
291
292
293
294
295
296
297
298
299
300
301
302
303
304
305
306
307
308
309
310
311
312
313
314
315
316
317
318
319
320
321
322
323
324
325
326
327
328
329
330
331
332
333
334
335
336
337
338
339
340
341
342
343
344
345
346
347
348
349
350
351
352
353
354
355
356
357
358
359
360
361
362
363
364
365
366
367
368
369
370
371
372
373
374
375
376
377
378
379
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400
401
402
403
404
405
406
407
408

1
2
3
4
5 1 or more disadvantaged areas. Finally, a longer duration of these episodes was observed among
6
7 2 females or patients attending practices in lower socioeconomic areas.

8
9 3 The increase in the prevalence of long-term opioid prescriptions is consistent with other
10
11 4 Australian studies using PBS data (9, 22).^{9 20 27} Some authors suggest the increase in opioid
12
13 5 use/prescription is related to the ageing population with higher rates of MSK, availability of
14
15 6 slow-release opioid formulations and aggressive marketing of opioids by pharmaceutical
16
17 7 companies.^{1 2 21} Moreover, the observed increase in Australia is probably related to the
18
19 8 prescription of potent opioids. A previous study using PBS data found that between 2006-2015
20
21 9 weaker opioid use remained stable or declined, while there was a 238% increase in persons
22
23 10 dispensed only strong opioids.²⁰ Nonetheless, there is evidence that long-term opioid
24
25 11 prescription for patients with MSK in the UK and North America reached a plateau around
26
27 12 2009-2011.^{21 22 44}

28
29 13 Previous studies have also reported the incidence of opioid use has either decreased or
30
31 14 remained unchanged in recent years, despite a rise in the prevalence.⁴⁵⁻⁴⁷ In consonance with
32
33 15 these studies, we found a steady incidence between 2012-2016, followed by a lower incidence
34
35 16 in 2018. Interestingly, the duration of long-term opioid prescription also declined in newly
36
37 17 incident cases in 2017 and 2018 compared to the previous five years. Although results for
38
39 18 2018 might reflect an insufficient follow-up of incident cases in that year, it would not explain
40
41 19 the findings observed in 2017. Recent education strategies among GPs and health policy
42
43 20 changes may have helped reduced opioid initiation and duration when prescribing to someone
44
45 21 affected by MSK.^{8 13 15 39} However, the increasing prevalence between 2012-2018 with an
46
47 22 upsurging number of patients starting opioids in previous years (i.e. 'prevalent' cases) may
48
49 23 suggest insufficient pro-active opioid de-prescribing is being undertaken. Factors such as
50
51 24 limited time of clinicians, insufficient training on de-prescribing, or restricted access to
52
53 25 resources for monitoring patients using opioids are recognised barriers that affect strategies
54
55 26 aiming to improve opioid prescription practices in primary care.⁴⁸

56
57 27 Our finding that the elderly, patients living in lower socioeconomic areas, attending practices
58
59 28 located in more disadvantaged settings or from rural and remote Australia have higher rates of
60
1 long-term opioid prescription is consistent with British and American studies,^{21 22 49} as well as
2 with results based on PBS data.^{9 30 31} These groups are also more likely to be affected by chronic
3 MSK conditions^{5 21}. Perhaps a maldistribution of support services or access to tertiary based

1
2
3
4
5 1 pain clinics could partially explain these differences⁴⁸, but further studies would be necessary
6
7 2 to investigate the underlying causes in the Australian context.

8 9 3 **Strengths and limitations**

10
11 4 The study has significant strengths: a national sample including adult patients of all age groups,
12
13 5 ethnicity, or sex, and practices from all Australian states, socioeconomic areas, or remoteness.
14
15 6 Despite the novelty in the use of a national general practice database that allows the
16
17 7 identification of patients with MSK and the reason for opioid prescription, differentiates
18
19 8 between incident and prevalent cases, and provides data on different associated factors, some
20
21 9 limitations have to be recognised. First, our study did not distinguish between the strength of
22
23 10 preparations (i.e. presented as either morphine equivalent doses or defined daily dose).
24
25 11 However, previous studies found that up to 40% of the dispensed pain medications for non-
26
27 12 cancer pain are potent opioids, and their use has increased over the years.^{14 17 20} Second,
28
29 13 individuals attending multiple clinics for prescriptions are not tracked by MedicineInsight, and
30
31 14 this may underestimate the real frequency of long-term opioid prescriptions. However, the
32
33 15 observed trends and associations are consistent with the available literature.^{9 20-22 27 44} Third,
34
35 16 the place/professional that initiated the prescriptions (e.g. Emergency Department, hospital,
36
37 17 private specialist) cannot be investigated. Nonetheless, according to PBS data, half of the
38
39 18 opioids prescribed in Australia are initiated by general practitioners¹⁷ and most patients with
40
41 19 chronic pain requiring long-term opioid prescriptions are managed in primary care settings.⁴⁸
42
43 20 Finally, medicine-use information from MedicineInsight relates to records of GP prescribing,
44
45 21 and not all prescriptions and repeats will be dispensed or taken by the patient. Therefore, results
46
47 22 from this study reflect prescription patterns rather than opioid use.

48 49 23 **CONCLUSION**

50
51 24 The overall prevalence of long-term opioid prescribing for MSK conditions has increased in
52
53 25 Australia between 2012 and 2018, despite a lower incidence and duration of these prescriptions
54
55 26 in the last couple of years. This trend towards an increase in the prevalence of long-term opioid
56
57 27 prescribing is of great concern, as current literature reports an overall escalation in the rates of
58
59 28 opioid harms and deaths.^{8 9 13 15} Our study highlights the need for ongoing efforts to reduce the
60
61 29 opioid burden, especially among those living and attending practices in more disadvantaged
62
63 30 areas and considering the higher risk of adverse effect in elderly patients. This should come
64
65 31 not only by reducing opioid initiation but also by proactively de-prescribing for suitable
66

1
2
3
4 1 patients.^{8 13} While GPs are in an optimal position for this role⁴⁸, opioid stewardship is the
5
6 2 responsibility of all prescribing medical practitioners and allied health professionals dealing
7
8 3 with MSK pain management.
9

10 4
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1
2
3
4
5 16
7 **2 ACKNOWLEDGEMENTS**8
9 3 The authors acknowledge NPS MedicineWise for their support in the development of this
10 4 research.11
12
13 **5 AUTHOR CONTRIBUTIONS**14
15 6 All authors made significant contributions to the manuscript and are responsible for its content.
16 7 NS and SBT conceived the idea and planned this study. DGC was responsible for data
17 8 extraction and analysis, interpreting and presenting the results. SBT and DGC wrote the first
18 9 draft and the revisions. NS contributed to the manuscript refinement. All authors have read and
19 10 approved the final manuscript.20
21
22 **11 FUNDING**23
24 12 This research received no specific grant from any funding agency in the public, commercial or
25 13 not-for-profit sectors.26
27
28 **14 COMPETING INTERESTS**29
30 15 None declared.31
32
33 **16 ETHICS APPROVAL**34
35 17 The Human Research Ethics Committee of the University of Adelaide exempted this study of
36 18 an ethical review as only non-identifiable data was used. Access to the data for this study was
37 19 approved by the MedicineInsight Data Governance Committee (project 2016–004 and 2019-
38 20 029).39
40
41 **21 DATA SHARING STATEMENT**42
43 22 No additional data are available, as the original dataset belongs to a third party.
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Blyth FM, Briggs AM, Schneider CH, et al. The Global Burden of Musculoskeletal Pain-Where to From Here? *Am J Public Health* 2019;109(1):35-40. doi: 10.2105/AJPH.2018.304747 [published Online First: 2018/11/30]
2. Briggs AM, Shiffman J, Shawar YR, et al. Global health policy in the 21st century: Challenges and opportunities to arrest the global disability burden from musculoskeletal health conditions. *Best Pract Res Clin Rheumatol* 2020;101549. doi: 10.1016/j.berh.2020.101549 [published Online First: 2020/07/28]
3. Australian Institute of Health and Welfare. Arthritis and other musculoskeletal conditions across the life stages. Canberra: AIHW; 2014. [cited 2019 Sep 20]. Available from: <http://www.aihw.gov.au/publication-detail/?id=60129547059>
4. Cooke G, Valenti L, Glasziou P, et al. Common general practice presentations and publication frequency. *Aust Fam Physician* 2013;42(1-2):65-8. [published Online First: 2013/03/27]
5. Gonzalez-Chica DA, Vanlint S, Hoon E, et al. Epidemiology of arthritis, chronic back pain, gout, osteoporosis, spondyloarthropathies and rheumatoid arthritis among 1.5 million patients in Australian general practice: NPS MedicineWise MedicineInsight dataset. *BMC Musculoskelet Disord* 2018;19(1):20. doi: 10.1186/s12891-018-1941-x [published Online First: 2018/01/20]
6. Australian Institute of Health and Welfare. Health-care expenditure on arthritis and other musculoskeletal conditions 2008–09. Canberra: AIHW; 2014. [cited 2019 Sep 13]. Available from: <http://www.aihw.gov.au/publication-detail/?id=60129548392>.
7. Gonzalez-Chica DA, Hill CL, Gill TK, et al. Individual diseases or clustering of health conditions? Association between multiple chronic diseases and health-related quality of life in adults. *Health Qual Life Outcomes* 2017;15(1):244. doi: 10.1186/s12955-017-0806-6 [published Online First: 2017/12/23]
8. Pain Australia. National Pain Strategy, Pain Management for all Australians, Australia.: Pain Australia; 2014. [cited 2019 Aug 16]. Available from: <http://www.painaustralia.org.au/improving-policy/national-pain-strategy>.
9. Australian Institute of Health and Welfare. Opioid harm in Australia: and comparisons between Australia and Canada. Canberra: AIHW; 2018. [cited 2020 Jun 05]. Available from: <https://www.aihw.gov.au/reports/illicit-use-of-drugs/opioid-harm-in-australia/contents/table-of-contents>.
10. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA* 2011;305(13):1315-21. doi: 10.1001/jama.2011.370 [published Online First: 2011/04/07]
11. Ray WA, Chung CP, Murray KT, et al. Prescription of Long-Acting Opioids and Mortality in Patients With Chronic Noncancer Pain. *JAMA* 2016;315(22):2415-23. doi: 10.1001/jama.2016.7789 [published Online First: 2016/06/15]

- 1 12. Krebs EE, Gravely A, Nugent S, et al. Effect of Opioid vs Nonopioid Medications on Pain-Related
2 Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE
3 Randomized Clinical Trial. *JAMA* 2018;319(9):872-82. doi: 10.1001/jama.2018.0899 [published
4 Online First: 2018/03/07]
- 5 13. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain —
6 United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49; 2016. [cited 2020 Mar 05].
7 Available from <http://dx.doi.org/10.15585/mmwr.rr6501e1>.
- 8 14. Ashaye T, Hounsome N, Carnes D, et al. Opioid prescribing for chronic musculoskeletal pain in
9 UK primary care: results from a cohort analysis of the COPERS trial. *BMJ Open* 2018;8(6):e019491.
10 doi: 10.1136/bmjopen-2017-019491 [published Online First: 2018/06/09]
- 11 15. The Royal Australian College of General Practitioners. Guideline for the management of knee and
12 hip osteoarthritis. 2nd edn. East Melbourne, Vic: RACGP; 2018. [cited 2020 Apr 03]. Available from:
13 [https://www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/guideline-for-the-](https://www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/guideline-for-the-management-of-knee-and-hip-0a-2nd-edition.pdf)
14 [management-of-knee-and-hip-0a-2nd-edition.pdf](https://www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/guideline-for-the-management-of-knee-and-hip-0a-2nd-edition.pdf).
- 15 16. La Frenais FL, Bedder R, Vickerstaff V, et al. Temporal Trends in Analgesic Use in Long-Term
16 Care Facilities: A Systematic Review of International Prescribing. *J Am Geriatr Soc* 2018;66(2):376-
17 82. doi: 10.1111/jgs.15238 [published Online First: 2017/12/24]
- 18 17. Lalic S, Ilomaki J, Bell JS, et al. Prevalence and incidence of prescription opioid analgesic use in
19 Australia. *Br J Clin Pharmacol* 2019;85(1):202-15. doi: 10.1111/bcp.13792 [published Online First:
20 2018/10/20]
- 21 18. Manchikanti L, Sanapati J, Benyamin RM, et al. Reframing the Prevention Strategies of the Opioid
22 Crisis: Focusing on Prescription Opioids, Fentanyl, and Heroin Epidemic. *Pain Physician*
23 2018;21(4):309-26. [published Online First: 2018/07/27]
- 24 19. Shipton EA, Shipton EE, Shipton AJ. A Review of the Opioid Epidemic: What Do We Do About
25 It? *Pain Ther* 2018;7(1):23-36. doi: 10.1007/s40122-018-0096-7 [published Online First: 2018/04/07]
- 26 20. Karanges EA, Buckley NA, Brett J, et al. Trends in opioid utilisation in Australia, 2006-2015:
27 Insights from multiple metrics. *Pharmacoepidemiol Drug Saf* 2018;27(5):504-12. doi:
28 10.1002/pds.4369 [published Online First: 2017/12/28]
- 29 21. Bedson J, Chen Y, Hayward RA, et al. Trends in long-term opioid prescribing in primary care
30 patients with musculoskeletal conditions: an observational database study. *Pain* 2016;157(7):1525-31.
31 doi: 10.1097/j.pain.0000000000000557 [published Online First: 2016/03/24]
- 32 22. Curtis JR, Xie F, Smith C, et al. Changing Trends in Opioid Use Among Patients With Rheumatoid
33 Arthritis in the United States. *Arthritis Rheumatol* 2017;69(9):1733-40. doi: 10.1002/art.40152
34 [published Online First: 2017/06/22]

