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Supporting Information

Supplementary methods and results

This appendix was part of the submitted manuscript and has been peer reviewed.
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Appendix to: Koch FC, Olivier J, Brett J, et al. Tighter prescribing restrictions for PBS-subsidised opioid medicines and the introduction of half-pack sizes, Australia, 2020–21: an interrupted time series analysis of their impact. *Med J Aust* 2024; doi: 10.5694/mja2.52257.

Table 1. Opioid medications included in our analysis

Opioid	ATC code	Formulation	Minimum prescribing restriction before 1 June 2020	Minimum prescribing restriction from 1 June 2020	Half-pack sizes available from 1 June 2020
Buprenorphine	N02AE01	CR	- Restricted Benefit	- Authority Required (streamlined)	-
Codeine	R05DA04*	IR	- Unrestricted Benefit	- Restricted Benefit	✓
Codeine/ paracetamol	N02AJ06	IR	- Unrestricted Benefit	- Restricted Benefit - Repeat prescribing Authority Required	✓
Fentanyl	N02AB03	CR	- Restricted Benefit	- Authority Required (streamlined)	-
Hydromorphone	N02AA03	IR	- Unrestricted Benefit	- Restricted Benefit	✓
		CR	- Restricted Benefit	- Authority Required (streamlined)	-
Methadone	N02AC52	CR†	- Restricted Benefit	- Authority Required (streamlined)	-
Morphine	N02AA01	IR	- Unrestricted Benefit	- Restricted Benefit	✓
		CR	- Restricted Benefit	- Authority Required (streamlined)	-
Oxycodone	N02AA05	IR	- Restricted Benefit	- Restricted Benefit‡	✓
		CR	- Restricted Benefit	- Authority Required (streamlined)	-
Oxycodone/naloxone	N02AA55	CR	- Restricted Benefit	- Authority Required (streamlined)	-
Tapentadol	N02AX06	CR	- Restricted Benefit	- Authority Required (streamlined)	-
Tramadol	N02AX02	IR	- Restricted Benefit	- Restricted Benefit‡ - Repeat prescribing Authority Required	✓
		CR	- Restricted Benefit	- Authority Required (streamlined)	-

ATC = Anatomical Therapeutic Chemical; IR = immediate release; CR = controlled release.

* Listings under the R05DA04 code are also used for treating pain.[1]

† While methadone formulations are listed on the PBS are not controlled-release, they are regulated in the same fashion as all other controlled-release opioid medicines, and for analytic purposes we have classified methadone as a controlled-release opioid.

‡ No restriction level change was made to these formulations, however, clinical guidelines were amended to clarify use to manage post-operative pain (oxycodone) and that non-opioid analgesics are insufficient for pain management (oxycodone and tramadol).

Unrestricted benefits Medicines available for general use without limits on the subsidised indication for prescribing.

Restricted benefits Medicines available for the treatment of certain indications or patient groups. If the medicine is prescribed outside the PBS-specified indication, prescribers are required to write private (unsubsidised) prescriptions.

Authority required benefits An authority prescription is required for certain restricted medicines and for cases where a higher dose or quantity of the medicine is required than the maximum approved on the PBS. Authority benefits fall into two categories: (a) Authority required prescriptions, which require the prescriber to obtain written or telephone approval before dispensing is permitted; and (b) Authority required (STREAMLINED) prescriptions, which do not require prior approval, but a streamlined authority code must be provided on the prescription.[2]

References

1 Karanges EA, Blanch B, Buckley NA, Pearson SA. Twenty-five years of prescription opioid use in Australia: a whole-of-population analysis using pharmaceutical claims. Br J Clin Pharmacol 2016; 82: 255-267.

2 Mellish L, Karanges EA, Litchfield MJ, et al. The Australian Pharmaceutical Benefits Scheme data collection: a practical guide for researchers. BMC Res Notes 2015; 8: 634.

Table 2. Opioid medicines included in our analysis: PBS item codes, formulation, strength, and oral morphine equivalent milligram (OME) conversion factor.

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Buprenorphine CR	08866P	Transdermal patch 10 mg	10	2.2
Buprenorphine CR	10770W	Transdermal patch 15 mg	15	2.2
Buprenorphine CR	08867Q	Transdermal patch 20 mg	20	2.2
Buprenorphine CR	10756D	Transdermal patch 25 mg	25	2.2
Buprenorphine CR	10755C	Transdermal patch 30 mg	30	2.2
Buprenorphine CR	10746N	Transdermal patch 40 mg	40	2.2
Buprenorphine CR	08865N	Transdermal patch 5 mg	5	2.2
Buprenorphine CR	10948F	Transdermal patch 10 mg	10	2.2
Buprenorphine CR	10953L	Transdermal patch 15 mg	15	2.2
Buprenorphine CR	10970J	Transdermal patch 20 mg	20	2.2
Buprenorphine CR	10964C	Transdermal patch 25 mg	25	2.2
Buprenorphine CR	10949G	Transdermal patch 30 mg	30	2.2
Buprenorphine CR	10959T	Transdermal patch 40 mg	40	2.2
Buprenorphine CR	10957Q	Transdermal patch 5 mg	5	2.2
Codeine IR	12054K	Tablet containing codeine phosphate hemihydrate 30 mg	30	0.1
Codeine IR	12065B	Tablet containing codeine phosphate hemihydrate 30 mg	30	0.1
Codeine IR	01214X	Tablet containing codeine phosphate hemihydrate 30 mg	30	0.1
Codeine IR	05063L	Tablet containing codeine phosphate hemihydrate 30 mg	30	0.1
Codeine IR + paracetamol	08785J	Tablet containing codeine phosphate hemihydrate 30 mg with paracetamol 500 mg	30	0.1
Codeine IR + paracetamol	12022R	Tablet containing codeine phosphate hemihydrate 30 mg with paracetamol 500 mg	30	0.1
Codeine IR + paracetamol	12066C	Tablet containing codeine phosphate hemihydrate 30 mg with paracetamol 500 mg	30	0.1
Codeine IR + paracetamol	01215Y	Tablet containing codeine phosphate hemihydrate 30 mg with paracetamol 500 mg	30	0.1

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Codeine IR + paracetamol	03316M	Tablet containing codeine phosphate hemihydrate 30 mg with paracetamol 500 mg	30	0.1
Fentanyl CR	05265D	Transdermal patch 1.28 mg	12	2.7
Fentanyl CR	05280X	Transdermal patch 10.20 mg	100	2.7
Fentanyl CR	05440H	Transdermal patch 12.375 mg	75	2.7
Fentanyl CR	08893C	Transdermal patch 12.6 mg	75	2.7
Fentanyl CR	05441J	Transdermal patch 16.5 mg	100	2.7
Fentanyl CR	08894D	Transdermal patch 16.8 mg	100	2.7
Fentanyl CR	05437E	Transdermal patch 2.063 mg	12	2.7
Fentanyl CR	08878G	Transdermal patch 2.1 mg	12	2.7
Fentanyl CR	05277R	Transdermal patch 2.55 mg	25	2.7
Fentanyl CR	05438F	Transdermal patch 4.125 mg	25	2.7
Fentanyl CR	08891Y	Transdermal patch 4.2 mg	25	2.7
Fentanyl CR	05278T	Transdermal patch 5.10 mg	50	2.7
Fentanyl CR	05279W	Transdermal patch 7.65 mg	75	2.7
Fentanyl CR	05439G	Transdermal patch 8.25 mg	50	2.7
Fentanyl CR	08892B	Transdermal patch 8.4 mg	50	2.7
Fentanyl CR	10722H	Tablet (orally disintegrating) 600 micrograms (as citrate)	600	0.1
Fentanyl CR	10713W	Tablet (orally disintegrating) 600 micrograms (as citrate)	600	0.1
Fentanyl CR	05405L	Lozenge 1200 micrograms (as citrate)	1,200	0.1
Fentanyl CR	05411T	Lozenge 1200 micrograms (as citrate)	1,200	0.1
Fentanyl CR	05412W	Lozenge 1600 micrograms (as citrate)	1,600	0.1
Fentanyl CR	05401G	Lozenge 200 micrograms (as citrate)	200	0.1
Fentanyl CR	05407N	Lozenge 200 micrograms (as citrate)	200	0.1
Fentanyl CR	05402H	Lozenge 400 micrograms (as citrate)	400	0.1
Fentanyl CR	05408P	Lozenge 400 micrograms (as citrate)	400	0.1
Fentanyl CR	05403J	Lozenge 600 micrograms (as citrate)	600	0.1
Fentanyl CR	05409Q	Lozenge 600 micrograms (as citrate)	600	0.1
Fentanyl CR	05404K	Lozenge 800 micrograms (as citrate)	800	0.1
Fentanyl CR	05410R	Lozenge 800 micrograms (as citrate)	800	0.1

