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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Krawczyk N, Rivera BD, Levin E, Dooling BCE. Synthesising evidence of the effects of COVID-19 regulatory changes on methadone treatment for opioid use disorder: implications for policy. *Lancet Public Health* 2023; **8**: e238–46.

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Appendix 1. Search strategy by database

| Database | Strategy |
|-----------------------|--|
| PubMed | 1 ("Methadone" AND ("take-home" OR "take-home")) |
| | 2 1 OR "Methadone maintenance therapy" OR "OTP" OR "Opioid treatment program" |
| | 3 2 OR "Opiate Substitution Treatment"[MeSH Terms] |
| | 4 "Methadone" OR "Methadone maintenance therapy" OR "OTP" OR "Opioid treatment program" OR "Opiate Substitution Treatment"[MeSH Terms] |
| | 5 "Methadone" OR "Methadone maintenance therapy" OR "OTP" OR "Opioid treatment program" |
| | 6 ("COVID-19"[Mesh]) AND ("Methadone" OR "MMT" OR "Methadone maintenance therapy" OR "methadone maintenance treatment" OR "OTP" OR "Opioid treatment program") |
| | 7 6 OR "take-home" OR "take-home" |
| | 8 ("COVID-19"[Mesh] OR "Pandemics"[Mesh]) AND ("Methadone/therapeutic use"[Mesh] OR "Methadone/administration and dosage"[MeSH] OR "MMT" OR "Methadone Maintenance Therapy" OR "Methadone Maintenance Treatment" OR "OTP" OR "OTPs" OR "Opioid treatment program" OR "opioid treatment programs" OR "take-home" OR "Take-home" OR "Opioid-Related Disorders/drug therapy"[Mesh] OR "Opioid-Related Disorders/therapy"[Mesh] OR "Opiate Substitution Treatment"[MeSH Terms] OR "Opioid-Related Disorders/prevention and control"[Mesh]) |
| 9 8 AND 1 | |
| PsycInfo | 1 covid-19.mp. or exp COVID-19/ |
| | 2 exp Pandemics/ or exp Severe Acute Respiratory Syndrome/ or sars-cov-2.mp. |
| | 3 1 or 2 |
| | 4 exp Methadone Maintenance/ or exp Methadone/ or methadone.mp. |
| | 5 3 AND 4 |
| Google Scholar | allintitle: methadone AND (pandemic OR change OR covid OR policy OR "expanded" OR "take-home" OR otp OR "opioid treatment program" OR mmt OR "maintenance therapy" OR "maintenance treatment") |