- 1
2
3
4 1 23. Fernandes K, Martins D, Juurlink D, et al. High-Dose Opioid Prescribing and Opioid-Related
5 Hospitalization: A Population-Based Study. *PLoS One* 2016;11(12):e0167479. doi:
6 10.1371/journal.pone.0167479 [published Online First: 2016/12/16]
7
8 24. Larochelle MR, Zhang F, Ross-Degnan D, et al. Trends in opioid prescribing and co-prescribing of
9 sedative hypnotics for acute and chronic musculoskeletal pain: 2001-2010. *Pharmacoepidemiol Drug*
10 *Saf* 2015;24(8):885-92. doi: 10.1002/pds.3776 [published Online First: 2015/04/25]
11
12 25. Steinman MA, Komaiko KD, Fung KZ, et al. Use of opioids and other analgesics by older adults in
13 the United States, 1999-2010. *Pain Med* 2015;16(2):319-27. doi: 10.1111/pme.12613 [published Online
14 First: 2014/10/30]
15
16 26. Woodard D, Van Demark RE, Jr. The Opioid Epidemic in 2017: Are We Making Progress? *S D*
17 *Med* 2017;70(10):467-71. [published Online First: 2017/09/29]
18
19 27. Donovan PJ, Arroyo D, Pattullo C, et al. Trends in opioid prescribing in Australia: a systematic
20 review. *Aust Health Rev* 2020;44(2):277-87. doi: 10.1071/AH18245 [published Online First:
21 2020/04/04]
22
23 28. Hollingworth SA, Symons M, Khatun M, et al. Prescribing databases can be used to monitor trends
24 in opioid analgesic prescribing in Australia. *Aust N Z J Public Health* 2013;37(2):132-8. doi:
25 10.1111/1753-6405.12030 [published Online First: 2013/04/05]
26
27 29. Gisev N, Pearson SA, Karanges EA, et al. To what extent do data from pharmaceutical claims under-
28 estimate opioid analgesic utilisation in Australia? *Pharmacoepidemiol Drug Saf* 2018;27(5):550-55.
29 doi: 10.1002/pds.4329 [published Online First: 2017/10/20]
30
31 30. Islam MM, McRae IS, Mazumdar S, et al. Prescription opioid dispensing in New South Wales,
32 Australia: spatial and temporal variation. *BMC Pharmacol Toxicol* 2018;19(1):30. doi:
33 10.1186/s40360-018-0219-0 [published Online First: 2018/06/20]
34
35 31. Islam MM, Wollersheim D. Variation in Prescription Opioid Dispensing across Neighborhoods of
36 Diverse Socioeconomic Disadvantages in Victoria, Australia. *Pharmaceuticals (Basel)* 2018;11(4) doi:
37 10.3390/ph11040116 [published Online First: 2018/11/06]
38
39 32. Busingye D, Gianacas C, Pollack A, et al. Data Resource Profile: MedicineInsight, an Australian
40 national primary health care database. *Int J Epidemiol* 2019;48(6):1741-41h. doi: 10.1093/ije/dyz147
41 [published Online First: 2019/07/12]
42
43 33. Badmus D, Menzies R. Using general practice data to monitor influenza vaccination coverage in
44 the medically at risk: a data linkage study. *BMJ Open* 2019;9(9):e031802. doi: 10.1136/bmjopen-2019-
45 031802 [published Online First: 2019/09/19]
46
47 34. Bernardo CO, Gonzalez-Chica D, Stocks N. Influenza-like illness and antimicrobial prescribing in
48 Australian general practice from 2015 to 2017: a national longitudinal study using the MedicineInsight
49 dataset. *BMJ Open* 2019;9(4):e026396. doi: 10.1136/bmjopen-2018-026396 [published Online First:
50 2019/05/03]
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4
5 1 35. Gonzalez-Chica D, Stocks N. Changes to the frequency and appropriateness of vitamin D testing
6 2 after the introduction of new Medicare criteria for rebates in Australian general practice: evidence from
7 3 1.5 million patients in the NPS MedicineInsight database. *BMJ Open* 2019;9(3):e024797. doi:
8 4 10.1136/bmjopen-2018-024797 [published Online First: 2019/03/11]
9
10 36. Khanam MA, Kitsos A, Stankovich J, et al. Chronic kidney disease monitoring in Australian general
11 5 practice. *Aust J Gen Pract* 2019;48(3):132-37. doi: 10.31128/AJGP-07-18-4630 [published Online
12 6 First: 2019/07/01]
13 7
14 37. Lee CMY, Mnatzaganian G, Woodward M, et al. Sex disparities in the management of coronary
15 8 heart disease in general practices in Australia. *Heart* 2019;105(24):1898-904. doi: 10.1136/heartjnl-
16 9 2019-315134 [published Online First: 2019/07/25]
17 10
18 38. SNOMED International. SNOMED CT; 2020. [cited 2020 Jun 13] Available from:
19 11 <http://www.snomed.org/>.
20 12
21 39. Australian Department of Health. The Pharmaceutical Benefits Scheme. TGA Prescription Opioid
22 13 Regulatory Reforms. Canberra; 2019. [cited 2020 Jan 30]. Available from:
23 14 [https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2019-12/tga-prescription-](https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2019-12/tga-prescription-opioid-regulatory-reforms)
24 15 [opioid-regulatory-reforms](https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2019-12/tga-prescription-opioid-regulatory-reforms).
25 16
26 40. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a
27 17 cohort study. *Ann Intern Med* 2010;152(2):85-92. doi: 10.7326/0003-4819-152-2-201001190-00006
28 18 [published Online First: 2010/01/20]
29 19
30 41. Australian Bureau of Statistics. Census of Population and Housing: Socio-Economic Indexes for
31 20 Areas (SEIFA), Australia. Cat. No. 2033.0.55.001. Canberra; 2018. [cited 2019 May 03]. Available
32 21 from: <http://www.abs.gov.au/ausstats/abs@.nsf/mf/2033.0.55.001>.
33 22
34 42. Tajeu GS, Sen B, Allison DB, et al. Misuse of odds ratios in obesity literature: an empirical analysis
35 23 of published studies. *Obesity (Silver Spring)* 2012;20(8):1726-31. doi: 10.1038/oby.2012.71 [published
36 24 Online First: 2012/03/23]
37 25
38 43. Goldstein BA, Bhavsar NA, Phelan M, et al. Controlling for Informed Presence Bias Due to the
39 26 Number of Health Encounters in an Electronic Health Record. *Am J Epidemiol* 2016;184(11):847-55.
40 27 doi: 10.1093/aje/kww112 [published Online First: 2016/11/18]
41 28
42 44. Han L, Allore H, Goulet J, et al. Opioid dosing trends over eight years among US Veterans with
43 29 musculoskeletal disorders after returning from service in support of recent conflicts. *Ann Epidemiol*
44 30 2017;27(9):563-69 e3. doi: 10.1016/j.annepidem.2017.08.015 [published Online First: 2017/09/12]
45 31
46 45. Fassio V, Aspinall SL, Zhao X, et al. Trends in opioid and nonsteroidal anti-inflammatory use and
47 32 adverse events. *Am J Manag Care* 2018;24(3):e61-e72. [published Online First: 2018/03/20]
48 33
49 46. Mosher HJ, Krebs EE, Carrel M, et al. Trends in prevalent and incident opioid receipt: an
50 34 observational study in Veterans Health Administration 2004-2012. *J Gen Intern Med* 2015;30(5):597-
51 35 604. doi: 10.1007/s11606-014-3143-z [published Online First: 2014/12/19]
52 36
53
54
55
56
57
58
59
60

- 1
2
3
4 1 47. Smolina K, Gladstone EJ, Rutherford K, et al. Patterns and trends in long-term opioid use for non-
5 2 cancer pain in British Columbia, 2005-2012. *Can J Public Health* 2016;107(4-5):e404-e09. doi:
6 3 10.17269/cjph.107.5413 [published Online First: 2016/12/28]
7
8 4 48. Cheatle MD, Barker C. Improving opioid prescription practices and reducing patient risk in the
9 5 primary care setting. *J Pain Res* 2014;7:301-11. doi: 10.2147/jpr.S37306 [published Online First:
10 6 2014/06/27]
11
12 7 49. Mordecai L, Reynolds C, Donaldson LJ, et al. Patterns of regional variation of opioid prescribing
13 8 in primary care in England: a retrospective observational study. *Br J Gen Pract* 2018;68(668):e225-
14 9 e33. doi: 10.3399/bjgp18X695057 [published Online First: 2018/02/15]
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1. Cumulative incidence of long-term opioid prescription for the management of musculoskeletal conditions according to practice and patient's characteristics. regular patients^a aged 18+ years. Australia, 2012-2018.

		Long-term opioids - incidence (%)						
Year		2012	2013	2014	2015	2016	2017	2018
regular patients with a MSK 'at risk'^a		157,528	185,358	210,089	231,961	253,648	281,655	190,074
		3.6	3.6	3.8	3.7	3.8	3.5	3.0
Overall incidence - % (95%CI)		(3.4;3.8)	(3.4;3.8)	(3.6;4.0)	(3.5;3.9)	(3.6;4.0)	(3.4;3.7)	(2.8;3.1)
Practice characteristics^c	% ^d							
State								
NSW	36.2	3.6	3.5	3.8	3.7	3.7	3.4	2.8
VIC	21.5	3.7	3.6	3.9	3.9	3.9	3.7	3.1
QLD	14.3	3.3	3.5	3.8	3.6	3.5	3.6	2.7
WA	11.3	3.7	3.8	3.9	3.8	4.3	4.1	3.5
TAS	10.4	3.3	3.3	3.4	3.4	3.4	3.1	2.8
SA	3.0	3.2	3.8	3.2	3.9	3.7	3.8	2.9
ACT	2.7	6.0	4.6	5.1	4.8	4.2	4.5	3.3
NT	0.6	2.6	3.6	3.5	2.5	3.7	2.6	2.6
Rurality								
Major cities	60.0	3.1	3.2	3.4	3.4	3.3	3.2	2.7
Inner regional	26.7	3.8	4.0	4.0	3.9	4.1	3.9	3.2
Outer regional/Remote	13.3	4.9	4.5	5.0	4.8	5.0	4.5	3.7
IRSAD Quintile								
Very high	25.8	2.8	2.9	3.1	2.9	3.1	2.8	2.4
High	16.7	3.4	3.4	3.4	3.4	3.6	3.4	3.0
Middle	22.8	3.8	3.6	3.9	4.0	4.0	3.9	3.1
Low	15.6	3.8	3.7	4.0	4.0	3.8	3.6	3.0
Very Low	19.1	4.0	4.3	4.5	4.4	4.4	4.1	3.3
Patient's characteristics^e								
Gender								
Male	44.5	3.4	3.4	3.6	3.7	3.7	3.4	3.0

Female	55.5	3.7	3.7	3.9	3.8	3.8	3.6	2.9
Age								
18-34 years	18.9	1.9	2.0	1.8	1.7	1.7	1.5	1.3
35-49 years	23.9	2.9	2.9	3.0	2.9	2.8	2.6	2.2
50-64 years	28.8	3.2	3.1	3.2	3.1	3.2	3.0	2.4
65-79 years	21.9	4.4	4.4	4.6	4.5	4.5	4.2	3.6
80+ years	6.5	6.5	6.5	7.0	7.4	7.6	7.3	6.2
Aboriginal/Torres Strait Islander								
No	77.9	3.6	3.6	3.8	3.8	3.8	3.5	3.0
Yes	1.9	6.5	6.0	6.5	7.3	7.0	6.5	5.3
Not recorded	20.2	3.0	3.1	3.1	3.0	3.3	3.3	2.7
IRSAD Quintile								
Very high	23.9	2.8	2.8	2.9	2.8	3.0	2.8	2.5
High	16.9	3.3	3.4	3.8	3.7	3.6	3.4	2.7
Middle	23.0	3.8	3.6	3.8	4.0	3.8	3.8	3.0
Low	17.3	3.7	3.7	4.0	3.8	4.2	3.7	3.2
Very Low	18.7	4.1	4.4	4.3	4.3	4.4	3.9	3.4

^a At least three consultations in any two consecutive years from 2012 to 2018. Numbers (n) represent the number of regular patients with a musculoskeletal condition in that year, excluding those who were already on opioids (i.e. patients “at risk”)

^b Values in parenthesis represent the 95% confidence intervals of the incidence

^c Logistic regression models with all practice characteristics mutually adjusted. Values in ‘bold’ represent those associations with a p-value <0.01

^d Values represent the sample distribution according to these characteristics

^e Logistic regression models with all patient characteristics mutually adjusted + adjustment for practice characteristics. Values in ‘bold’ represent those associations with a p-value <0.01

MSK: Musculoskeletal condition; IRSAD: Index of Relative Socioeconomic Advantage and Disadvantage.

Table 2. Average time on long-term opioid prescription for the management of musculoskeletal conditions among incident cases according to practice and patient's characteristics. regular patients^a aged 18+ years. Australia, 2012-2018.