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Fentanyl CR	10684H	Tablet (orally disintegrating) 100 micrograms (as citrate)	100	0.1
Fentanyl CR	10729Q	Tablet (orally disintegrating) 100 micrograms (as citrate)	100	0.1
Fentanyl CR	10697B	Tablet (orally disintegrating) 200 micrograms (as citrate)	200	0.1
Fentanyl CR	10698C	Tablet (orally disintegrating) 200 micrograms (as citrate)	200	0.1
Fentanyl CR	10737D	Tablet (orally disintegrating) 400 micrograms (as citrate)	400	0.1
Fentanyl CR	10739F	Tablet (orally disintegrating) 400 micrograms (as citrate)	400	0.1
Fentanyl CR	10738E	Tablet (orally disintegrating) 800 micrograms (as citrate)	800	0.1
Fentanyl CR	10601Y	Tablet (sublingual) 100 micrograms (as citrate)	100	0.1
Fentanyl CR	10602B	Tablet (sublingual) 100 micrograms (as citrate)	100	0.1
Fentanyl CR	10600X	Tablet (sublingual) 200 micrograms (as citrate)	200	0.1
Fentanyl CR	10607G	Tablet (sublingual) 200 micrograms (as citrate)	200	0.1
Fentanyl CR	10606F	Tablet (sublingual) 300 micrograms (as citrate)	300	0.1
Fentanyl CR	10610K	Tablet (sublingual) 300 micrograms (as citrate)	300	0.1
Fentanyl CR	10603C	Tablet (sublingual) 400 micrograms (as citrate)	400	0.1
Fentanyl CR	10608H	Tablet (sublingual) 400 micrograms (as citrate)	400	0.1
Fentanyl CR	10604D	Tablet (sublingual) 600 micrograms (as citrate)	600	0.1
Fentanyl CR	10613N	Tablet (sublingual) 600 micrograms (as citrate)	600	0.1
Fentanyl CR	10611L	Tablet (sublingual) 800 micrograms (as citrate)	800	0.1
Fentanyl CR	10612M	Tablet (sublingual) 800 micrograms (as citrate)	800	0.1
Hydromorphone IR	11467M	Oral liquid containing hydromorphone hydrochloride 1 mg per mL, 200 mL	200	5
Hydromorphone IR	05115F	Tablet containing hydromorphone hydrochloride 2 mg	2	5
Hydromorphone IR	08541M	Tablet containing hydromorphone hydrochloride 2 mg	2	5
Hydromorphone IR	08542N	Tablet containing hydromorphone hydrochloride 4 mg	4	5
Hydromorphone IR	08543P	Tablet containing hydromorphone hydrochloride 8 mg	8	5
Hydromorphone IR	12047C	Tablet containing hydromorphone hydrochloride 2 mg	2	5
Hydromorphone IR	12046B	Tablet containing hydromorphone hydrochloride 4 mg	4	5
Hydromorphone IR	12016K	Tablet containing hydromorphone hydrochloride 8 mg	8	5
Hydromorphone IR	08421F	Injection containing hydromorphone hydrochloride 10 mg in 1 mL	10	17.5
Hydromorphone IR	08420E	Injection containing hydromorphone hydrochloride 2 mg in 1 mL	2	17.5
Hydromorphone IR	08422G	Injection containing hydromorphone hydrochloride 50 mg in 5 mL	50	17.5

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Hydromorphone IR	08423H	Injection containing hydromorphone hydrochloride 500 mg in 50 mL	500	17.5
Hydromorphone IR	08424J	Oral liquid containing hydromorphone hydrochloride 1 mg per mL, 473 mL	473	5
Hydromorphone CR	09407D	Tablet (modified release) containing hydromorphone hydrochloride 16 mg	16	5
Hydromorphone CR	09408E	Tablet (modified release) containing hydromorphone hydrochloride 32 mg	32	5
Hydromorphone CR	09299K	Tablet (modified release) containing hydromorphone hydrochloride 4 mg	4	5
Hydromorphone CR	09409F	Tablet (modified release) containing hydromorphone hydrochloride 64 mg	64	5
Hydromorphone CR	09406C	Tablet (modified release) containing hydromorphone hydrochloride 8 mg	8	5
Methadone	01606M	Injection containing methadone hydrochloride 10 mg in 1 mL	10	13.5
Methadone	01609Q	Tablet containing methadone hydrochloride 10 mg	10	4.7
Methadone	05399E	Oral liquid containing methadone hydrochloride 25 mg per 5 mL, 200 mL	1000	4.7
Methadone	05400F	Oral liquid containing methadone hydrochloride 25 mg per 5 mL, 200 mL	1000	4.7
Morphine IR	02124T	Oral solution containing morphine hydrochloride trihydrate 10 mg per mL, 200 mL	2000	1
Morphine IR	02122Q	Oral solution containing morphine hydrochloride trihydrate 2 mg per mL, 200 mL	400	1
Morphine IR	05237P	Oral solution containing morphine hydrochloride trihydrate 2 mg per mL, 200 mL	400	1
Morphine IR	02123R	Oral solution containing morphine hydrochloride trihydrate 5 mg per mL, 200 mL	1000	1
Morphine IR	01646P	Tablet containing morphine sulfate pentahydrate 30 mg	30	1
Morphine IR	12009C	Tablet containing morphine sulfate pentahydrate 30 mg	30	1
Morphine IR	10864T	Injection containing morphine hydrochloride trihydrate 10 mg in 1 mL	10	3
Morphine IR	10878M	Injection containing morphine hydrochloride trihydrate 100 mg in 5 mL	100	3
Morphine IR	10874H	Injection containing morphine hydrochloride trihydrate 20 mg in 1 mL	20	3
Morphine IR	10869C	Injection containing morphine hydrochloride trihydrate 50 mg in 5 mL	50	3
Morphine IR	01644M	Injection containing morphine sulfate pentahydrate 10 mg in 1 mL	10	3
Morphine IR	01645N	Injection containing morphine sulfate pentahydrate 15 mg in 1 mL	15	3
Morphine IR	01647Q	Injection containing morphine sulfate pentahydrate 30 mg in 1 mL	30	3
Morphine IR	02332R	Injection containing morphine sulphate 10 mg in 1 mL (with preservative)	10	3
Morphine IR	01607N	Injection containing morphine tartrate 120 mg in 1.5 mL	120	3