Appendix 2: Summary of reviewed articles

| | First Author, Year | Research Questions Addressed | Study Design | Study Period (pre, post pandemic) | Setting | Study Population | Sample Size |
|----|--------------------|---|---|--|---|---|--------------------------|
| 1 | Amram, 2021 | Implementation, Overdose, Illicit drug use/diversion | Observational outcomes study | Pre: 270 days prior to Mar. 1, 2020 Post: 270 days after April 1, 2020 | One OTP, Spokane WA | English-speaking clients age 18 years and older receiving methadone for OUD | 183 |
| 2 | Amram, 2022 | Implementation | Observational outcomes study | Pre: Dec. 1 2019 – Feb. 29, 2020 Post: Apr. 1 2020 – Jun, 30 2020 | One OTP, Spokane WA | English-speaking clients age 18 years and older receiving methadone for OUD | 194 |
| 3 | Bart, 2022 | Illicit drug use/diversion | Observational outcomes study | Pre: Jul. 2019 Post: Jul. 2020 | One OTP, Minneapolis, MN | Clients receiving methadone for OUD | 613 |
| 4 | Brothers, 2021 | Implementation, Overdose, Illicit drug use/diversion | Observational outcomes study | OTP survey: Jul 8- Aug. 18, 2020 Death data: 2020 Pre: 2015-201 Post: Jan.- Aug. | Multiple OTPs, Mortality data, CT | Clients receiving methadone for OUD | 24,261 |
| | Dunn, 2021 | Implementation, Illicit drug use/diversion, Patient Experience | Randomized Trial | Mar. 2018 – Mar. 2020 | One OTP, Baltimore, MD | Clients age 18 years and older receiving methadone for OUD | 25 |
| 6 | El-Bassel, 2022 | Patient experience | Quantitative content analysis | Mar. 1- May 22, 2020 | Reddit, subreddits: r/opiates, r/OpiatesRecovery, r/suboxone, and r/Methadone | Clients receiving methadone for OUD | 9,809 |
| 7 | Ezie, 2022 | Overdose, Illicit drug use/diversion | Observational outcomes study | Pre: Dec. 16, 2019 – Mar. 15, 2020 Post: Mar. 16- June 15, 2020 | One OTP, New York, NY | Veterans receiving methadone for OUD | 129 |
| 8 | Figgatt, 2021 | Implementation, Illicit drug use/diversion | Closed end survey of practices/perceptions | Pre/Post March 1, 2020 | Multiple OTPs, Greensboro, NC | Clients receiving methadone for OUD | 104 |
| 9 | Goldsamt, 2021 | Implementation, Provider experiences | Qualitative study | "Early pandemic" | Multiple OTPs, Multi-state | MOUD Providers | 25 |
| 10 | Harris, 2022 | Patient experience | Qualitative study | Aug. – Oct. 2020 | One OTP, Boston, MA | Adults 18-65 with overdose in last 3 years | 20 |
| 11 | Hoffman, 2022 | Implementation, Illicit drug use/diversion, Initiation/Retention Tx, Patient Experience | Observational outcomes study ; qualitative interviews | Pre: Sep. 1, 2019 – Feb. 28, 2020 Post: Apr. 1, 2020 – Sep. 30, 2020 | Multiple OTPs, OR | Clients receiving methadone | 377 (quant) 32 (qual) |

| | First Author, Year | Research Questions Addressed | Study Design | Study Period (pre, post pandemic) | Setting | Study Population | Sample Size |
|----|---------------------------|--|-------------------------------|---|--|--|--------------------|
| 12 | Hunter, 2021 | Implementation, Provider experiences | Qualitative study | May 14, 2020 - June 19, 2020 | Multiple OTPs, Multi-state | MOUD Providers | 20 |
| 13 | Jacka, 2021 | Implementation | Observational outcomes study | May - July 2020 | Multiple OTPs, Multi-state | Clients age 18 years + receiving methadone for OUD | 135 |
| 14 | Jones, 2022 | Overdose | Observational outcomes study | Pre: Jan. 2019- Feb 2020 Post: Apr. 2020- Aug 2021 | Mortality data, Multi-state | Adults 18 + | N/A |
| 15 | Joseph, 2021 | Implementation, Overdose | Observational outcomes study | Mar. 16, 2020 - May 31, 2020 | Multiple OTPs, Bronx NY | Clients receiving methadone | 3,600+ |
| 16 | Kidorf, 2021 | Implementation, Illicit drug use/diversion | Observational outcomes study | Apr. 8– Jul. 6, 2020 | One OTP, Baltimore, MD | Clients receiving methadone | 42 |
| 17 | Krawczyk, 2021 | Patient experience | Qualitative study | Mar. 5- May 13, 2020 | Reddit: subreddits: r/opiates, r/OpiatesRecovery, | Clients receiving methadone | 2,000 |
| 18 | Krawczyk, 2022 | Implementation, Provider experiences | Closed end survey | Sep.- Nov. 2020 | Multiple OTPs, PA | Clinical directors of OTPs | 47 |
| 19 | Levander, 2021 | Patient experience | Qualitative study | Pre: Aug.- Oct. 2020 Peri: Nov. 2020 – Jan. 2021 | Multiple OTPs, OR | English-speaking clients age 18+ receiving methadone | 46 |
| 20 | Levander, 2022 | Implementation, Provider experiences | Closed end survey | Sep. – Nov. 2020 | Multiple OTPs, Multi-state | OTP leaders | 170 |
| 21 | Madden, 2021 | Provider experience | Qualitative study | Feb. 17, 2017 – Aug. 31, 2020 | Multiple OTPs, Multi-state | OTP staff | 59 |
| 22 | McIlveen, 2021 | Implementation | Observational outcomes study | Pre: Feb. and first half of Mar, 2020 Post: Mar-Jun 2020 | Multiple OTPs, OR | Clients receiving methadone | 7,792 |
| 23 | Nobles, 2021 | Patient experience | Qualitative study | Jan. 31- Sep. 30, 2020 | Reddit Subreddits: r/methadone | Clients receiving methadone | 215 |
| 24 | Saloner, 2022 | Implementation | Closed end survey | Aug.19, 2020 – Jan. 29, 2021 | Convenience sample of substance use treatment and harm reduction programs, Multi-state | Individuals receiving substance use treatment | 243 |
| 25 | Sarker, 2022 | Patient experience | Quantitative content analysis | Pre: Jan. 1, 2019 – Feb. 29, 2020 Peri: Mar. 1, 2020 – Nov. 30, 2020 | Reddit | Clients receiving methadone | 820 |