	Time on long-term opioids among incident cases (days)						
	2012	2013	2014	2015	2016	2017	2018
Incident cases	5,621	6,647	7,944	8,652	9,572	9,958	5,672
Median duration (95%CI)^b	287 (266;308)	301 (281;321)	295 (279;311)	288 (272;304)	294 (281;307)	229 (221;237)	140 (135;145)
Practice characteristics^c							
State							
NSW	266	299	308	273	292	210	134
VIC	283	309	312	313	268	230	141
QLD	342	243	264	278	297	244	146
WA	294	288	281	333	336	246	141
TAS	339	367	205	367	292	241	138
SA	269	393	255	292	402	214	154
ACT	327	299	431	338	321	267	186
NT	249	683	261	206	237	116	108
Rurality							
Major cities	301	327	288	309	290	221	137
Inner regional	309	313	319	290	316	234	142
Outer regional/Remote	242	243	310	309	284	240	148
IRSAD Quintile							
Very high	203	214	244	203	247	186	128
High	231	300	285	299	263	221	143
Middle	263	319	290	302	320	222	142
Low	393	341	361	341	293	259	145
Very Low	349	346	322	355	333	251	141
Patient's characteristics^d							
Gender							
Male	278	272	272	259	271	211	137
Female	311	349	329	336	323	238	143

Age							
18-34 years	230	361	276	363	247	233	147
35-49 years	335	361	345	327	350	257	154
50-64 years	299	337	320	293	306	221	142
65-79 years	278	257	277	279	242	203	132
80+ years	336	371	326	336	379	249	143
Aboriginal/Torres Strait Islander							
No	302	319	308	303	303	224	139
Yes	442	376	415	405	381	274	158
Not recorded	245	315	278	296	279	232	146
IRSAD Quintile							
Very high	238	287	236	268	277	230	127
High	249	315	258	296	292	218	140
Middle	278	315	306	297	319	233	139
Low	358	333	360	323	303	216	134
Very Low	343	337	343	330	308	232	159

^a At least three consultations in any two consecutive years from 2012 to 2018.

^b Values in parenthesis represent the 95% confidence intervals of the median time on opioids. The corresponding interquartile values are 2012=91-1177; 2013=98-1214; 2014=98-1145; 2015=94-989; 2016=97-759; 2017=91-474; 2018=78-255.

^c Quantile regression models with all practice characteristics mutually adjusted. Values in 'bold' represent those associations with a p-value <0.01

^d Quantile regression models with all patient characteristics mutually adjusted + adjustment for practice characteristics. Values in 'bold' represent those associations with a p-value <0.01

MSK: Musculoskeletal condition; IRSAD: Index of Relative Socioeconomic Advantage and Disadvantage.

1
2
3
4 **Figure 1. Algorithm of data extraction from MedicineInsight database for the diagnosis**
5 **of MSK and opioid prescriptions. Period 2012-2018**
6
7
8

9 **Figure 2. Frequency of long-term opioid prescription for the management of**
10 **musculoskeletal conditions. regular patients^a aged 18+ years. Australia, 2012-2018.**
11 **Number in parenthesis (n) represent the total number of regular patients with a musculoskeletal**
12 **condition in that year from a total of 811,174 regular patients investigated over the whole**
13 **period.**
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

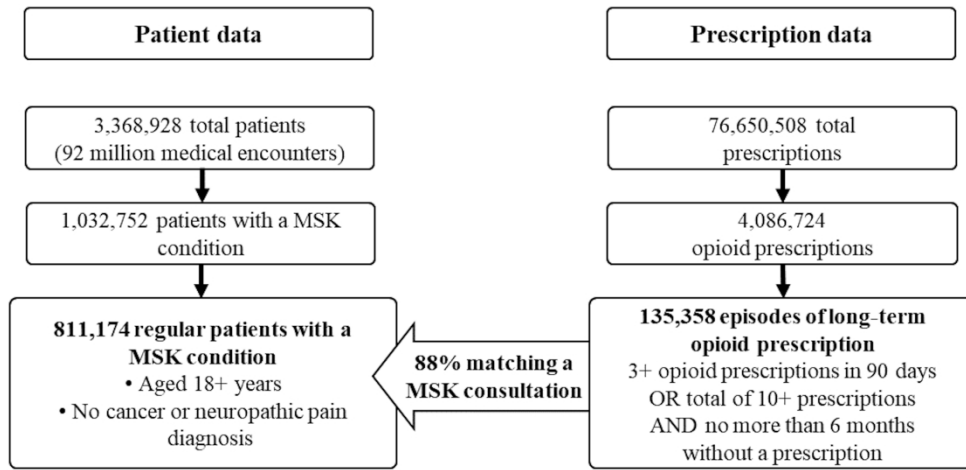


Figure 1. Algorithm of data extraction from MedicineInsight database for the diagnosis of MSK and opioid prescriptions. Period 2012-2018

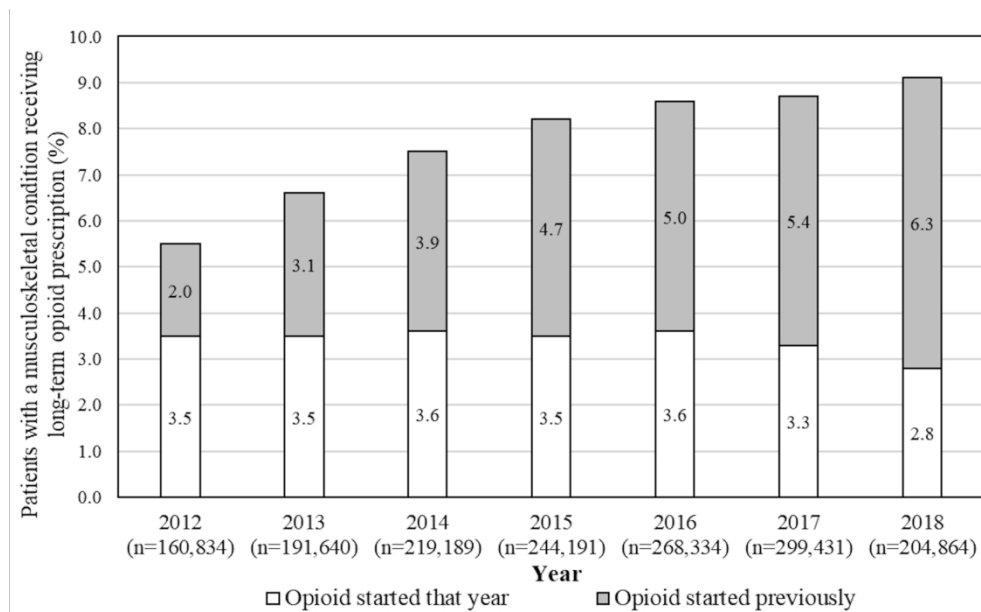


Figure 2. Frequency of long-term opioid prescription for the management of musculoskeletal conditions. regular patients aged 18+ years. Australia, 2012-2018. Number in parenthesis (n) represent the total number of regular patients with a musculoskeletal condition in that year from a total of 811,174 regular patients investigated over the whole period.

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

	Item No	Recommendation	Page No
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	1,2 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
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	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
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	6-7
Bias	9	Describe any efforts to address potential sources of bias	6-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
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	8 - 6-7 - -
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	6,9, Tables 1,2 - Fig.1
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)	9, Table 1 9, Table 1 9, Table 1

1	Outcome data	15*	Report numbers of outcome events or summary measures over time	9, 10, Fig. 2, Tables 1,2
---	--------------	-----	--	------------------------------------

2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For peer review only

1	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	9-10, tables 1,2
2			(b) Report category boundaries when continuous variables were categorized	9-10, tables 1,2
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-10, tables 1,2
4	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
5	Discussion			
6	Key results	18	Summarise key results with reference to study objectives	10
7	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	12
8	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
9	Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
10	Other information			
11	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	13

*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>.

BMJ Open

Trends in long-term opioid prescriptions for musculoskeletal conditions in Australian general practice: a national longitudinal study using MedicineInsight, 2012-2018

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2020-045418.R1
Article Type:	Original research
Date Submitted by the Author:	01-Feb-2021
Complete List of Authors:	Black-Tiong, Sean; The University of Adelaide Faculty of Health and Medical Sciences, Discipline of General Practice, Adelaide Medical School Gonzalez-Chica, David; The University of Adelaide Faculty of Health and Medical Sciences, Discipline of General Practice, Adelaide Medical School; The University of Adelaide, Adelaide Rural Clinical School Stocks, Nigel; The University of Adelaide Faculty of Health and Medical Sciences, Discipline of General Practice
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Pharmacology and therapeutics, Epidemiology, General practice / Family practice, Medical management, Public health
Keywords:	Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, PAIN MANAGEMENT, EPIDEMIOLOGY, Back pain < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE, PUBLIC HEALTH

SCHOLARONE™
Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our [licence](#).

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which [Creative Commons](#) licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

1
2
3
4 **1 Trends in long-term opioid prescriptions for musculoskeletal conditions in Australian**
5 **2 general practice: a national longitudinal study using MedicineInsight, 2012-2018**

6
7
8
9 3 Short Title: Trends in long-term opioid prescribing in Australia

10
11 4
12
13 5
14
15 6 Sean Black-Tiong¹

16
17 7 sean.black-tiong@adelaide.edu.au

18
19 8 David Alejandro Gonzalez-Chica^{1,2}

20
21 9 david.gonzalez@adelaide.edu.au

22
23 10 Nigel Stocks¹

24
25 11 nigel.stocks@adelaide.edu.au

26
27 12
28
29 13 ¹ Discipline of General Practice, Adelaide Medical School, The University of Adelaide,
30 14 Adelaide, SA, Australia

31
32 15 ² Adelaide Rural Clinical School, The University of Adelaide, Adelaide, SA, Australia

33
34 16
35
36 17 Corresponding author:

37
38 18 David Alejandro Gonzalez-Chica

39
40 19 Discipline of General Practice, The University of Adelaide, Helen Mayo North building, 109
41 20 Frome Road, Level 1, Room 113. Adelaide, 5005, South Australia, Australia.

42
43 21 E-mail: david.gonzalez@adelaide.edu.au

44
45 22 Phone: +61 8 8313 1631

46
47 23
48
49 24
50
51 25
52
53 26
54
55 27 Word count: 3,958

1 ABSTRACT

2 **Objective:** Describe trends and patterns in long-term opioid prescriptions among adults with
3 musculoskeletal conditions (MSK).

4 **Design:** Interrupted time-series analysis based on an open cohort study

5 **Setting:** A representative sample of 402 Australian general practices contributing data to the
6 MedicineInsight database.

7 **Participants:** 811,174 patients aged 18+ years with a MSK diagnosis and three or more
8 consultations in any two consecutive years between 2012 and 2018. Males represented 44.5%
9 of the sample, 28.4% had 65+ years, and 1.9% were Aboriginal or Torres Strait Islanders.

10 **Primary and secondary outcome measures:** Annual prevalence and cumulative incidence
11 (%) of long-term opioid prescribing (3+ prescriptions in 90 days) among patients with a MSK.
12 Average duration of these episodes in each year between 2012 and 2018.

13 **Results:** The prevalence of long-term opioid prescribing increased from 5.5% (95%CI 5.2-5.8)
14 in 2012 to 9.1% (95%CI 8.8-9.7) in 2018 [annual change OR=1.09 IC95% 1.08-1.09], but a
15 slightly lower incidence was observed in 2018 [3.0% vs 3.6-3.8% in other years; annual change
16 OR=0.99 IC95% 0.98-0.99]. The incidence was between 37%-52% higher among practices
17 located in rural Australia or lower socioeconomic areas. Individual risk factors included
18 increasing age (3.4 times higher among those aged 80+ years than the 18-34-year group in
19 2012, increasing to 4.8% in 2018), identifying as Aboriginal or Torres Strait Islander (1.7-1.9
20 higher incidence than their peers), or living in disadvantaged areas (36%-57% more likely than
21 among those living in wealthiest areas). Long-term opioid prescriptions lasted in average 287-
22 301 days between 2012-2016, reducing to 229 days in 2017 and 140 days in 2018. A longer
23 duration was observed in practices from more disadvantaged areas and females in all years,
24 except in 2018.

25 **Conclusions:** The continued rise in the prevalence of long-term opioid prescribing is of
26 concern, despite a recent reduction in the incidence and duration of opioid management.

27 **Keywords:** Narcotic Analgesics, Electronic Health Records, Musculoskeletal Diseases,
28 Chronic Pain, Incidence

1 **ARTICLE SUMMARY**

2 **Strengths and limitations of this study**

- 3 • A national sample including 135,358 instances of long-term opioid prescriptions (3+ opioid
4 prescriptions in 90 days) and 811,174 adult patients with musculoskeletal conditions from
5 Australian general practice over seven years.
- 6 • Patients and practices from all Australian states, with different socioeconomic and
7 demographic profiles, and from urban and rural regions are included in the study.
- 8 • The study explores the incidence and duration of long-term opioid prescriptions over time
9 and their association with sociodemographic characteristics.
- 10 • Individuals attending multiple clinics for prescriptions are not tracked by MedicineInsight,
11 which may underestimate the real frequency. Moreover, the findings reflect prescribing
12 patterns rather than medication use, and the available data does not allow the investigation
13 of the place/professional that initiated these prescriptions.