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Morphine IR	05393W	Tablet containing morphine sulfate pentahydrate 10 mg	10	1
Morphine IR	05395Y	Tablet containing morphine sulfate pentahydrate 10 mg	10	1
Morphine IR	08669G	Tablet containing morphine sulfate pentahydrate 10 mg	10	1
Morphine IR	05394X	Tablet containing morphine sulfate pentahydrate 20 mg	20	1
Morphine IR	05396B	Tablet containing morphine sulfate pentahydrate 20 mg	20	1
Morphine IR	08670H	Tablet containing morphine sulfate pentahydrate 20 mg	20	1
Morphine CR	08349K	Capsule containing morphine sulfate pentahydrate 10 mg (containing sustained release pellets)	10	1
Morphine CR	02841M	Capsule containing morphine sulfate pentahydrate 100 mg (containing sustained release pellets)	100	1
Morphine CR	08494C	Capsule containing morphine sulfate pentahydrate 120 mg (controlled release)	120	1
Morphine CR	02839K	Capsule containing morphine sulfate pentahydrate 20 mg (containing sustained release pellets)	20	1
Morphine CR	08491X	Capsule containing morphine sulfate pentahydrate 30 mg (controlled release)	30	1
Morphine CR	02840L	Capsule containing morphine sulfate pentahydrate 50 mg (containing sustained release pellets)	50	1
Morphine CR	08492Y	Capsule containing morphine sulfate pentahydrate 60 mg (controlled release)	60	1
Morphine CR	08493B	Capsule containing morphine sulfate pentahydrate 90 mg (controlled release)	90	1
Morphine CR	08306E	Sachet containing controlled release granules for oral suspension, containing morphine sulfate pentahydrate 100 mg per sachet	100	1
Morphine CR	08490W	Sachet containing controlled release granules for oral suspension, containing morphine sulfate pentahydrate 20 mg per sachet	20	1
Morphine CR	08146R	Sachet containing controlled release granules for oral suspension, containing morphine sulfate pentahydrate 30 mg per sachet	30	1
Morphine CR	08305D	Sachet containing controlled release granules for oral suspension, containing morphine sulfate pentahydrate 60 mg per sachet	60	1
Morphine CR	01653B	Tablet containing morphine sulfate pentahydrate 10 mg (controlled release)	10	1
Morphine CR	01656E	Tablet containing morphine sulfate pentahydrate 100 mg (controlled release)	100	1
Morphine CR	08489T	Tablet containing morphine sulfate pentahydrate 15 mg (controlled release)	15	1

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Morphine CR	01654C	Tablet containing morphine sulfate pentahydrate 30 mg (controlled release)	30	1
Morphine CR	08035X	Tablet containing morphine sulfate pentahydrate 5 mg (controlled release)	5	1
Morphine CR	01655D	Tablet containing morphine sulfate pentahydrate 60 mg (controlled release)	60	1
Morphine CR	12055L	Tablet containing morphine sulfate pentahydrate 200 mg (controlled release)	200	1
Morphine CR	11760Y	Capsule containing morphine sulfate pentahydrate 10 mg (containing sustained release pellets)	10	1
Morphine CR	11761B	Capsule containing morphine sulfate pentahydrate 20 mg (containing sustained release pellets)	20	1
Morphine CR	05391R	Tablet containing morphine sulfate pentahydrate 200 mg (controlled release)	200	1
Morphine CR	05392T	Tablet containing morphine sulfate pentahydrate 200 mg (controlled release)	200	1
Morphine CR	08453X	Tablet containing morphine sulfate pentahydrate 200 mg (controlled release)	200	1
Oxycodone IR	05197M	Capsule containing oxycodone hydrochloride 10 mg	10	1.5
Oxycodone IR	08501K	Capsule containing oxycodone hydrochloride 10 mg	10	1.5
Oxycodone IR	08502L	Capsule containing oxycodone hydrochloride 20 mg	20	1.5
Oxycodone IR	05191F	Capsule containing oxycodone hydrochloride 5 mg	5	1.5
Oxycodone IR	08464L	Capsule containing oxycodone hydrochloride 5 mg	5	1.5
Oxycodone IR	05190E	Oral solution containing oxycodone hydrochloride 1 mg per mL, 250 mL	250	1.5
Oxycodone IR	08644Y	Oral solution containing oxycodone hydrochloride 1 mg per mL, 250 mL	250	1.5
Oxycodone IR	02481N	Suppository 30 mg (as pectinate)	30	1.5
Oxycodone IR	02622B	Tablet containing oxycodone hydrochloride 5 mg	5	1.5
Oxycodone IR	05195K	Tablet containing oxycodone hydrochloride 5 mg	5	1.5
Oxycodone IR	12031F	Capsule containing oxycodone hydrochloride 10 mg	10	1.5
Oxycodone IR	12074L	Capsule containing oxycodone hydrochloride 10 mg	10	1.5
Oxycodone IR	12044X	Capsule containing oxycodone hydrochloride 5 mg	5	1.5
Oxycodone IR	12023T	Tablet containing oxycodone hydrochloride 5 mg	5	1.5
Oxycodone IR	12048D	Tablet containing oxycodone hydrochloride 5 mg	5	1.5
Oxycodone CR	08385H	Tablet containing oxycodone hydrochloride 10 mg (controlled release)	10	1.5
Oxycodone CR	09399Q	Tablet containing oxycodone hydrochloride 15 mg (controlled release)	15	1.5
Oxycodone CR	08386J	Tablet containing oxycodone hydrochloride 20 mg (controlled release)	20	1.5
Oxycodone CR	09400R	Tablet containing oxycodone hydrochloride 30 mg (controlled release)	30	1.5

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Oxycodone CR	08387K	Tablet containing oxycodone hydrochloride 40 mg (controlled release)	40	1.5
Oxycodone CR	08388L	Tablet containing oxycodone hydrochloride 80 mg (controlled release)	80	1.5
Oxycodone CR	08681X	Tablet containing oxycodone hydrochloride 5 mg (controlled release)	5	1.5
Oxycodone CR + naloxone	08934F	Tablet (controlled release) containing oxycodone hydrochloride 10 mg with naloxone hydrochloride 5 mg	10	1.5
Oxycodone CR + naloxone	10757E	Tablet (controlled release) containing oxycodone hydrochloride 15 mg with naloxone hydrochloride 7.5 mg	15	1.5
Oxycodone CR + naloxone	10776E	Tablet (controlled release) containing oxycodone hydrochloride 2.5 mg with naloxone hydrochloride 1.25 mg	2.5	1.5
Oxycodone CR + naloxone	08935G	Tablet (controlled release) containing oxycodone hydrochloride 20 mg with naloxone hydrochloride 10 mg	20	1.5
Oxycodone CR + naloxone	10758F	Tablet (controlled release) containing oxycodone hydrochloride 30 mg with naloxone hydrochloride 15 mg	30	1.5
Oxycodone CR + naloxone	08936H	Tablet (controlled release) containing oxycodone hydrochloride 40 mg with naloxone hydrochloride 20 mg	40	1.5
Oxycodone CR + naloxone	08000C	Tablet (controlled release) containing oxycodone hydrochloride 5 mg with naloxone hydrochloride 2.5 mg	5	1.5
Oxycodone CR + naloxone	11102H	Tablet (controlled release) containing oxycodone hydrochloride 60 mg with naloxone hydrochloride 30 mg	60	1.5
Oxycodone CR + naloxone	11111T	Tablet (controlled release) containing oxycodone hydrochloride 80 mg with naloxone hydrochloride 40 mg	80	1.5
Tapentadol CR	10094G	Tablet (modified release) 100 mg (as hydrochloride)	100	0.4
Tapentadol CR	10100N	Tablet (modified release) 150 mg (as hydrochloride)	150	0.4
Tapentadol CR	10091D	Tablet (modified release) 200 mg (as hydrochloride)	200	0.4
Tapentadol CR	10092E	Tablet (modified release) 250 mg (as hydrochloride)	250	0.4
Tapentadol CR	10096J	Tablet (modified release) 50 mg (as hydrochloride)	50	0.4
Tramadol IR	05232J	Capsule containing tramadol hydrochloride 50 mg	50	0.2
Tramadol IR	08455B	Capsule containing tramadol hydrochloride 50 mg	50	0.2
Tramadol IR	08582Q	Injection containing tramadol hydrochloride 100 mg in 2 mL	100	0.2
Tramadol IR	05150C	Oral drops containing tramadol hydrochloride 100 mg per mL, 10 mL	100	0.2

