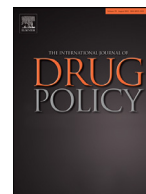




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## Review

## Medication for opioid use disorder in the Arab World: A systematic review



Jude Alawa<sup>a</sup>, Muzzammil Muhammad<sup>b</sup>, Maryam Kazemitabar<sup>c</sup>, Daniel J Bromberg<sup>c</sup>,  
Danilo Garcia<sup>d,e</sup>, Kaveh Khoshnood<sup>c</sup>, Lilian Ghandour<sup>f,\*</sup>

<sup>a</sup> Stanford University School of Medicine, 291 Campus Drive, Stanford, CA 94305, United States

<sup>b</sup> Yale University School of Medicine, 333 Cedar St, New Haven, CT 06510, United States

<sup>c</sup> Yale University School of Public Health, 60 College St, New Haven, CT 06510, United States

<sup>d</sup> Centre for Ethics, Law and Mental Health (CELAM), University of Gothenburg, Box 100, 405 30 Gothenburg, Gothenburg, Sweden

<sup>e</sup> Department of Behavioral Sciences and Learning, Linköping University, SE 581 83, Linköping, Sweden

<sup>f</sup> Department of Epidemiology and Population Health, Faculty of Health Sciences, American University of Beirut, Van Dyck Building, PO Box 11-0236, Riad El-Solh Beirut, 1107 2020, Lebanon

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## ABSTRACT

**Background:** Opioid use disorder (OUD) is a global public health concern. The standard of care for OUD involves treatment using medications such as buprenorphine, methadone, or naltrexone. No known review exists to assess the contextual factors associated with medication for opioid use disorder (MOUD) in the Arab World. This systematic review serves as an implementation science study to address this research gap and improve the uptake of MOUD in the Arab World.

**Methods:** Systematic searches of Medline, PsycINFO, and EMBASE, and a citation analysis, were used to identify peer-reviewed articles with original data on MOUD in the Arab World. Quality assessment was conducted using the CASP appraisal tools, and main findings were extracted and coded according to the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) framework.

**Results:** 652 research articles were identified, and 10 met inclusion criteria for final review. Four studies considered health-systems aspects of MOUD administration, such as cost-effectiveness, the motivations for and impact of national MOUD policies, the types of social, political, and scientific advocacy that led to the adoption of MOUD in Arab countries, and the challenges limiting its wide-scale adoption in the Arab World. Six papers considered MOUD at individual and group patient levels by evaluating patient quality of life, addiction severity, patient satisfaction, and patient perspectives on opioid agonist therapy.

**Conclusion:** Despite financial and geographic barriers that limit access to MOUD in the Arab World, this review found MOUD to be cost-effective and associated with positive health outcomes for OUD patients in the Arab World. MOUD can be successfully established and scaled to the national level in the Arab context, and strong coalitions of health practitioners can lobby to establish MOUD programs in Arab countries. Still, the relative novelty of MOUD in this context precludes an abundance of research to address its long-term delivery in the Arab World.

## Introduction

Opioid use disorder (OUD) is a global public health issue impacting the Middle East and North Africa (MENA). High rates of opioid use have been observed in as many as 12 Arab countries, with particularly high rates seen in Bahrain and Kuwait (Wilby & Wilbur, 2017). The MENA region is also one of just three Joint United Nations Programme on HIV/AIDS (UNAIDS) regions with a worsening HIV epidemic, and people who inject opioids via non-sterile means are particularly vulnerable to HIV infection (UNAIDS, 2021).

The three medications supported by World Health Organization (WHO) guidelines for the treatment of OUD are opioid agonist therapies (OAT's): methadone, buprenorphine, and extended-release naltrexone (WHO, 2009). Studies considering the effectiveness of medication for opioid use disorder (MOUD) have associated MOUD with decreased overall mortality (Ma et al., 2019; Pierce et al., 2016; Sordo et al., 2017), reduced opioid overdose deaths (Schwartz et al., 2013), decreased incidence of other drug use (Thomas et al., 2014), lower risk of behaviors linked to HIV infection (Altice et al., 2011), lower risk of hepatitis C (Alavian et al., 2013), and less involvement in crime (Sun et al., 2015).

\* Corresponding author.

E-mail address: [lg01@aub.edu.lb](mailto:lg01@aub.edu.lb) (L. Ghandour).

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Despite significant evidence for its efficacy, MOUD has not been broadly adopted in the MENA region. In 2020, MOUD was only available as a treatment modality for OUD in four of the 19 World Bank-classified MENA states — Lebanon, Morocco, Iran, and the Palestinian Territories. This coincides with the limited adoption of other major harm reduction programs for substance use disorders in the region, with Needle and Syringe Programs present in only seven MENA states, overdose response programs in just two MENA states, and no Drug Consumption Rooms in any MENA state. The limited adoption of these harm reduction measures reflects the widespread criminalization of narcotic possession and use throughout the region, regional stigma against people with OUD, and a lack of attention given to this vulnerable population and public health issue (Harm Reduction International, 2020).