1 INTRODUCTION

2 Musculoskeletal conditions (MSK) represent a public health problem worldwide due to their
3 substantial impact on the quality of life, increasing prevalence, and contribution to the global
4 burden of disability.^{1 2} In Australia, MSK affect approximately 30% of adults (6.1 million
5 individuals), but its prevalence is even higher in lower socioeconomic groups and the elderly.³⁻⁵
6 In terms of health costs, MSK accounted for \$5,690 million in 2008-09, representing 9% of the
7 total Australian health-care expenditure in that year and the fourth most expensive group of
8 diseases in the country.⁶ MSK are among the ten most frequent problems managed by general
9 practitioners (GPs).⁴ The principal symptom associated with these visits is chronic pain.^{1 3 5-7}

10 Countries such as Australia, the United States, Canada, Belgium and the United Kingdom
11 recognise MSK and chronic pain management as a public health priority and have developed
12 national policies aiming to improve prevention and management.^{1 8} The strategies and actions
13 include models of care orientated toward high-value care options for MSK pain management,
14 as well as regular monitoring of their prevalence, patterns of medication use/prescription, and
15 side effects related to the use of these medications.^{1 2 8} Current guidelines recommend non-
16 pharmacological interventions as the primary initial approach for managing MSK pain.
17 Simultaneously, non-steroidal anti-inflammatory drugs (NSAIDs) represent the first-line
18 pharmacological therapy.⁸⁻¹⁰ The use of opioids for pain management is discouraged due to the
19 increased risk of severe side effects, especially in elderly patients or among long-term users.
20 ⁸⁻¹⁵ Harmful effects associated with opioid use include sedation, falls, respiratory depression,
21 and death, as well as an increased risk of dependence and diversion. Moreover, long-term use
22 of opioids can potentiate chronic pain mechanisms, reducing the effect of these drugs at
23 standard doses.^{8 9 14}

24 Despite their recognised harmful effects, opioid use has increased in the last decades, especially
25 among high-income countries such as the United States, Canada, the United Kingdom,
26 Germany, Norway, Australia and New Zealand.¹⁶⁻²⁰ In the United States, for example, the use
27 of opioids (licit and illicit) escalated 10-14 times in the last two decades, while in Australia
28 there was a 238% increase in the number of people receiving potent opioids between 2006 and
29 2015.^{19 20} However, some countries have reported an apparent plateau of opioid use among
30 patients with MSK in recent years.^{15 21-26} In Australia, a systematic review showed a significant
31 rise in opioid use up to 2017, mainly driven by oxycodone.²⁷ Nonetheless, most data regarding
32 opioid use in Australia analysed data from the Pharmaceutical Benefits Scheme (PBS)

1 database.²⁷ PBS data represent an efficient and cost-effective way to monitor dispensed
2 medicines and trends over time²⁸. However, studies based on dispensed medications tend to
3 underestimate opioid use²⁹, the investigation of patterns is usually restricted to age and sex
4 distribution, and the use of aggregated data cannot distinguish between incident users,
5 prevalent users or long-term users.²⁷ Understanding the determinants and patterns of long-term
6 opioid prescription/use is fundamental to inform stakeholders and propose targeted
7 interventions aiming to reduce their use for MSK management.^{11-13 18 27} In Australia, only a
8 few studies have examined opioid prescribing and its association with sociodemographic
9 characteristics at the local level but not across states or including urban and rural areas.^{30 31}

10 In this sense, MedicineInsight is a national longitudinal database established in 2011 by NPS
11 MedicineWise to collect comprehensive, de-identified patient data from GP electronic medical
12 records (EMR) across Australia.³² Data from MedicineInsight has been previously used to
13 assess trends and patterns of preventive activities, medication prescriptions and laboratory
14 requests for acute and chronic conditions managed in Australian general practice.^{5 32-37} This
15 study aims to utilise MedicineInsight data to estimate the prevalence and cumulative incidence
16 of long-term opioid prescriptions among adult patients with MSK. Furthermore, it describes
17 trends in opioid prescriptions between 2012-2018 and investigates associations with patient
18 and practice characteristics.

19 20 **METHODS**

21 *Study design*

22 This is an interrupted time-series study analysing data from MedicineInsight, a large general
23 practice database including patients from 662 general practices (8.2% of all general practices
24 in Australia) and over 2,700 GPs across Australia.³² Although practices participating in
25 MedicineInsight were recruited using a non-random process, all Australian states and regions
26 are represented, and the database includes practices vary in size and type of services offered.
27 Patients in the database have been found to be comparable with the general population as
28 measured by sociodemographic variables and clinical conditions.^{5 32} The information extracted
29 from MedicineInsight for the present study include EMR dating between 1 January 2011 and
30 31 December 2018.

1
2
3
4
5 1 Patients within a practice have a unique identifying number which allows all the EMR held in
6
7 2 the database for an individual to be linked and tracked over time. Patients' EMR are collected
8
9 3 monthly, de-identified and securely transferred to NPS MedicineWise's data warehouse.
10
11 4 Routinely collected information includes: demographics (gender, aboriginality, year of birth,
12
13 5 patient postcode and area of residence), clinical information (diagnoses, reasons for
14
15 6 consultation, immunisations), prescribed medications (generic and brand names, doses, active
16
17 7 ingredient and number of repeats reasons for prescription, known allergies, drug reactions),
18
19 8 pathology test results, clinical measurements (temperature, blood pressure, weight, height,
20
21 9 waist circumference), and smoking status.³²

22 *Participants*

23
24 11 To improve data quality, only practices established for at least two years before the end of the
25
26 12 analysis period, with recorded data (i.e., diagnosis, reason for encounter, or reason for
27
28 13 prescription) in at least 10% of clinical encounters, an average of 30 or more prescriptions per
29
30 14 week and a consistent number of consultations over time (i.e. ratio between the highest and
31
32 15 lowest number of annual total consultations lower than five, no gaps of more than six weeks in
33
34 16 the previous two years in practice data) were included.

35
36 17 The sample included all regular patients (i.e. individuals with three or more consultations in
37
38 18 any two consecutive years) aged 18 years or older (Figure 1). The sample was further restricted
39
40 19 to patients with at least one recorded visit in the 12 months preceding the initial opioid
41
42 20 prescription and follow-up time ended six months after the last medical encounter, in order to
43
44 21 differentiate between past and current patients on opioids.²¹ Therefore, despite data in
45
46 22 MedicineInsight was available since 2011, the analyses were restricted to the period 2012-
47
48 23 2018. Patients were also excluded if they had a record of cancer or neuropathic pain up to 12
49
50 24 months before or six months after the start date of the initial long-term opioid prescription
51
52 25 episode. Therefore, we used data from 811,174 regular adult patients with MSK attending 402
53
54 26 general practices across Australia.

55
56
57 27 *[FIGURE 1 HERE]*

58 *Musculoskeletal conditions*

59
60 29 Data regarding MSK conditions were extracted from the database using previously published
30
31 30 algorithms.⁵ The diagnosis, reason for encounter and reason for prescription fields were used

1 to identify patients with a potentially painful MSK condition, as these are typical fields used
2 by GPs to record morbidity in Australian general practice.³² Most general practices use coding
3 systems (i.e. 'Docle', 'Pyefinch' or the International Classification of Primary Care 2), and
4 these were mapped to the Systematized Nomenclature of Medicine - Clinical Terms
5 (SNOMED-CT).^{5 32 38} The list of MSK conditions included i) osteoarthritis, ii) osteoarthrosis,
6 iii) spondylarthritis, iv) fibromyalgia, v) polymyalgia rheumatica, vi) rheumatoid arthritis, vii)
7 myofascial pain, viii) chronic fatigue syndrome, ix) gout, x) Paget disease, xi) osteoporosis,
8 xii) tenosynovitis, xiii) chronic back pain and xiv) other conditions recorded as 'chronic
9 musculoskeletal pain'. Synonyms and misspellings of these terms were also used, considering
10 that GPs can also use free-text in the completion of the diagnosis. The data extraction
11 algorithms used in this study are available from the authors by request.

12 *Prescription data*

13 Data regarding opioid prescriptions (i.e. codeine, tramadol, tapentadol, oxycodone, morphine,
14 fentanyl, buprenorphine, hydromorphone) were extracted from the prescription dataset using
15 generic and brand names.³⁹ Using recommendations from the literature,^{21 40} a new 'episode of
16 opioid prescription' was defined as a prescription provided to the patient where no opioid was
17 prescribed within six months from the 'end of the last episode'. The 'end date' of an 'episode
18 of opioid prescription' was considered as being 28 days after the last prescription was provided
19 (i.e. in Australia, opioids can be prescribed for up to 28 days without repeats).^{8 39} An episode
20 of 'long-term opioid prescription' was defined as patients receiving i) three or more scripts
21 (including the initiating script) within 90 days of the initial script or ii) a total of 10 or more
22 consecutive scripts with an interval lower than 180 between 'episodes of opioid prescription',
23 even though the first three were not provided within 90 days. An episode of 'long-term opioid
24 prescription' ended when the patient had not received a prescription for opioids for six or more
25 months.^{8 39} A total of 135,358 instances of long-term opioid prescriptions were identified over
26 the period (Figure 1), with 88% of them matching a consultation when the GP recorded a MSK
27 as the reason for diagnosis, reason for encounter and/or reason for prescription (i.e. excluding
28 cancer or neuropathic pain) within a period lasting from 30 days before the initial opioid
29 prescription, or up to 120 days after it.^{8 39}

30 *Data analysis*

1
2
3
4
5 1 The prevalence of long-term opioid prescriptions was estimated as the percentage of regular
6 2 patients with MSK attending the practice that year that were on opioids (i.e. long-term opioid
7 3 prescription), either because these prescriptions started in that year or previous years. The
8 4 cumulative incidence of long-term opioid prescription was estimated as the percentage of
9 5 regular patients with MSK in any year between 2012 and 2018 starting opioids that year (i.e.
10 6 patients “at risk” not on opioids). The average annual change in the prevalence or incidence of
11 7 long term opioid prescription was investigated using logistic regression, and the results
12 8 expressed as odds ratios (OR) with their respective 95% confidence intervals (95% CI).

13
14
15
16
17
18
19 9 The association between sociodemographic characteristics and the incidence of long-term
20 10 opioid prescription was also explored using logistic regression, and the variables were included
21 11 in the models considering two hierarchical levels. The first level included practice
22 12 characteristics: state, rurality (i.e. major cities, inner regional, or outer regional/remote
23 13 Australia) and the practice’s Index of Relative Socioeconomic Advantage and Disadvantage
24 14 [IRSAD, as provided by MedicineInsight (based on the postcode of the practice) and divided
25 15 in quintiles]. IRSAD is a relative indicator of economic and social advantage/disadvantage of
26 16 people and households within an area generated by the Australian Bureau of Statistics and
27 17 based on a range of census variables.⁴¹ Higher IRSAD scores indicate that the practice is
28 18 located in a more advantaged area. The second level included patient characteristics: gender
29 19 (males/females), age in groups (18-34, 35-49, 50-64, 65-79, 80+ years), aboriginality
30 20 (Aboriginal or Torres Strait Islander: No, Yes, not recorded), and the patient’s IRSAD (divided
31 21 in quintiles).

32
33
34
35
36
37
38
39
40
41
42 22 Results of the logistic regression models were expressed as marginal predicted probabilities
43 23 (i.e. adjusted cumulative incidence) instead of odds ratio to facilitate interpretation of the
44 24 results, as many medical doctors, researchers and health policymakers are not familiar with
45 25 these measures of association.⁴² Wald tests for heterogeneity or trend were used to estimate the
46 26 p-values due to the use of clustered data (i.e. practice defined as the cluster).

47
48
49
50
51 27 Quantile regression models were used to investigate the variables associated with the median
52 28 duration (in days) of the long-term opioid prescription among incident cases, considering the
53 29 same levels of adjustment as above.

54
55
56
57 30 All analyses were performed using the statistical software STATA 15.0 (StataCorp, Texas,
58 31 USA) and conditioned to the patient’s probability of being in the sample to minimise selection
59
60

1 bias (i.e. the likelihood of receiving medical treatments or diagnosis increase with the number
2 of visits to the practice).⁴³

3 *Ethics approval*

4 The Human Research Ethics Committee of the University of Adelaide exempted this study of
5 an ethical review as only non-identifiable data was used. Access to the data for this study was
6 approved by the MedicineInsight Data Governance Committee (project 2016–004 and 2019-
7 029).

8 *Patient and public involvement*

9 Patients or the public were not directly involved in the design, conduct, reporting, or
10 dissemination plans of our research. However, the provision of information for the study
11 underwent a formal approval process guided by the MedicineInsight independent external Data
12 Governance Committee that includes GPs, consumer advocates, privacy experts and
13 researchers. Moreover, two of the authors are active GPs regularly attending patients affected
14 by MSK, which also supported the design of the study.

15 **RESULTS**

16 MedicineInsight included a total sample of 3,368,928 total patients, with 1,936,573 of them
17 aged 18 years or older (Figure 1). Most practices were from New South Wales (35.5%) and
18 Victoria (21.7%) and located in major cities (60.5%), but practices from all regions and with a
19 different socioeconomic profile were included (Supplementary Table 1). Males represented
20 42.2% of the adults in the database, while 28.7% were 65 years or older and 2.0% Aboriginals
21 or Torres Strait islanders. The most common MSK among patients aged 18+ years were chronic
22 back pain (16.6%), osteoarthritis (13.7%), tenosynovitis (6.7%) osteoporosis (4.2) and gout
23 (4.0%). The rest of the conditions showed a prevalence lower than 1%.