Opioid medicine	PBS item code	Formulation	Strength (mg)	OME conversion factor
Tramadol IR	08843K	Oral drops containing tramadol hydrochloride 100 mg per mL, 10 mL	100	0.2
Tramadol IR	08611F	Capsule containing tramadol hydrochloride 50 mg	50	0.2
Tramadol IR	12008B	Capsule containing tramadol hydrochloride 50 mg	50	0.2
Tramadol IR	12024W	Capsule containing tramadol hydrochloride 50 mg	50	0.2
Tramadol CR	08523N	Tablet (sustained release) containing tramadol hydrochloride 100 mg	100	0.2
Tramadol CR	08524P	Tablet (sustained release) containing tramadol hydrochloride 150 mg	150	0.2
Tramadol CR	08525Q	Tablet (sustained release) containing tramadol hydrochloride 200 mg	200	0.2
Tramadol CR	02527B	Tablet (sustained release) containing tramadol hydrochloride 50 mg	50	0.2
Tramadol CR	09199E	Tablet (extended release) containing tramadol hydrochloride 100 mg	100	0.2
Tramadol CR	09200F	Tablet (extended release) containing tramadol hydrochloride 200 mg	200	0.2
Tramadol CR	09201G	Tablet (extended release) containing tramadol hydrochloride 300 mg	300	0.2

PBS = Pharmaceutical Benefits Scheme; mg = milligrams; OME = oral morphine equivalent milligrams; IR = immediate release; CR = controlled release.

Statistical analysis

We used multivariate segmented regression models to quantify changes in oral morphine equivalent milligrams (OME) dispensed, sold, and the total market proportion of publicly-subsidised OME. We included a structural component to allow for seasonal effects to be jointly estimated across each of the opioid types. The response variables were OME/day with a weekly resolution for publicly-subsidised OME dispensed, OME/day with a monthly resolution for total market OME sold, and the ratio of publicly-subsidised OME dispensed to total market OME sold. The intervention on 1 June 2020 was modelled as an interaction with the intercept and slope components.

In March 2020 Australia entered a nation-wide lockdown in response to the outbreak of coronavirus disease 2019 (COVID-19). This prompted many Australians to fill outstanding prescriptions, resulting in substantial increases in dispensings/sales during the month, followed by corresponding decreases in April 2020.[1-4,] To control for these events in our models we included additional indicator variables for the periods 14/03/2020-28/03/2020 and 11/04/2020-25/04/2020.

The regression fit to model mean daily OME dispensed with a weekly resolution was:

$$Y_{t,i} = \beta_{0,i} + \beta_{1,i}t + I_A(t) \times \left(\beta_{2,i} + \beta_{3,i}t\right) + \beta_{3,i}I_B(t) + \beta_{4,i}I_C(t) + \sum_{k=1}^{W} \lambda_i \alpha_k I_{D,k}(t) + \varepsilon_{t,i}$$

where $Y_{t,i}$ is the outcome at time point t for opioid formulation i; $\beta_{0,i}$ is the intercept for opioid formulation i; $\beta_{1,i}$ is the slope for opioid formulation i; $I_A(t)$ is an indicator function which takes the value of 0 before the intervention and 1 after; $\beta_{2,i}$ is the effect of the intervention on

opioid formulation i; $\beta_{3,i}$is the effect of the interaction of the intervention with the slope; $I_B(t)$ is an indicator function which takes the value of 1 during the COVID-19 stockpiling event and 0 otherwise; $\beta_{3,i}$ is the effect of this stockpiling event on opioid formulation i; $I_C(t)$ is an indicator function which takes the value of 1 during the ban on elective surgeries due to the COVID-19 outbreak (see COVID-19 adjustments); $\beta_{4,i}$ is the effect of this ban opioid formulation i; λ_i is the seasonal scaling factor for opioid formulation i; α_k is the *k*th common seasonal effect; $I_{D,k}(t)$ is an indicator function which takes the value of 1 during the kth season and 0 otherwise; and $\varepsilon_{t,i}$ is the random error term at time t for opioid formulation i and is assumed to be normally distributed with 0 mean and constant variance σ_i^2. There were 51 seasonal effects estimated ($W = 51$), one for each week of the year excluding week 26 which was used as a baseline for model identifiability. Likewise, $\lambda_1 = 1$ was enforced for model identifiability. The response was modelled in units of OME/day. Trends, therefore, have units of change in OME/day^2 (OME per day, per day).

The regression fit to model mean daily OME sold as well as the ratio of OME sold to dispensed with a monthly resolution was:

$$Y_{t,i} = \beta_{0,i} + \beta_{1,i}t + I_A(t) \times \left(\beta_{2,i} + \beta_{3,i}t\right) + \sum_{k=1}^{M} \lambda_i \alpha_k I_{D,k}(t) + \varepsilon_{t,i}$$

where the variables have the same interpretation as the previous regression model, however, the two COVID-19 events could not be controlled for due to the monthly resolution of the data. Furthermore, there were 11 seasonal effects estimated ($\mathrm{M} = 11$), one for each month of the year, excluding June which was used as a baseline for model identifiability.

To protect the privacy of patients in the PBS 10% dataset, dispensing dates are subject to a random offset of ±14 days, with the direction of the offset being the same for all dispensing records for each person. To account for this offset of dispensing dates, we first constructed the regressor matrix for the level/trend components with a daily resolution instead of weekly. We then applied a rolling-mean filter to model these perturbations and account for the per-patient random offset in dispensing date.[5] Finally, we obtained the target regressor matrix by aggregating the smoothed matrix into weekly means. The observed information matrix and score function were derived for the regression models and maximum likelihood estimates were obtained for each parameter using Fisher's scoring algorithm.[6]

Autocorrelation (ACF) plots were visually inspected and Durbin-Watson tests were performed to verify that serial correlation was not present in the model residuals. Furthermore, residual quantile-quantile (Q-Q) plots were inspected to ensure that the model residuals could be well approximated by a normal distribution.

Repeat PBS dispensings

To investigate and quantify changes in the weekly proportion of opioid dispensings accounted for by repeat prescriptions, we performed a binomial test of proportions to detect significant changes in the proportion of repeat dispensings on the subsidised market.

Half-pack sizes dispensed

We identified dispensings of half pack opioids through the PBS item code. To determine the uptake of these packs and their impact on opioid use more broadly, we examined the proportion of opioid dispensings and OMEmg dispensed between July 2020 and June 2021 accounted for by half-pack sizes.