| | First Author, Year | Research Questions Addressed | Study Design | Study Period (pre, post pandemic) | Setting | Study Population | Sample Size |
|----|---------------------------|--|------------------------------|---|--|---|--|
| 26 | Suen, 2022 | Implementation, Provider experiences, Patient experience | Qualitative study | Provider: Aug, to Sep, 2020 Patient: Sep. to Nov. 2020 | One OTP, San Francisco, CA | MOUD providers, clients receiving methadone | 10 providers, 20 patients |
| 27 | Treitler, 2022 | Provider experience | Qualitative study | Sep. – Nov. 2020 | Providers from OTPs or office-based treatment, NJ | MOUD providers | 20 |
| 28 | Walters, 2022 | Patient experience | Qualitative study | Jun. – Oct.2020 | Substance use clinics/programs and craigslist ads, Northeast | Adults 18+ who use/used drugs; MOUD providers, clinic staff, or work at a regulatory agency | 21 clients 18 providers, or gov. agencies |
| 29 | Welsh, 2022 | Overdose | Observational outcomes study | Pre: Mar. 19, 2019 – Mar. 16, 2020 Post: Mar. 17, 2020 – Mar. 15, 2021 | Poison Control Center Data, Multi-state | Adults ≥ 18 years old | 2,461 |

Panel 1: Selected quotes from qualitative studies capturing patient and provider experiences, by theme

Theme 1: patient challenges with opioid treatment programme (OTP) resistance to implementing pandemic flexibilities

"I live with high risk people. I'm afraid that going to the clinic puts them at risk, but my clinic refuses to follow SAMHSA guidelines." (Nobles, 2021)²³

"I still had to get up and go every day. They weren't running trains. They weren't running the buses...I'm five miles away from [the] inner city. And here I am having to fucking ride the bike down the highway...We couldn't do anything, but it's okay to send the drug addicts out. The homeless guys out so that they can go get their food stamps and fucking methadone" (Harris, 2022)²⁴

"The most [take-home doses] one can get [at my OTP] is 1 week. I asked if they would have to make special exceptions because of the [COVID-19] crisis. I was told that nobody has to do anything for us" (Sarker, 2022)²⁵

"...my immune system is comprised. All documented via paperwork from doctors/emergency rooms plus my medication lists...I've not been given the take-home doses nor have others that have health issues causing us to be high risks [for COVID-19]. What can we do? I've talked to the drug board, and health department. As have others. We feel very afraid that we will die trying to get dosed. It's maddening knowing the clinic has permission to give take-homes but refuse. They just 'blow us off' saying they will call etc[.] etc. But no one of us has been called yet." (Sarker, 2022)²⁵

Theme 2: patient positive experiences with take-home flexibilities

"...I feel that it's given me a sense of responsibility. I wasn't sure if I was ready to handle—but of course, I rose to the challenge. That makes me feel proud of myself. It really does. Having that responsibility and taking care of them on my own." (Hoffman, 2022)²⁶

"[Take-home doses make] it much easier for me—probably more than most people, because it might not be a big deal to a lot of people but I live twenty four miles...Every day when I was coming in, it was almost forty-five minutes to an hour driving round trip every day just the driving. I did that for probably a couple of years. Six days a week." (Hoffman, 2022)²⁶