24 The analysed sample of unique regular adult patients with MSK attending one of the
25 MedicineInsight practices between 2012 and 2018 consisted of 811,174 individuals. As shown
26 in Figure 2, the number of these patients per year ranged between 160,834 and 299,431
27 individuals.

28 The overall ‘prevalence’ of long-term opioid prescribing (i.e. patients with MSK on opioids,
29 either because they started that year or in previous years) increased from 5.5% (95% CI 5.2-
30 5.8) in 2012 to 9.1% (95% CI 8.8-9.7) in 2018 [annual change OR=1.09 IC95% 1.08-1.09; p-

1
2
3
4
5 1 value for trend <0.001]. Figure 2 shows the increase was related to a higher proportion of
6
7 2 patients starting opioids in previous years, rather than a rise in incident cases (i.e. those who
8
9 3 started opioids in that year).

10 4 [FIGURE 2 HERE]

11
12
13 5 The MSK with the highest rate of long-term opioid prescribing were spondyloarthritis (13.8%)
14
15 6 and fibromyalgia (13.3%) in 2012, and Paget disease (22.2%) and fibromyalgia (21.4%) in
16
17 7 2018 (Supplementary Figure 1). Patients with fatigue syndrome or gout were less likely to be
18
19 8 on long-term opioids (4.4% and 3.4% in 2012; 8.6% and 6.9% in 2018, respectively).

20
21
22 9 Table 1 shows males represented 44.5% of the sample, 28.4% had 65+ years, and 1.9% were
23
24 10 Aboriginal or Torres Strait Islanders. Individuals from different socioeconomic settings were
25
26 11 all represented in the study, and 40.0% were for regional or remote areas. The cumulative
27
28 12 incidence of long-term opioid prescription (i.e. excluding those who were already on opioids)
29
30 13 among regular patients with a MSK ranged between 3.6% and 3.8% between 2012-2016,
31
32 14 dropping to 3.0% in 2018 [3.0%; annual change OR=0.99 IC95% 0.98-0.99; p-value for trend
33
34 15 0.002].

35
36
37 16 The same table also shows the sociodemographic factors associated with the cumulative
38
39 17 incidence of long-term opioid prescribing. In any investigated year, the cumulative incidence
40
41 18 was 37%-52% higher among individuals attending practices located in rural Australia or areas
42
43 19 with a very low IRSAD, compared to those attending practices located in major cities or areas
44
45 20 with a higher IRSAD. Individual risk factors associated with a higher incidence of long-term
46
47 21 opioid prescribing included increasing age (3.4 times higher among those aged 80+ years than
48
49 22 the 18-34-year group in 2012, increasing to 4.8% in 2018), identifying as an Aboriginal or
50
51 23 Torres Strait Islander (1.7-1.9 higher incidence than their peers), or living in areas with a lower
52
53 24 IRSAD (36%-57% more likely than among those living in wealthiest areas). Neither the state
54
55 25 where the practice was located nor the patient's gender was associated with this outcome.

56
57
58 26 [TABLE 1 HERE]

59
60
61 27 The average duration of the long-term opioid prescriptions among incident cases ranged from
62
63 28 287 to 301 days between 2012-2016, reducing to 229 days in 2017 and 140 days in 2018 (Table
64
65 29 2). The most consistent pattern observed over the investigated years was an increased duration
66
67 30 of prescribing among individuals attending practices located in lower socioeconomic areas (i.e.

1 up to 152 days longer than those attending practices located in the wealthiest areas) or females
2 (i.e. up to 77 days longer than in males). However, these differences were not evident in 2018.

3 [TABLE 2 HERE]

4 Figure 3 shows that 74.4% (CI 95% 72.9-75.8) of those that started long-term opioid
5 prescriptions in 2012 were still receiving these prescriptions after one year, while for those
6 starting opioids in 2017, the proportion was 76.3% (95% CI 75.0-77.6). The proportion of
7 patients in each cohort still on these prescriptions decreased to 54%-56% in year two and to
8 48-51% in year three after starting long-term opioid prescriptions, remaining steady at around
9 48% in subsequent years.

10 [FIGURE 3 HERE]

11 DISCUSSION

12 To the best of our knowledge, this is the first Australian study that uses EMR from a national
13 general practice database to investigate patterns of long-term opioid prescriptions for patients
14 with MSK.²⁷ Three main findings can be highlighted from the results. Firstly, the overall
15 prevalence of long-term opioid prescriptions increased between 2012 and 2018 as a
16 consequence of the progressive rise of patients starting opioids in previous years rather than
17 for an upsurge of incident cases. Secondly, factors associated with a higher incidence of long-
18 term opioid prescription included increasing age, identifying as Aboriginal or Torres Strait
19 Islander, living in a lower socioeconomic area, or attending practices located in a rural setting
20 or more disadvantaged areas. Finally, a longer duration of these episodes was observed among
21 females or patients attending practices in lower socioeconomic areas.

22 The increase in the prevalence of long-term opioid prescriptions is consistent with other
23 Australian studies using PBS data (9, 22).^{11 20 27} The observed increase in opioids prescriptions
24 represents a substantial ongoing burden for Australia. In 2015-16, the total direct cost related
25 to opioid use in Australia (i.e. premature mortality, health care, criminal justice) was estimated
26 in \$15.76 billion, with additional \$26.8 associated the loss of quality of life of users and co-
27 residents.⁴⁴ Some authors suggest the increase in opioid use/prescription is related to the ageing
28 population with higher rates of MSK, availability of slow-release opioid formulations and
29 aggressive marketing of opioids by pharmaceutical companies.^{1 2 21} Moreover, the observed
30 increase in Australia is probably related to the prescription of potent opioids. A previous study

1
2
3
4
5 1 using PBS data found that between 2006-2015 weaker opioid use remained stable or declined,
6 2 while there was a 238% increase in persons dispensed only strong opioids.²⁰ Nonetheless, there
7 3 is evidence that long-term opioid prescription for patients with MSK in the UK and North
8 4 America reached a plateau around 2009-2011.^{21 22 45}

11
12 5 Previous studies have also reported the incidence of opioid use has either decreased or
13 6 remained unchanged in recent years, despite a rise in the prevalence.⁴⁶⁻⁴⁸ In consonance with
14 7 these studies, we found a steady incidence between 2012-2016, followed by a lower incidence
15 8 in 2018. Interestingly, the duration of long-term opioid prescription also declined in newly
16 9 incident cases in 2017 and 2018 compared to the previous five years. Although results for
17 10 2018 might reflect an insufficient follow-up of incident cases in that year, it would not explain
18 11 the findings observed in 2017. Recent education strategies among GPs and health policy
19 12 changes may have helped reduce opioid initiation and duration when prescribing to someone
20 13 affected by MSK.^{8 9 14 39} However, the increasing prevalence between 2012-2018 with an
21 14 upsurging number of patients starting opioids in previous years (i.e. 'prevalent' cases) may
22 15 suggest insufficient pro-active opioid de-prescribing is being undertaken. This conclusion is
23 16 reinforced by the findings that four years or after starting long-term opioid prescriptions, half
24 17 the patients continued to receive these prescriptions. Therefore, after all that time receiving
25 18 opioids, it is likely that a considerable number of these patients became either dependent or
26 19 possibly addicted to opioids.^{8 11 19}

28
29 20 It is also overwhelming that sedative-hypnotics drugs (i.e. benzodiazepines and Z-drugs) are
30 21 being concomitantly prescribed with of opioids, increasing the risk of addiction,
31 22 hospitalisations and deaths.^{19 49 50} Preliminary findings using MedicineInsight data show that
32 23 the proportion of patients with MSK on long-term opioids prescriptions also receiving long-
33 24 term benzodiazepines/Z-drugs prescriptions increased from 24.4 % (95% CI 23.3-25.5) in 2012
34 25 to 30.0% (95% CI 29.0-30.9%). In contrast, among patients with MSK not receiving opioids,
35 26 only 7.1% received long-term benzodiazepines/Z-drugs prescriptions in 2012 or 2018
36 27 (unpublished results). These findings help explain the substantial increase of opioid-induced
37 28 deaths in Australia, which raised from 2.67 per 100,00 people in 2001 (514 out of 1,038 total
38 29 drug-induced deaths) to 4.36 per 100,000 people in 2018 (1,088 out of 1,740 total drug-induced
39 30 deaths).^{44 49}

40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58 31 Factors such as limited time of clinicians, insufficient training on de-prescribing, restricted
59 32 access to resources for monitoring patients using opioids are recognised barriers that affect

1 strategies aiming to improve opioid prescription practices in primary care.^{1 51} Moreover,
2 pharmaceutical companies' aggressive marketing strategies also influence opioid prescription
3 practices. In 2019, the Therapeutic Goods Administration fined Mundipharma \$302,400 for
4 infringement notices related to misleading, imbalanced and inaccurate claims of promotional
5 materials directed to Australian health professionals, all of them related to nine opioid
6 medicines marketed under the name Targin®.⁵²

7 Our finding that the elderly, patients living in lower socioeconomic areas, attending practices
8 located in more disadvantaged settings or from rural and remote Australia have higher rates of
9 long-term opioid prescription is consistent with British and American studies,^{21 22 53} as well as
10 with results based on PBS data.^{11 30 31} These groups are also more likely to be affected by
11 chronic MSK conditions^{5 21}. Perhaps a maldistribution of support services or access to tertiary
12 based pain clinics could partially explain these differences⁵¹, but further studies would be
13 necessary to investigate the underlying causes in the Australian context.

14 **Strengths and limitations**

15 The study has significant strengths: a national sample including adult patients of all age groups,
16 ethnicity, or sex, and practices from all Australian states, socioeconomic areas, or remoteness.
17 Despite the novelty in the use of a national general practice database that allows the
18 identification of patients with MSK and the reason for opioid prescription, differentiates
19 between incident and prevalent cases, and provides data on different associated factors, some
20 limitations have to be recognised.

21 First, medicine-use information from MedicineInsight relates to records of GP prescribing, and
22 not all prescriptions and repeats will be dispensed or taken by the patient. Therefore, results
23 from this study reflect prescription patterns rather than opioid use.

24 Second, our study did not distinguish between the strength of preparations (i.e. presented as
25 either morphine equivalent doses or defined daily dose). However, previous studies found that
26 up to 40% of the dispensed pain medications for non-cancer pain are potent opioids, and their
27 use has increased over the years.^{15 17 20}

28 Third, individuals attending multiple clinics for prescriptions are not tracked by
29 MedicineInsight, and this may underestimate the real frequency of long-term opioid
30 prescriptions. However, the observed trends and associations are consistent with the available
31 literature.^{11 20-22 27 45}

1
2
3
4
5 1 Finally, the place/professional that initiated the prescriptions (e.g. Emergency Department,
6 2 hospital, private specialist) cannot be investigated. Moreover, MedicineInsight does not
7 3 provide details on the size and type of practices or characteristics of the doctors prescribing
8 4 opioids (e.g. junior doctor, specialist, or GPs; years of experience, etc.) Nonetheless, according
9 5 to PBS data, half of the opioids prescribed in Australia are initiated by general practitioners¹⁷
10 6 and most patients with chronic pain requiring long-term opioid prescriptions are managed in
11 7 primary care settings.⁵¹
12
13
14
15
16

17 8 **CONCLUSION**

19 9 The overall prevalence of long-term opioid prescribing for MSK conditions has increased in
20 10 Australia between 2012 and 2018, despite a lower incidence and duration of these prescriptions
21 11 in the last couple of years. This trend towards an increase in the prevalence of long-term opioid
22 12 prescribing is of great concern, as current literature reports an overall escalation in the rates of
23 13 opioid harms and deaths.^{8 9 11 14} Our study highlights the need for ongoing efforts to reduce the
24 14 opioid burden, especially among those living and attending practices in more disadvantaged
25 15 areas and considering the higher risk of adverse effect in elderly patients. This should come
26 16 not only by reducing opioid initiation but also by proactively de-prescribing for suitable
27 17 patients.^{8 14} While GPs are in an optimal position for this role⁵¹, opioid stewardship is the
28 18 responsibility of all prescribing medical practitioners and allied health professionals dealing
29 19 with MSK pain management.
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1

2 **ACKNOWLEDGEMENTS**

3 The authors acknowledge NPS MedicineWise for their support in the development of this
4 research.

5 **AUTHOR CONTRIBUTIONS**

6 All authors made significant contributions to the manuscript and are responsible for its content.
7 NS and SBT conceived the idea and planned this study. DGC was responsible for data
8 extraction and analysis, interpreting and presenting the results. SBT and DGC wrote the first
9 draft and the revisions. NS contributed to the manuscript refinement. All authors have read and
10 approved the final manuscript.

11 **FUNDING**

12 This research received no specific grant from any funding agency in the public, commercial or
13 not-for-profit sectors.

14 **COMPETING INTERESTS**

15 None declared.

16 **ETHICS APPROVAL**

17 The Human Research Ethics Committee of the University of Adelaide exempted this study of
18 an ethical review as only non-identifiable data was used. Access to the data for this study was
19 approved by the MedicineInsight Data Governance Committee (project 2016–004 and 2019-
20 029).

21 **DATA SHARING STATEMENT**

22 Data may be obtained from MedicineInsight and are not publicly available. Third parties may
23 express an interest in the information collected through MedicineInsight. The provision of
24 information in these instances undergoes a formal approval process and is guided by the
25 MedicineInsight independent external Data Governance Committee. This Committee includes
26 GPs, consumer advocates, privacy experts and researchers.