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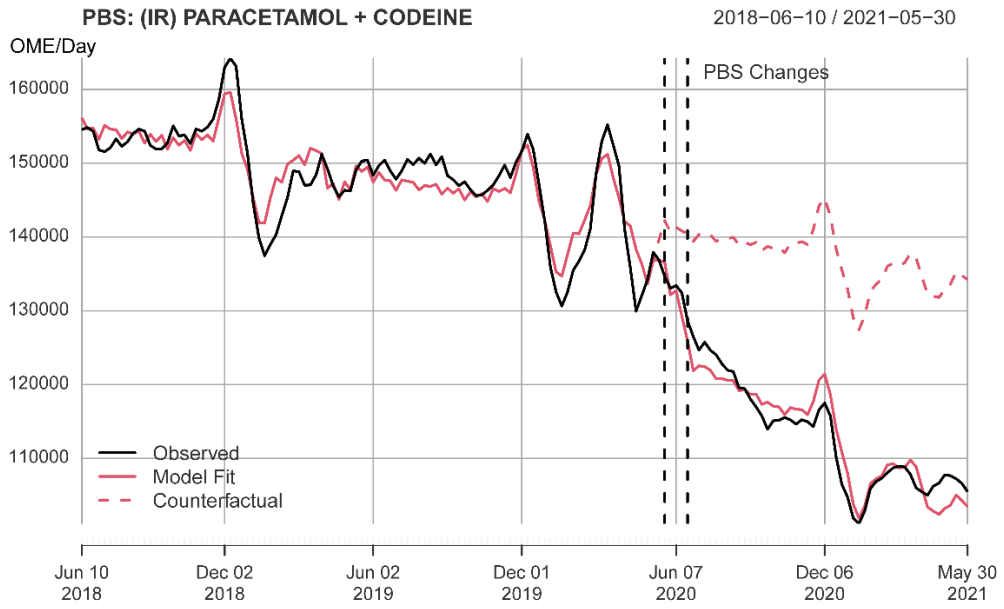
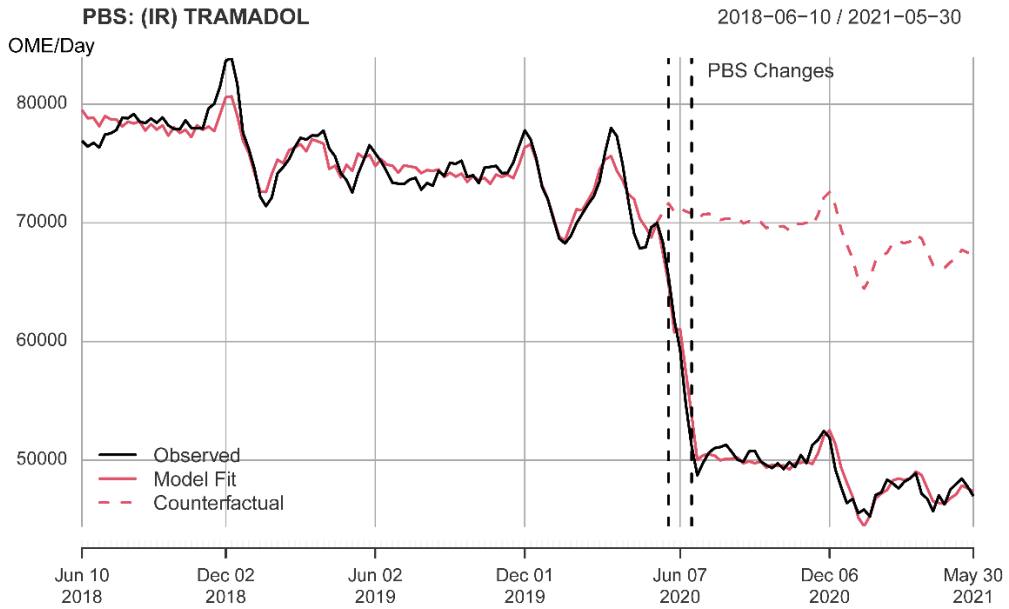
Figure 1. Publicly subsidised oral morphine equivalent milligrams (OME) dispensed with predicted values for immediate release paracetamol and codeine*



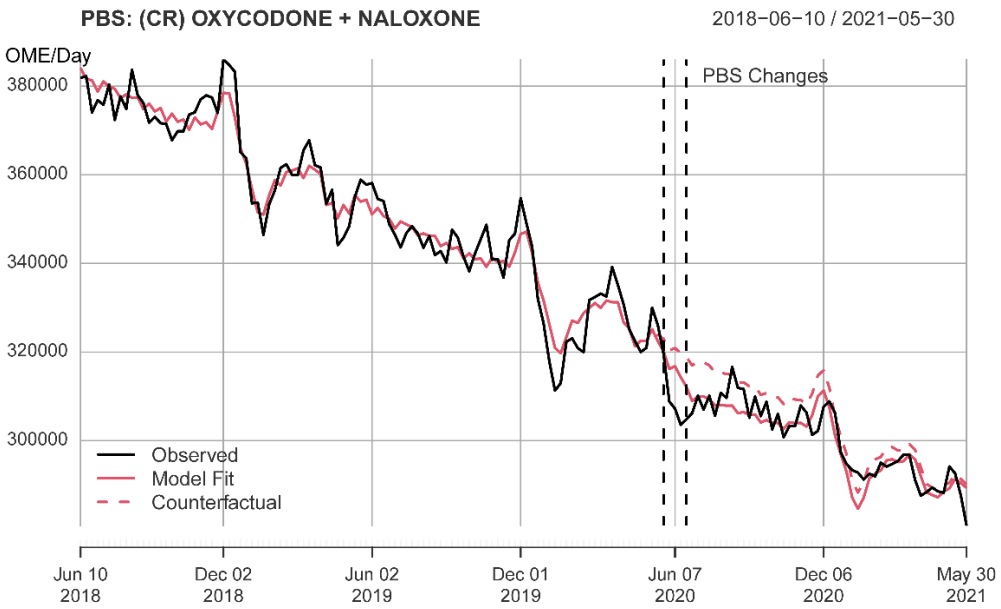
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 2. Publicly-subsidised oral morphine equivalent milligrams (OME) dispensed with predicted values for immediate release tramadol*



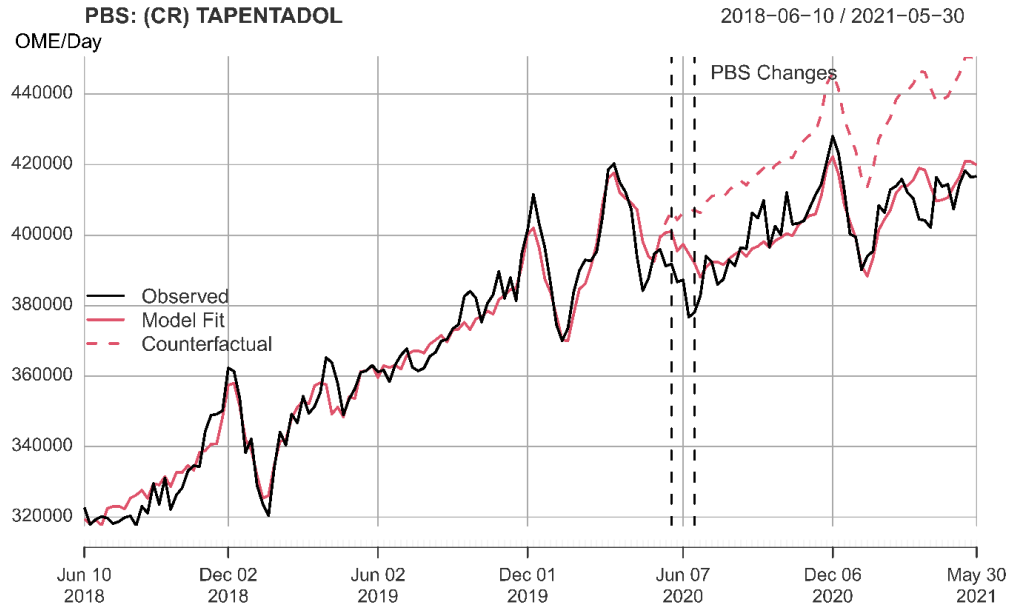
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 3. Publicly-subsidised oral morphine equivalent milligrams (OMEs) dispensed with predicted values for controlled release oxycodone and naloxone*