"I didn't feel nervous...that I would take them all at once or have trouble taking them every day. I didn't feel like I wasn't being monitored properly because I wasn't coming into the clinic all the time...When you get your take-homes it's like you feel you are being trusted to take care of yourself, and do the right thing...it felt great...that I was on the right track in my recovery." 39-year-old woman (Levander, 2021)²⁷

"[I am] able to live a normal life without having to come in every single day. I have a baby at home and stuff so that's initially why I joined the clinic...Not having to come in. I feel a little more independent. I feel when I do get a job it will be a lot

easier...just enjoy being able to be more like a normal person, just having my medication at home." 31-year-old woman (Levander, 2021)²⁷

"I was able to go camping with my mom and not have to worry about asking for extra doses. I went and saw my son and I didn't have to ask for extra doses 'cause I already had them. Just made it a little easier. A lot easier." 51-year-old woman (Levander, 2021)²⁷

"Before I would go every week. Now I'm going every two weeks... Definitely better...Well, the thing with work, not having to worry about being late for work on those days." (Walters, 2022)²⁸

Theme 3: patient negative experiences with take-home flexibilities

"Now, I like coming in every day because I think it keeps you on track...I think it's better for people at first...I wasn't even getting take-homes, and all of a sudden here I am getting two weeks of my medicine so it was kind of a lot...For me it just wasn't good at the time because I was still pretty new in my sobriety, you have to trust in yourself and everybody is different." 44-year-old woman (Levander, 2021)²⁷

"I found [the methadone take-home doses] very hard to do because I would drink a little extra on day four, and it would leave me running on empty...So I basically told on myself and told [the clinic] that I was having trouble with the take-homes, so they stopped giving them to me...I like it better because [going to the clinic] gets me up and ready for the day. I get up early, so I'm not sleeping all day. So it gets me motivated" 37-year-old man (Harris, 2022)²⁴

"When you're on the clinic, you go every single day, which means you got to get up and leave the house, and just go. Now, they were giving people take-homes, which means some people got three, and six, whatever. I ended up getting six bottles so I could stay home. In a way, it helped me, but then in a way it hurts too because I started that feeling again of not leaving the house... I think I probably shouldn't have got any take-homes and just continued going daily, and seeing the nurses and the counsellors that were there." 52-year-old woman (Harris, 2022)²⁴

Theme 4: provider positive experiences with take-home flexibilities

"Keeping it as loose as possible so that individual clinics could do what they think is clinically appropriate feels like it would be safer than the old ways of doing things...The idea [is] to help people achieve greater success and greater liberty from us. And it's been okay. We haven't had any terrible stuff from that." (Suen, 2022)²⁸

"This was the most surprising thing...getting the take-home medications that they have not earned, actually motivated them to change that they are now meeting the criteria...So that for them it's no longer a pandemic bottle, it is another bottle that I have earned" (Trietler, 2022)²⁹

(Panel 1 continues on next page)

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“But at the end of the day, a regulatory requirement that we must see people face-to-face for that visit, there is no question that there are people that will not be able to access care during that windowed timeframe. There will be people that overdose and die because, I mean, that will happen. We strongly advocate for that not being reinstated and that we are able to continue to deliver care” (Trietler, 2022)²⁹

“Our initial thinking that it was just going to be a complete mess...and it ended up not turning out that way at all” (Trietler, 2022)²⁹

“the levers for telemedicine, for take-home supplies of methadone have really been a game changer. And I’m really hoping that it’s something that is extended and we can move that up permanently” (Hunter, 2021)³⁰

Theme 5: provider negative experiences with take-home flexibilities

“As a contingency management tool, we’ve lost the ability to grant or remove take-home dosages from patients, either as an incentive for doing better or as something they would lose if they did worse. So, we’ve definitely lost a lot of tools” (Trietler, 2022)²⁹

“A pregnant mother that I can recall, she just needed the contact that came with daily dosing. She needed the support that we were giving her, and the love and attention we were giving her that she wasn’t getting at home to help her get through her pregnancy...I like that accountability piece of coming in every day, so we have eyes on them. That’s why I prefer methadone over Suboxone.” (Madden, 2021)³¹