27

28

29

30

31

32

1 1 **References**

- 2 1. Blyth FM, Briggs AM, Schneider CH, et al. The Global Burden of Musculoskeletal Pain-Where to
3 From Here? *Am J Public Health* 2019;109(1):35-40. doi: 10.2105/AJPH.2018.304747
4 [published Online First: 2018/11/30]
- 5 2. Briggs AM, Shiffman J, Shawar YR, et al. Global health policy in the 21st century: Challenges and
6 opportunities to arrest the global disability burden from musculoskeletal health conditions.
7 *Best Pract Res Clin Rheumatol* 2020;101549. doi: 10.1016/j.berh.2020.101549 [published
8 Online First: 2020/07/28]
- 9 3. Australian Institute of Health and Welfare. Arthritis and other musculoskeletal conditions across
10 the life stages. Canberra: AIHW; 2014. [cited 2019 Sep 20]. Available from:
11 <http://www.aihw.gov.au/publication-detail/?id=60129547059>
- 12 4. Cooke G, Valenti L, Glasziou P, et al. Common general practice presentations and publication
13 frequency. *Aust Fam Physician* 2013;42(1-2):65-8. [published Online First: 2013/03/27]
- 14 5. Gonzalez-Chica DA, Vanlint S, Hoon E, et al. Epidemiology of arthritis, chronic back pain, gout,
15 osteoporosis, spondyloarthropathies and rheumatoid arthritis among 1.5 million patients in
16 Australian general practice: NPS MedicineWise MedicineInsight dataset. *BMC Musculoskelet*
17 *Disord* 2018;19(1):20. doi: 10.1186/s12891-018-1941-x [published Online First: 2018/01/20]
- 18 6. Australian Institute of Health and Welfare. Health-care expenditure on arthritis and other
19 musculoskeletal conditions 2008–09. Canberra: AIHW; 2014. [cited 2019 Sep 13]. Available
20 from: <http://www.aihw.gov.au/publication-detail/?id=60129548392>.
- 21 7. Gonzalez-Chica DA, Hill CL, Gill TK, et al. Individual diseases or clustering of health conditions?
22 Association between multiple chronic diseases and health-related quality of life in adults.
23 *Health Qual Life Outcomes* 2017;15(1):244. doi: 10.1186/s12955-017-0806-6 [published
24 Online First: 2017/12/23]
- 25 8. Pain Australia. National Pain Strategy, Pain Management for all Australians, Australia.: Pain
26 Australia; 2014. [cited 2019 Aug 16]. Available from:
27 <http://www.pinaustralia.org.au/improving-policy/national-pain-strategy>.
- 28 9. The Royal Australian College of General Practitioners. Guideline for the management of knee and
29 hip osteoarthritis. 2nd edn. East Melbourne, Vic: RACGP; 2018. [cited 2020 Apr 03].
30 Available from:
31 [https://www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/guideline-for-](https://www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/guideline-for-the-management-of-knee-and-hip-oa-2nd-edition.pdf)
32 [the-management-of-knee-and-hip-oa-2nd-edition.pdf](https://www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/guideline-for-the-management-of-knee-and-hip-oa-2nd-edition.pdf).
- 33 10. Krebs EE, Gravely A, Nugent S, et al. Effect of Opioid vs Nonopioid Medications on Pain-
34 Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The

- 1
2
3
4 1 SPACE Randomized Clinical Trial. *JAMA* 2018;319(9):872-82. doi: 10.1001/jama.2018.0899
5
6 2 [published Online First: 2018/03/07]
7
8 3 11. Australian Institute of Health and Welfare. Opioid harm in Australia: and comparisons between
9 4 Australia and Canada. Canberra: AIHW; 2018. [cited 2020 Jun 05]. Available from:
10 5 [https://www.aihw.gov.au/reports/illicit-use-of-drugs/opioid-harm-in-australia/contents/table-](https://www.aihw.gov.au/reports/illicit-use-of-drugs/opioid-harm-in-australia/contents/table-of-contents)
11 6 [of-contents](https://www.aihw.gov.au/reports/illicit-use-of-drugs/opioid-harm-in-australia/contents/table-of-contents).
12
13
14 7 12. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and
15 8 opioid overdose-related deaths. *JAMA* 2011;305(13):1315-21. doi: 10.1001/jama.2011.370
16 9 [published Online First: 2011/04/07]
17
18 10 13. Ray WA, Chung CP, Murray KT, et al. Prescription of Long-Acting Opioids and Mortality in
19 11 Patients With Chronic Noncancer Pain. *JAMA* 2016;315(22):2415-23. doi:
20 12 10.1001/jama.2016.7789 [published Online First: 2016/06/15]
21
22
23 13 14. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain —
24 14 United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49; 2016. [cited 2020 Mar
25 15 05]. Available from <http://dx.doi.org/10.15585/mmwr.rr6501e1>.
26
27
28 16 15. Ashaye T, Hounsome N, Carnes D, et al. Opioid prescribing for chronic musculoskeletal pain in
29 17 UK primary care: results from a cohort analysis of the COPERS trial. *BMJ Open*
30 18 2018;8(6):e019491. doi: 10.1136/bmjopen-2017-019491 [published Online First: 2018/06/09]
31
32
33 19 16. La Frenais FL, Bedder R, Vickerstaff V, et al. Temporal Trends in Analgesic Use in Long-Term
34 20 Care Facilities: A Systematic Review of International Prescribing. *J Am Geriatr Soc*
35 21 2018;66(2):376-82. doi: 10.1111/jgs.15238 [published Online First: 2017/12/24]
36
37
38 22 17. Lalic S, Ilomaki J, Bell JS, et al. Prevalence and incidence of prescription opioid analgesic use in
39 23 Australia. *Br J Clin Pharmacol* 2019;85(1):202-15. doi: 10.1111/bcp.13792 [published
40 24 Online First: 2018/10/20]
41
42
43 25 18. Manchikanti L, Sanapati J, Benyamin RM, et al. Reframing the Prevention Strategies of the
44 26 Opioid Crisis: Focusing on Prescription Opioids, Fentanyl, and Heroin Epidemic. *Pain*
45 27 *Physician* 2018;21(4):309-26. [published Online First: 2018/07/27]
46
47
48 28 19. Shipton EA, Shipton EE, Shipton AJ. A Review of the Opioid Epidemic: What Do We Do About
49 29 It? *Pain Ther* 2018;7(1):23-36. doi: 10.1007/s40122-018-0096-7 [published Online First:
50 30 2018/04/07]
51
52 31 20. Karanges EA, Buckley NA, Brett J, et al. Trends in opioid utilisation in Australia, 2006-2015:
53 32 Insights from multiple metrics. *Pharmacoepidemiol Drug Saf* 2018;27(5):504-12. doi:
54 33 10.1002/pds.4369 [published Online First: 2017/12/28]
55
56
57 34 21. Bedson J, Chen Y, Hayward RA, et al. Trends in long-term opioid prescribing in primary care
58 35 patients with musculoskeletal conditions: an observational database study. *Pain*

- 1
2
3
4
5 1 2016;157(7):1525-31. doi: 10.1097/j.pain.0000000000000557 [published Online First:
6 2 2016/03/24]
7
8 3 22. Curtis JR, Xie F, Smith C, et al. Changing Trends in Opioid Use Among Patients With
9 4 Rheumatoid Arthritis in the United States. *Arthritis Rheumatol* 2017;69(9):1733-40. doi:
10 5 10.1002/art.40152 [published Online First: 2017/06/22]
11
12 6 23. Fernandes K, Martins D, Juurlink D, et al. High-Dose Opioid Prescribing and Opioid-Related
13 7 Hospitalization: A Population-Based Study. *PLoS One* 2016;11(12):e0167479. doi:
14 8 10.1371/journal.pone.0167479 [published Online First: 2016/12/16]
15
16 9 24. Larochelle MR, Zhang F, Ross-Degnan D, et al. Trends in opioid prescribing and co-prescribing
17 10 of sedative hypnotics for acute and chronic musculoskeletal pain: 2001-2010.
18 11 *Pharmacoepidemiol Drug Saf* 2015;24(8):885-92. doi: 10.1002/pds.3776 [published Online
19 12 First: 2015/04/25]
20
21 13 25. Steinman MA, Komaiko KD, Fung KZ, et al. Use of opioids and other analgesics by older adults
22 14 in the United States, 1999-2010. *Pain Med* 2015;16(2):319-27. doi: 10.1111/pme.12613
23 15 [published Online First: 2014/10/30]
24
25 16 26. Woodard D, Van Demark RE, Jr. The Opioid Epidemic in 2017: Are We Making Progress? *SD*
26 17 *Med* 2017;70(10):467-71. [published Online First: 2017/09/29]
27
28 18 27. Donovan PJ, Arroyo D, Pattullo C, et al. Trends in opioid prescribing in Australia: a systematic
29 19 review. *Aust Health Rev* 2020;44(2):277-87. doi: 10.1071/AH18245 [published Online First:
30 20 2020/04/04]
31
32 21 28. Hollingworth SA, Symons M, Khatun M, et al. Prescribing databases can be used to monitor
33 22 trends in opioid analgesic prescribing in Australia. *Aust N Z J Public Health* 2013;37(2):132-
34 23 8. doi: 10.1111/1753-6405.12030 [published Online First: 2013/04/05]
35
36 24 29. Gisev N, Pearson SA, Karanges EA, et al. To what extent do data from pharmaceutical claims
37 25 under-estimate opioid analgesic utilisation in Australia? *Pharmacoepidemiol Drug Saf*
38 26 2018;27(5):550-55. doi: 10.1002/pds.4329 [published Online First: 2017/10/20]
39
40 27 30. Islam MM, McRae IS, Mazumdar S, et al. Prescription opioid dispensing in New South Wales,
41 28 Australia: spatial and temporal variation. *BMC Pharmacol Toxicol* 2018;19(1):30. doi:
42 29 10.1186/s40360-018-0219-0 [published Online First: 2018/06/20]
43
44 30 31. Islam MM, Wollersheim D. Variation in Prescription Opioid Dispensing across Neighborhoods of
45 31 Diverse Socioeconomic Disadvantages in Victoria, Australia. *Pharmaceuticals (Basel)*
46 32 2018;11(4) doi: 10.3390/ph11040116 [published Online First: 2018/11/06]
47
48 33 32. Busingye D, Gianacas C, Pollack A, et al. Data Resource Profile: MedicineInsight, an Australian
49 34 national primary health care database. *Int J Epidemiol* 2019;48(6):1741-41h. doi:
50 35 10.1093/ije/dyz147 [published Online First: 2019/07/12]
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4
5 1 33. Badmus D, Menzies R. Using general practice data to monitor influenza vaccination coverage in
6 2 the medically at risk: a data linkage study. *BMJ Open* 2019;9(9):e031802. doi:
7 3 10.1136/bmjopen-2019-031802 [published Online First: 2019/09/19]
8
9 4 34. Bernardo CO, Gonzalez-Chica D, Stocks N. Influenza-like illness and antimicrobial prescribing in
10 5 Australian general practice from 2015 to 2017: a national longitudinal study using the
11 6 MedicineInsight dataset. *BMJ Open* 2019;9(4):e026396. doi: 10.1136/bmjopen-2018-026396
12 7 [published Online First: 2019/05/03]
13
14 8 35. Gonzalez-Chica D, Stocks N. Changes to the frequency and appropriateness of vitamin D testing
15 9 after the introduction of new Medicare criteria for rebates in Australian general practice:
16 10 evidence from 1.5 million patients in the NPS MedicineInsight database. *BMJ Open*
17 11 2019;9(3):e024797. doi: 10.1136/bmjopen-2018-024797 [published Online First: 2019/03/11]
18
19 12 36. Khanam MA, Kitsos A, Stankovich J, et al. Chronic kidney disease monitoring in Australian
20 13 general practice. *Aust J Gen Pract* 2019;48(3):132-37. doi: 10.31128/AJGP-07-18-4630
21 14 [published Online First: 2019/07/01]
22
23 15 37. Lee CMY, Mnatzaganian G, Woodward M, et al. Sex disparities in the management of coronary
24 16 heart disease in general practices in Australia. *Heart* 2019;105(24):1898-904. doi:
25 17 10.1136/heartjnl-2019-315134 [published Online First: 2019/07/25]
26
27 18 38. SNOMED International. SNOMED CT; 2020. [cited 2020 Jun 13] Available from:
28 19 <http://www.snomed.org/>.
29
30 20 39. Australian Department of Health. The Pharmaceutical Benefits Scheme. TGA Prescription Opioid
31 21 Regulatory Reforms. Canberra; 2019. [cited 2020 Jan 30]. Available from:
32 22 [https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2019-12/tga-](https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2019-12/tga-prescription-opioid-regulatory-reforms)
33 23 [prescription-opioid-regulatory-reforms](https://www.pbs.gov.au/info/industry/listing/elements/pbac-meetings/psd/2019-12/tga-prescription-opioid-regulatory-reforms).
34
35 24 40. Dunn KM, Saunders KW, Rutter CM, et al. Opioid prescriptions for chronic pain and overdose: a
36 25 cohort study. *Ann Intern Med* 2010;152(2):85-92. doi: 10.7326/0003-4819-152-2-201001190-
37 26 00006 [published Online First: 2010/01/20]
38
39 27 41. Australian Bureau of Statistics. Census of Population and Housing: Socio-Economic Indexes for
40 28 Areas (SEIFA), Australia. Cat. No. 2033.0.55.001. Canberra; 2018. [cited 2019 May 03].
41 29 Available from: <http://www.abs.gov.au/ausstats/abs@.nsf/mf/2033.0.55.001>.
42
43 30 42. Tajeu GS, Sen B, Allison DB, et al. Misuse of odds ratios in obesity literature: an empirical
44 31 analysis of published studies. *Obesity (Silver Spring)* 2012;20(8):1726-31. doi:
45 32 10.1038/oby.2012.71 [published Online First: 2012/03/23]
46
47 33 43. Goldstein BA, Bhavsar NA, Phelan M, et al. Controlling for Informed Presence Bias Due to the
48 34 Number of Health Encounters in an Electronic Health Record. *Am J Epidemiol*
49 35 2016;184(11):847-55. doi: 10.1093/aje/kww112 [published Online First: 2016/11/18]
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3
4
5 1 44. Australian Institute of Health and Welfare (AIHW). Alcohol, tobacco & other drugs in Australia.
6 2 AIHW 2020. accessed date 4/12/2020. [https://www.aihw.gov.au/reports/phe/221/alcohol-](https://www.aihw.gov.au/reports/phe/221/alcohol-tobacco-other-drugs-australia/contents/drug-types/non-medical-use-of-pharmaceutical-drugs)
7 3 [tobacco-other-drugs-australia/contents/drug-types/non-medical-use-of-pharmaceutical-drugs](https://www.aihw.gov.au/reports/phe/221/alcohol-tobacco-other-drugs-australia/contents/drug-types/non-medical-use-of-pharmaceutical-drugs).
8 4 doi: 10.25816/c9x6-gy43
- 9
10
11 5 45. Han L, Allore H, Goulet J, et al. Opioid dosing trends over eight years among US Veterans with
12 6 musculoskeletal disorders after returning from service in support of recent conflicts. *Ann*
13 7 *Epidemiol* 2017;27(9):563-69 e3. doi: 10.1016/j.annepidem.2017.08.015 [published Online
14 8 First: 2017/09/12]
- 15
16
17 9 46. Fassio V, Aspinall SL, Zhao X, et al. Trends in opioid and nonsteroidal anti-inflammatory use and
18 10 adverse events. *Am J Manag Care* 2018;24(3):e61-e72. [published Online First: 2018/03/20]
- 19
20
21 11 47. Mosher HJ, Krebs EE, Carrel M, et al. Trends in prevalent and incident opioid receipt: an
22 12 observational study in Veterans Health Administration 2004-2012. *J Gen Intern Med*
23 13 2015;30(5):597-604. doi: 10.1007/s11606-014-3143-z [published Online First: 2014/12/19]
- 24
25 14 48. Smolina K, Gladstone EJ, Rutherford K, et al. Patterns and trends in long-term opioid use for non-
26 15 cancer pain in British Columbia, 2005-2012. *Can J Public Health* 2016;107(4-5):e404-e09.
27 16 doi: 10.17269/cjph.107.5413 [published Online First: 2016/12/28]
- 28
29
30 17 49. Man N, Chrzanowska A, Dobbins T, Degenhardt L, Peacock A, 2019. Trends in drug induced
31 18 death in Australia, 1997-2018. National Drug and Alcohol Research Centre, University of
32 19 New South Wales, Sydney, NSW 2052, Australia. Accessed 20/01/2021
33 20 [https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Drug%20Induced%20Death](https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Drug%20Induced%20Deaths%20December%202019%20Bulletin_1.pdf)
34 21 [s%20December%202019%20Bulletin_1.pdf](https://ndarc.med.unsw.edu.au/sites/default/files/ndarc/resources/Drug%20Induced%20Deaths%20December%202019%20Bulletin_1.pdf).
- 35
36
37 22 50. Caughey GE, Gadzhanova S, Shakib S, et al. Concomitant prescribing of opioids and
38 23 benzodiazepines in Australia, 2012-2017. *Med J Aust* 2019;210(1):39-40. doi:
39 24 10.5694/mja2.12026 [published Online First: 2019/01/14]
- 40
41
42 25 51. Cheatle MD, Barker C. Improving opioid prescription practices and reducing patient risk in the
43 26 primary care setting. *J Pain Res* 2014;7:301-11. doi: 10.2147/jpr.S37306 [published Online
44 27 First: 2014/06/27]
- 45
46
47 28 52. Woodley M. Mundipharma fined for misleading advertising of opioids. The Royal Australian
48 29 College of General Practitioners - News. [cited 2021 Jan 21]. Available from
49 30 [https://www1.racgp.org.au/newsgp/professional/mundipharma-fined-for-misleading-](https://www1.racgp.org.au/newsgp/professional/mundipharma-fined-for-misleading-advertising-of-op)
50 31 [advertising-of-op](https://www1.racgp.org.au/newsgp/professional/mundipharma-fined-for-misleading-advertising-of-op). 2019
- 51
52
53 32 53. Mordecai L, Reynolds C, Donaldson LJ, et al. Patterns of regional variation of opioid prescribing
54 33 in primary care in England: a retrospective observational study. *Br J Gen Pract*
55 34 2018;68(668):e225-e33. doi: 10.3399/bjgp18X695057 [published Online First: 2018/02/15]
- 56
57
58
59 35
60