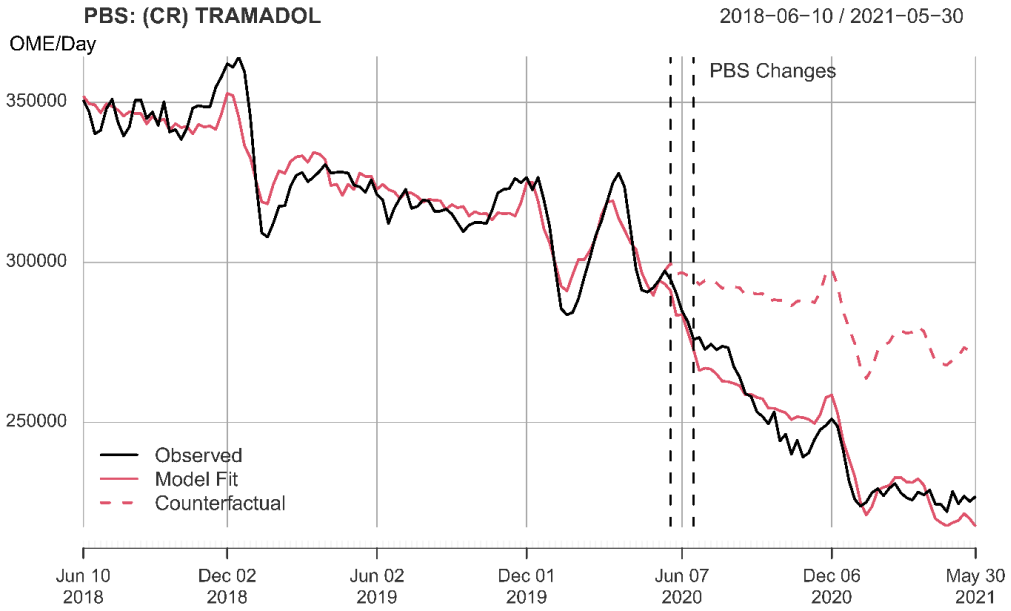
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 4. Publicly-subsidised oral morphine equivalent milligrams dispensed with predicted values for controlled release tapentadol*



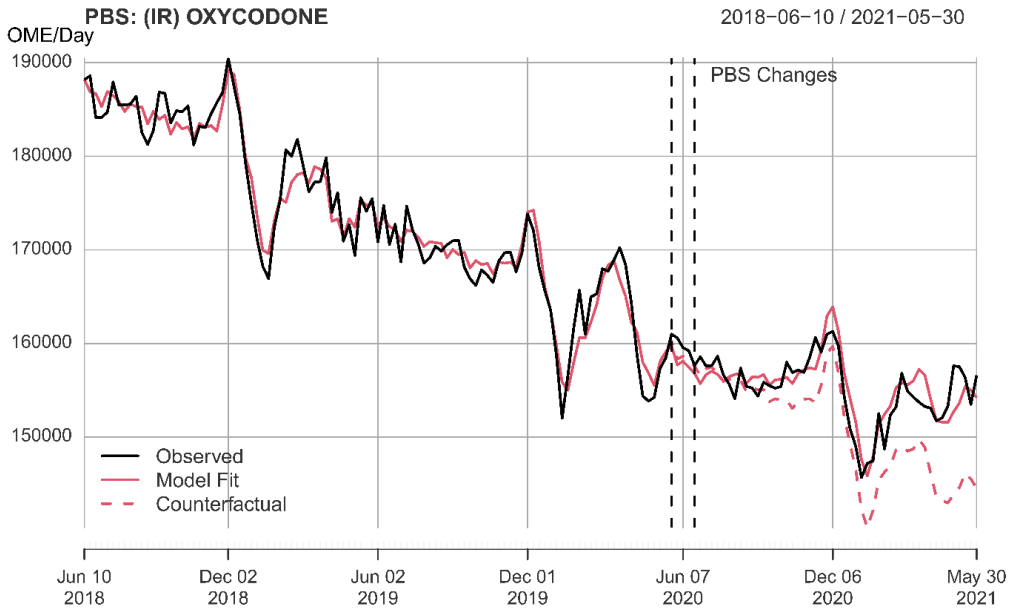
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 5. Publicly-subsidised oral morphine equivalent milligrams dispensed with predicted values for controlled release tramadol*



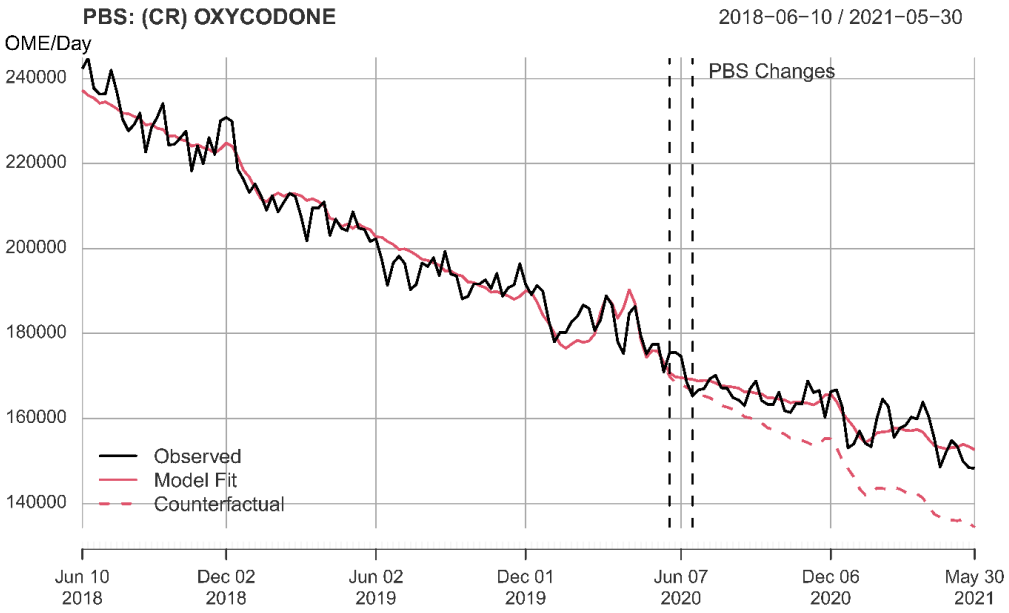
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 6. Publicly-subsidised oral morphine equivalent milligrams dispensed with predicted values for immediate release oxycodone*



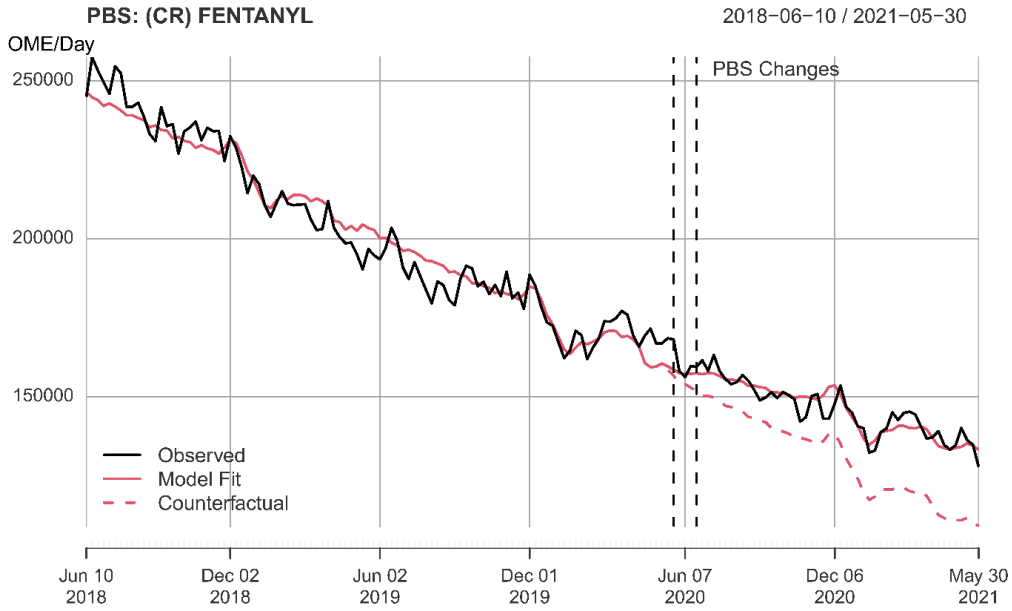
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 7. Publicly-subsidised oral morphine equivalent milligrams dispensed with predicted values for controlled release oxycodone*



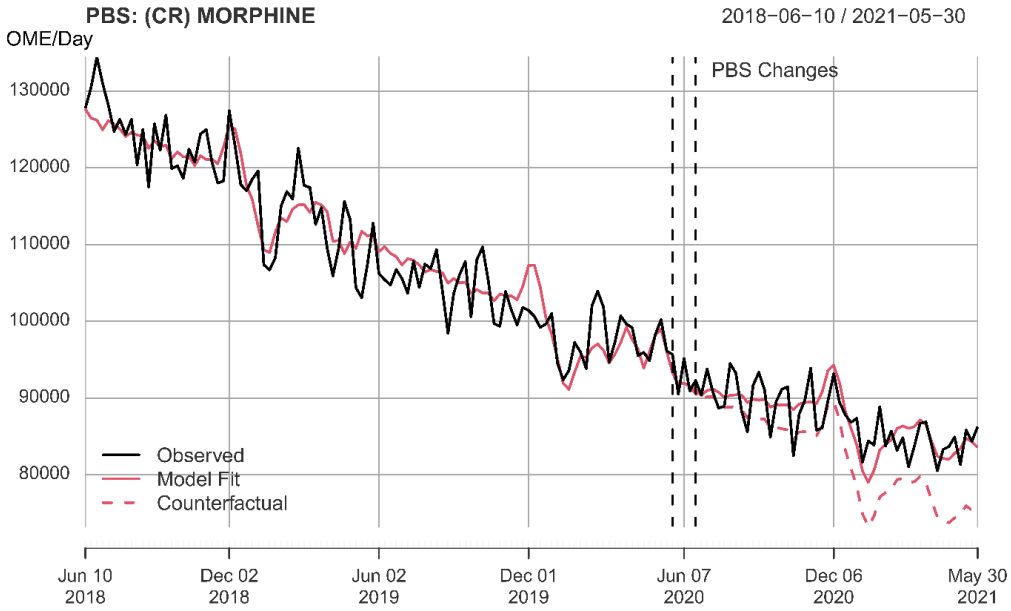
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 8. Publicly-subsidised oral morphine equivalent milligrams dispensed with predicted values for controlled release fentanyl*



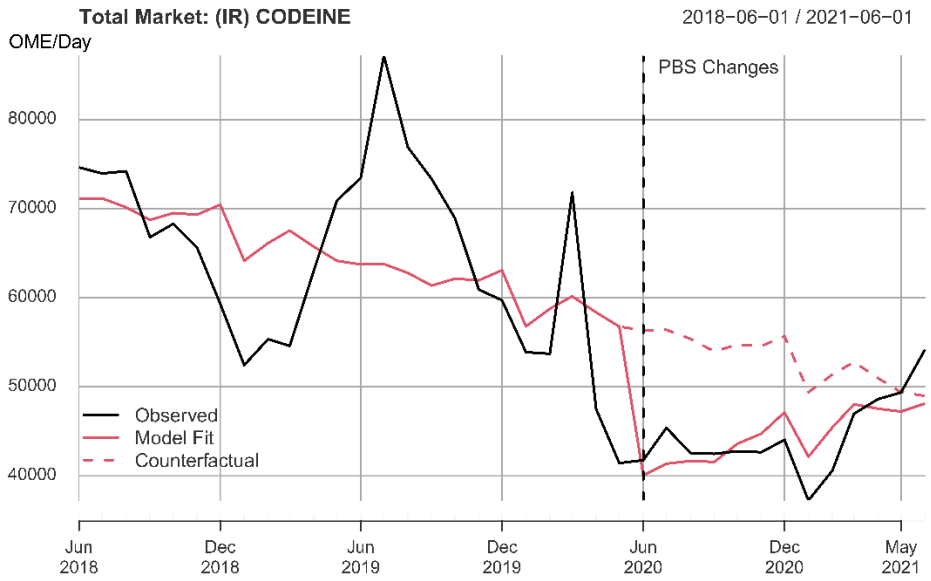
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 9. Publicly-subsidised oral morphine equivalent milligrams dispensed with predicted values for controlled release morphine*



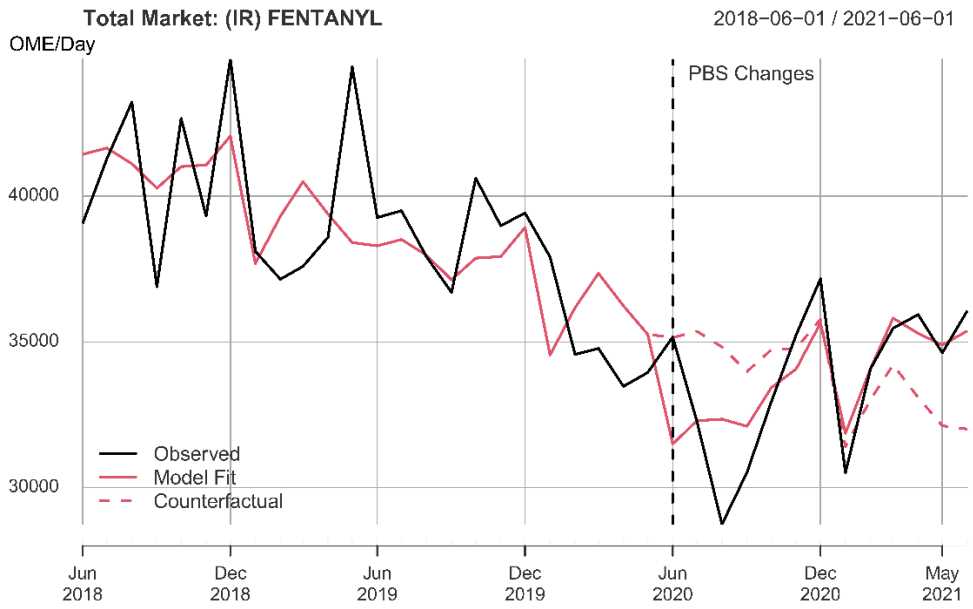
* To enhance readability, three-week rolling series means are depicted. Vertical dashed lines indicate the week that prescribing restrictions and half-pack sizes were introduced.