Table 1. Cumulative incidence of long-term opioid prescription for the management of musculoskeletal conditions according to practice and patient's characteristics. regular patients^a aged 18+ years. Australia, 2012-2018.

Long-term opioids - incidence (%)								
Year	2012	2013	2014	2015	2016	2017	2018	
regular patients with a MSK 'at risk'^a	157,528	185,358	210,089	231,961	253,648	281,655	190,074	
	3.6	3.6	3.8	3.7	3.8	3.5	3.0	
Overall incidence - % (95%CI)	(3.4;3.8)	(3.4;3.8)	(3.6;4.0)	(3.5;3.9)	(3.6;4.0)	(3.4;3.7)	(2.8;3.1)	
Practice characteristics^c	% ^d							
State								
NSW	36.2	3.6	3.5	3.8	3.7	3.7	3.4	2.8
VIC	21.5	3.7	3.6	3.9	3.9	3.9	3.7	3.1
QLD	14.3	3.3	3.5	3.8	3.6	3.5	3.6	2.7
WA	11.3	3.7	3.8	3.9	3.8	4.3	4.1	3.5
TAS	10.4	3.3	3.3	3.4	3.4	3.4	3.1	2.8
SA	3.0	3.2	3.8	3.2	3.9	3.7	3.8	2.9
ACT	2.7	6.0	4.6	5.1	4.8	4.2	4.5	3.3
NT	0.6	2.6	3.6	3.5	2.5	3.7	2.6	2.6
Rurality								
Major cities	60.0	3.1	3.2	3.4	3.4	3.3	3.2	2.7
Inner regional	26.7	3.8	4.0	4.0	3.9	4.1	3.9	3.2
Outer regional/Remote	13.3	4.9	4.5	5.0	4.8	5.0	4.5	3.7
IRSAD Quintile								
Very high	25.8	2.8	2.9	3.1	2.9	3.1	2.8	2.4
High	16.7	3.4	3.4	3.4	3.4	3.6	3.4	3.0
Middle	22.8	3.8	3.6	3.9	4.0	4.0	3.9	3.1
Low	15.6	3.8	3.7	4.0	4.0	3.8	3.6	3.0
Very Low	19.1	4.0	4.3	4.5	4.4	4.4	4.1	3.3
Patient's characteristics^e								
Gender								
Male	44.5	3.4	3.4	3.6	3.7	3.7	3.4	3.0

Female	55.5	3.7	3.7	3.9	3.8	3.8	3.6	2.9
Age								
18-34 years	18.9	1.9	2.0	1.8	1.7	1.7	1.5	1.3
35-49 years	23.9	2.9	2.9	3.0	2.9	2.8	2.6	2.2
50-64 years	28.8	3.2	3.1	3.2	3.1	3.2	3.0	2.4
65-79 years	21.9	4.4	4.4	4.6	4.5	4.5	4.2	3.6
80+ years	6.5	6.5	6.5	7.0	7.4	7.6	7.3	6.2
Aboriginal/Torres Strait Islander								
No	77.9	3.6	3.6	3.8	3.8	3.8	3.5	3.0
Yes	1.9	6.5	6.0	6.5	7.3	7.0	6.5	5.3
Not recorded	20.2	3.0	3.1	3.1	3.0	3.3	3.3	2.7
IRSAD Quintile								
Very high	23.9	2.8	2.8	2.9	2.8	3.0	2.8	2.5
High	16.9	3.3	3.4	3.8	3.7	3.6	3.4	2.7
Middle	23.0	3.8	3.6	3.8	4.0	3.8	3.8	3.0
Low	17.3	3.7	3.7	4.0	3.8	4.2	3.7	3.2
Very Low	18.7	4.1	4.4	4.3	4.3	4.4	3.9	3.4

^a At least three consultations in any two consecutive years from 2012 to 2018. Numbers (n) represent the number of regular patients with a musculoskeletal condition in that year, excluding those who were already on opioids (i.e. patients “at risk”)

^b Values in parenthesis represent the 95% confidence intervals of the incidence

^c Logistic regression models with all practice characteristics mutually adjusted. Values in ‘bold’ represent those associations with a p-value <0.01

^d Values represent the sample distribution according to these characteristics

^e Logistic regression models with all patient characteristics mutually adjusted + adjustment for practice characteristics. Values in ‘bold’ represent those associations with a p-value <0.01

MSK: Musculoskeletal condition; IRSAD: Index of Relative Socioeconomic Advantage and Disadvantage.

Table 2. Average time on long-term opioid prescription for the management of musculoskeletal conditions among incident cases according to practice and patient's characteristics. regular patients^a aged 18+ years. Australia, 2012-2018.

	Time on long-term opioids among incident cases (days)						
	2012	2013	2014	2015	2016	2017	2018
Incident cases	5,621	6,647	7,944	8,652	9,572	9,958	5,672
Median duration (95%CI)^b	287 (266;308)	301 (281;321)	295 (279;311)	288 (272;304)	294 (281;307)	229 (221;237)	140 (135;145)
Practice characteristics^c							
State							
NSW	266	299	308	273	292	210	134
VIC	283	309	312	313	268	230	141
QLD	342	243	264	278	297	244	146
WA	294	288	281	333	336	246	141
TAS	339	367	205	367	292	241	138
SA	269	393	255	292	402	214	154
ACT	327	299	431	338	321	267	186
NT	249	683	261	206	237	116	108
Rurality							
Major cities	301	327	288	309	290	221	137
Inner regional	309	313	319	290	316	234	142
Outer regional/Remote	242	243	310	309	284	240	148
IRSAD Quintile							
Very high	203	214	244	203	247	186	128
High	231	300	285	299	263	221	143
Middle	263	319	290	302	320	222	142
Low	393	341	361	341	293	259	145
Very Low	349	346	322	355	333	251	141
Patient's characteristics^d							
Gender							
Male	278	272	272	259	271	211	137
Female	311	349	329	336	323	238	143

Age							
18-34 years	230	361	276	363	247	233	147
35-49 years	335	361	345	327	350	257	154
50-64 years	299	337	320	293	306	221	142
65-79 years	278	257	277	279	242	203	132
80+ years	336	371	326	336	379	249	143
Aboriginal/Torres Strait Islander							
No	302	319	308	303	303	224	139
Yes	442	376	415	405	381	274	158
Not recorded	245	315	278	296	279	232	146
IRSAD Quintile							
Very high	238	287	236	268	277	230	127
High	249	315	258	296	292	218	140
Middle	278	315	306	297	319	233	139
Low	358	333	360	323	303	216	134
Very Low	343	337	343	330	308	232	159

^a At least three consultations in any two consecutive years from 2012 to 2018.

^b Values in parenthesis represent the 95% confidence intervals of the median time on opioids. The corresponding interquartile values are 2012=91-1177; 2013=98-1214; 2014=98-1145; 2015=94-989; 2016=97-759; 2017=91-474; 2018=78-255.

^c Quantile regression models with all practice characteristics mutually adjusted. Values in 'bold' represent those associations with a p-value <0.01

^d Quantile regression models with all patient characteristics mutually adjusted + adjustment for practice characteristics. Values in 'bold' represent those associations with a p-value <0.01

MSK: Musculoskeletal condition; IRSAD: Index of Relative Socioeconomic Advantage and Disadvantage.