Figure 10. Total market OMEs sold with predicted values for immediate release codeine



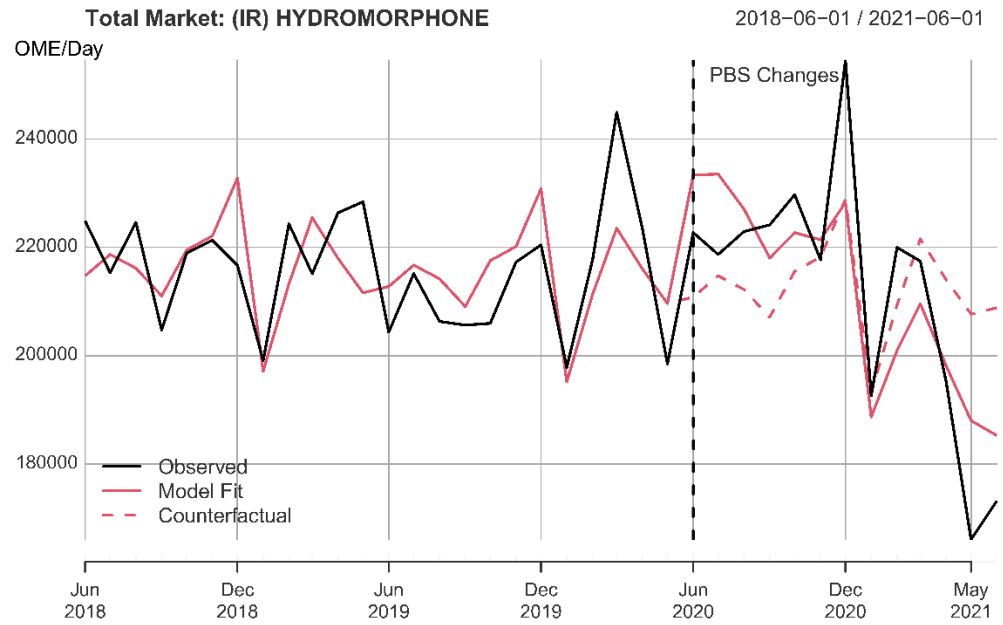
Vertical dashed line indicates the week that prescribing restrictions and half pack sizes were introduced.

Figure 11. Total market OMEs sold with predicted values for immediate release fentanyl (not available through the PBS during the study period)



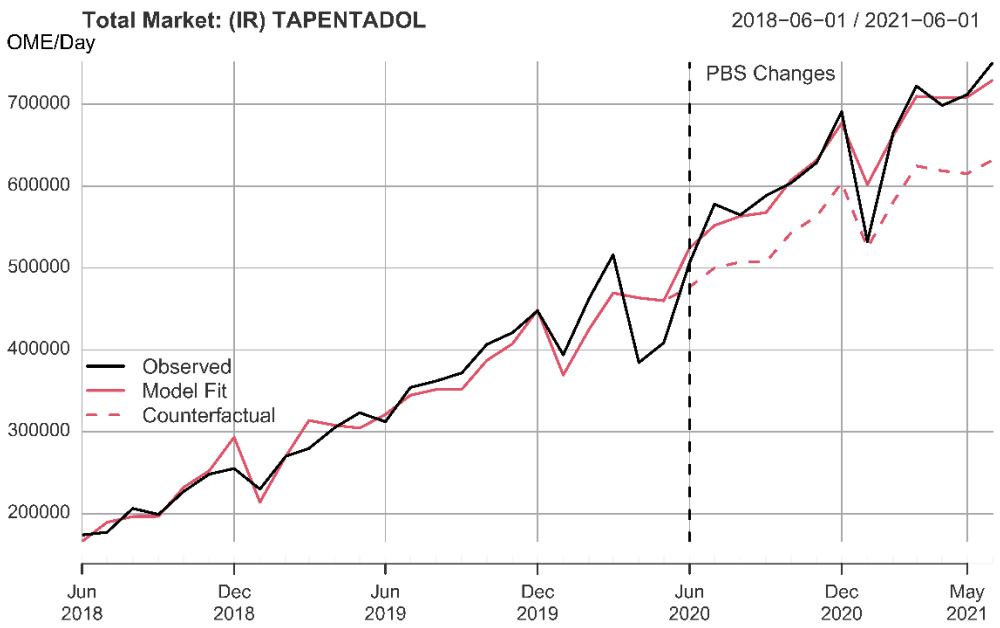
Vertical dashed line indicates the week that prescribing restrictions and half pack sizes were introduced. Please note: Because of ethical restrictions, graph for fentanyl CR could not be included in this article.

Figure 12 Total market OMEmg sold with predicted values for immediate release hydromorphone



Vertical dashed line indicates the week that prescribing restrictions and half pack sizes were introduced.

Figure 13. Total market OME sold with predicted values for immediate release tapentadol (not available through the PBS during the study period)



Vertical dashed line indicates the week that prescribing restrictions and half pack sizes were introduced.

Table 3. Estimates in changes of mean percentage of oral morphine equivalent milligrams accounted for by repeat dispensing

Opioid medicine	Pre-June 2020 Level, percentage of repeat OMEs	Change in level from June 2020, percentage points (95%CI)	Change in level as percentage of the pre-June 2020 level
Buprenorphine CR	9.3%	-1.2 (-1.8, -0.6)	-13.4%
Codeine IR	11.9%	-0.7 (-4.2, 2.9)	-5.8%
Codeine/paracetamol IR	47.0%	-9.9 (-12.3, -7.4)	-21.0%
Fentanyl CR	7.1%	-1.0 (-2.2, 0.1)	-14.1%
Hydromorphone IR	6.7%	-0.9 (-3.8, 2.1)	-13.0%
Hydromorphone CR	9.4%	0.0 (-2.8, 2.8)	-0.3%
Methadone CR	16.4%	-2.4 (-5.1, 0.2)	-14.8%
Morphine IR	6.2%	0.8 (-1.8, 3.3)	12.3%
Morphine CR	8.4%	-0.8 (-2.5, 0.9)	-9.7%
Oxycodone IR	2.5%	-0.1 (-0.5, 0.3)	-5.3%
Oxycodone CR	6.9%	-1.2 (-2.3,-0.2)	-17.9%
Oxycodone/naloxone	4.5%	-0.5 (-1.0, -0.1)	-11.8%
Tapentadol	5.1%	-0.2 (-0.8, 0.3)	-4.6%
Tramadol IR	45.4%	-33.7 (-35.9, -31.6)	-74.4%
Tramadol CR	59.2%	-9.7 (-12.8, -6.6)	-16.4%

Table 4. Proportion of all immediate release opioid dispensing and OME dispensed from June 2020 accounted for by half pack sizes

Opioid medicine	Proportion of dispensing	Half-pack IR counts	Full-pack IR counts	Proportion of dispensed OME	Half-pack IR OME	Full-pack IR OME
All immediate release formulations	8.5%	56,003	602,710	2.8%	3,580,749	124,343,028
Codeine	8.7%	349	3685	1.9%	10,797	547,011
Codeine/paracetamol	4.7%	14,514	295,733	1.2%	449,607	37,781,469
Hydromorphone	1.5%	106	6820	0.4%	29,340	7,543,085
Morphine	<0.1%*	*	*	<0.1 %*	*	*
Oxycodone	14.9%	35,959	205,899	4.8%	2,569,665	50,997,038
Tramadol	6.5%	5068	72,523	3.1%	519,420	16,115,030

* Cells suppressed because of ethical restrictions regarding small cell counts.