1
2
3
4 **Figure 1. Algorithm of data extraction from MedicineInsight database for the diagnosis**
5 **of MSK and opioid prescriptions. Period 2012-2018**
6
7

8
9 **Figure 2. Frequency of long-term opioid prescription for the management of**
10 **musculoskeletal conditions. Period 2012-2018.** Number in parenthesis (n) represent the total
11 number of regular patients with a musculoskeletal condition in that year from a total of 811,174
12 regular patients investigated over the whole period.
13
14

15
16
17 **Figure 3. Proportion of patients starting long-term opioid prescriptions in any year that**
18 **were still receiving these prescriptions in subsequent years. Period 2012-2018.** Each
19 connected line represents a different cohort followed over time. Numbers in parenthesis (n)
20 represent the total number of regular patients with a musculoskeletal condition that started long-
21 term opioid prescriptions in that year.
22
23

24
25
26 **Supplementary Table 1. Practice and patient characteristics in the whole sample. Regular**
27 **patients^a aged 18+ years. MedicineInsight data, 2018.**
28

29
30
31 **Supplementary Figure 1. Rate of long-term opioid prescribing for different**
32 **musculoskeletal conditions in 2012 and 2018.**
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

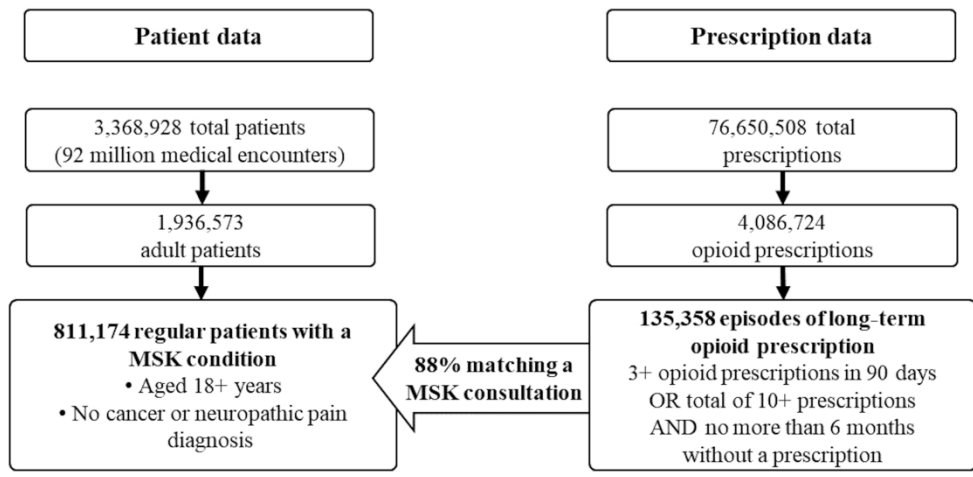


Figure 1. Algorithm of data extraction from MedicineInsight database for the diagnosis of MSK and opioid prescriptions. Period 2012-2018

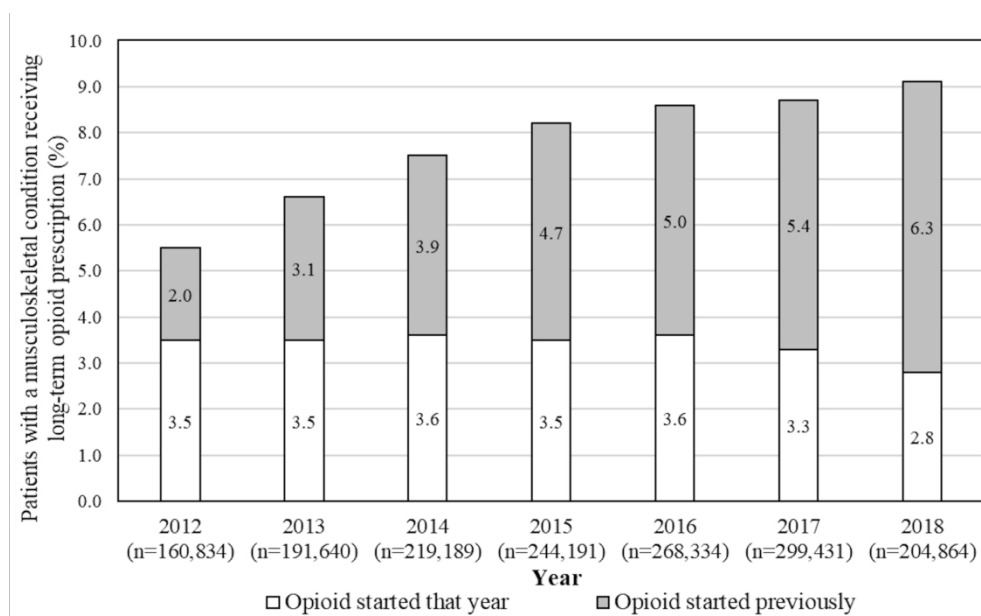


Figure 2. Frequency of long-term opioid prescription for the management of musculoskeletal conditions. regular patients aged 18+ years. Australia, 2012-2018. Number in parenthesis (n) represent the total number of regular patients with a musculoskeletal condition in that year from a total of 811,174 regular patients investigated over the whole period.

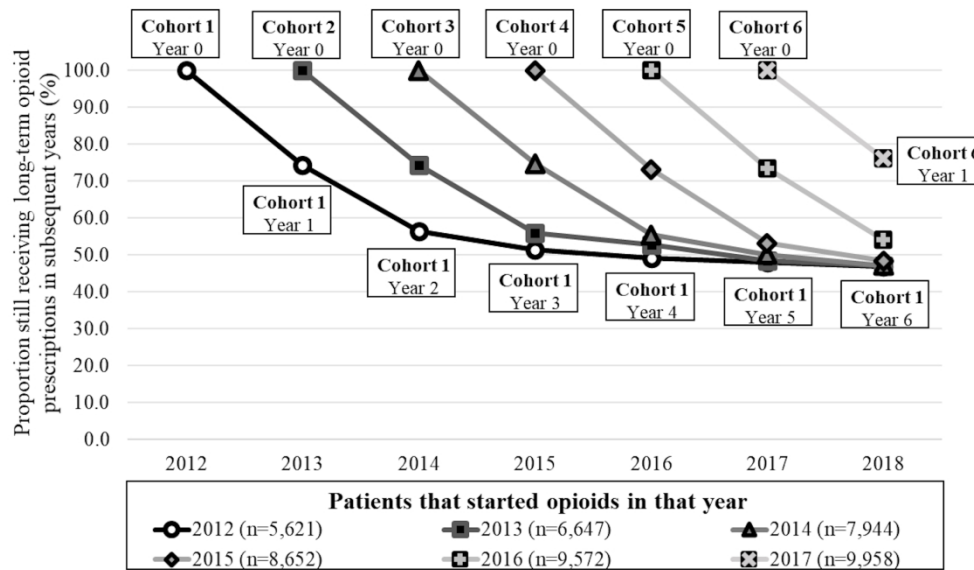


Figure 3. Proportion of patients starting long-term opioid prescriptions in any year that were still receiving these prescriptions in subsequent years. Period 2012-2018. Each connected line represents a different cohort followed over time. Numbers in parenthesis (n) represent the total number of regular patients with a musculoskeletal condition that started long-term opioid prescriptions in that year.

Supplementary Table 1. Practice and patient characteristics in the whole sample. Regular patients^a aged 18+ years. MedicineInsight data, 2018.

Practice characteristics	%^b	95% CI
State		
NSW	35.5	30.1-41.2
VIC	21.7	17.1-27.2
QLD	14.4	10.9-18.8
WA	12.0	8.5-16.6
TAS	10.0	6.8-14.4
SA	2.6	1.4-5.0
ACT	2.8	1.3-6.1
NT	1.0	0.4-2.4
Rurality		
Major cities	60.5	54.7-66.1
Inner regional	25.9	21.1-31.4
Outer regional/Remote	13.5	10.2-17.8
IRSAD Quintile		
Very high	27.0	22.0-32.7
High	16.4	12.6-21.0
Middle	22.6	18.0-28.1
Low	18.8	11.3-18.9
Very Low	18.8	14.5-24.1
Patient's characteristics		
Gender		
Male	42.2	41.7-42.8
Female	57.7	57.1-58.2
Age		
18-34 years	23.0	22.1-23.9
35-49 years	23.2	22.6-23.9
50-64 years	25.1	24.7-25.5
65-79 years	15.4	14.9-16.0
80+ years	13.3	12.6-14.0
Aboriginal/Torres Strait Islander		
No	76.9	73.9-79.6
Yes	2.0	1.1-2.3
Not recorded	21.1	18.4-24.2
IRSAD Quintile		
Very high	25.0	21.3-29.2
High	16.9	14.6-19.4
Middle	22.7	19.5-26.3
Low	16.5	13.9-19.5
Very Low	18.1	15.0-21.8
Chronic musculoskeletal conditions^c		
Chronic back pain	16.6	15.9-17.2
Osteoarthritis	13.7	13.1-14.3
Tenosynovitis	6.7	6.4-7.1
Osteoporosis	4.2	4.0-4.4
Gout	4.0	3.8-4.1
Rheumatoid arthritis	0.89	0.85-0.94
Fibromyalgia	0.69	0.64-0.73

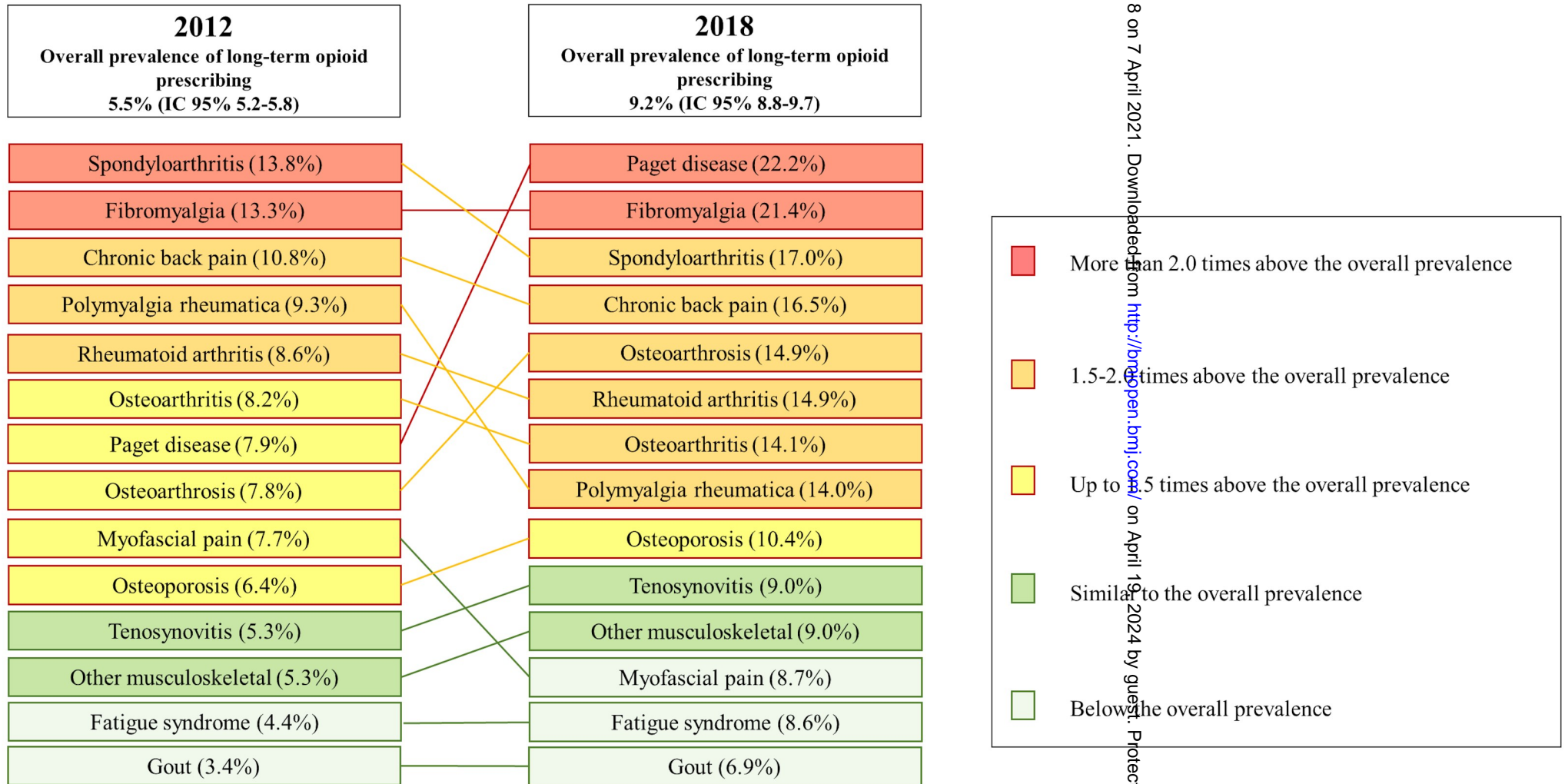
1			
2			
3	Polymyalgia_rheumatica	0.68	0.63-0.74
4	Osteoarthritis	0.38	0.34-0.43
5	Spondyloarthritis	0.28	0.26-0.31
6	Fatigue syndrome	0.22	0.20-0.24
7	Paget disease	0.11	0.01-0.12
8	Myofascial pain	0.03	0.02-0.05
9			

10 ^a At least three consultations in any two consecutive years

11 ^b Values represent the distribution (prevalence) in the whole sample of regular patients aged 18+ years
12 according to these characteristics

13 ^c List of chronic musculoskeletal conditions diagnosed at any time between 2011 and 2018

14 IRSAD: Index of Relative Socioeconomic Advantage and Disadvantage.
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



6/bmjopen-2020-045418 on 7 April 2021. Downloaded from <http://bmjopen.bmj.com/> on April 19, 2024 by guest. Protected by copyright.

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

	Item No	Recommendation	Page No
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	1,2 2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
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	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
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	6-7
Bias	9	Describe any efforts to address potential sources of bias	6-8
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
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	8 - 6-7 - -
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	6,9, Tables 1,2 - Fig.1
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)	9, Table 1 9, Table 1 9, Table 1

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Outcome data

15*

Report numbers of outcome events or summary measures over time

9, 10,
Fig. 2,
Tables
1,2

For peer review only

1	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	9-10, tables 1,2
2			(b) Report category boundaries when continuous variables were categorized	9-10, tables 1,2
3			(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-10, tables 1,2
4				
5	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
6	Discussion			
7	Key results	18	Summarise key results with reference to study objectives	10
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	12
9	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
10	Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
11	Other information			
12	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	13

*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>.