While MOUD has been adopted and well-studied in Iran and countries neighboring MENA, such as Israel and Turkey, where Arabic is not the major official language, MOUD remains extremely understudied in Arab contexts. Beyond using the same language, countries comprising the Arab World largely share similar cultural values, religious outlooks, and historical backgrounds. Despite differences in population size and wealth, these core characteristics that Arab nations share are considered to shape their attitudes, legislation, and programming surrounding substance use, harm reduction, and MOUD more specifically. For instance, drug use is legally prohibited and often socially stigmatized in the Arab World, which may impact reported usage metrics that could be used to justify the development of robust treatment programs (Ghandour et al., 2016). At least five Arab states have adopted MOUD, including Morocco, Palestine, the United Arab Emirates, Lebanon, and Bahrain (Ghaddar, Abbas, & Haddad, 2017). However, no known study has conducted a systematic review of the peer-reviewed literature surrounding MOUD in the Arab World. As such, this paper serves as an implementation science-oriented review of MOUD in the Arab World that aims to identify the contextual factors associated with MOUD uptake and to help adapt the evidence-based intervention of MOUD for application in Arab contexts.

## Methods

The methodology for this study is summarized in the associated International Prospective Register of Systematic Reviews protocol (ID = CRD42020222941).

### Search strategy

A systematic review of all studies of MOUD in the Arab World was conducted. MOUD studies were defined as those that focus on methadone, buprenorphine, or naltrexone. The Arab World was defined as countries that are member states, both active and suspended, of the League of Arab States (Arab League). Therefore, countries where Arabic is an official, but not necessarily the most spoken, language (e.g., Somalia) were included in the search strategy. Though this study focuses on the implementation factors associated with MOUD, our search strategy was not limited to any particular study design, methodology, or theoretical framework; this was done to obtain the broadest set of retrieved studies and to include articles that may contain relevant information but do not explicitly define themselves as implementation science studies.

Our search strategy was designed to retrieve articles using title-abstract keywords and, where appropriate, controlled vocabulary for the following concepts: 1) MOUD and 2) the Arab World. Our search string is displayed in Table 1. The search strategy was tested against a validated set of articles and applied in three bibliographic databases via OVID: 1) MEDLINE; 2) Embase; and, 3) PsycINFO. Similar searches were conducted in each database; however, minor adjustments were made where controlled vocabulary schema differed by database. We did not apply human subjects, date, or language restrictions to the search. All searches were conducted on January 4th, 2021.

### Study selection

To be included in the present review, a study had to: 1) Include data on MOUD (buprenorphine, methadone, or naltrexone); 2) include data on any member state of the League of Arab States; 3) contain original data (reviews, commentaries, opinion pieces, etc. were excluded); and 4) be peer-reviewed.

Titles and abstracts of all retrieved articles were exported to End-Note (Hupe, 2019), deduplicated, and uploaded to Covidence software for management (Covidence, 2019). Then, each title and abstract was independently reviewed against inclusion criteria by at least two reviewers (JA, MM, MK, DB) to identify potentially relevant studies. Disagreements were resolved by consensus or arbitration by a third reviewer. Next, full texts of articles identified during title and abstract review were read and evaluated against inclusion criteria. At least two study team members (JA, MM, MK, DB) had to agree on all inclusions and exclusions. Where reviewers had conflicting votes regarding inclusions, a third team member would resolve the disagreement. Citations of all included articles were then reviewed to identify other potentially relevant articles.

### Data extraction & analysis

From all sources included in the final dataset, study team members (JA, MM, MK, DB) extracted the study characteristics and main findings, and reviewed and coded articles according to the Reach, Effectiveness, Adoption, Implementation, or Maintenance framework (RE-AIM; Glasgow et al., 2019). The RE-AIM framework is a time-tested tool in translational research and was selected because one of the main goals of this review is to inform MOUD implementation in the Arab World. RE-AIM designates five criteria with which to evaluate health interventions: 1) how well they reach their target populations, 2) their effectiveness and/or efficacy, 3) the extent and experience of their adoption by target staff, settings, or institutions, 4) their implementation consistency, costs, and adaptations made during delivery, and 5) the maintenance of their effects in individuals and populations over time. We applied the RE-AIM framework to our evaluation by considering the following:

- 1) Reach: How can MOUD be scaled to reach patients with OUD in the Arab World?
- 2) Effectiveness: How effective is MOUD in the Arab World?
- 3) Adoption: How can organizational/institutional support be developed to support the delivery of MOUD in the Arab World?
- 4) Implementation: How can we ensure that MOUD is delivered properly in the Arab World?
- 5) Maintenance: How can we incorporate MOUD so that it is delivered over the long term?

Because of the heterogeneity of the study methodologies and outcomes of the studies included in this review, findings were summarized in a narrative fashion.

### Risk of bias

Quality assessment of included studies was conducted by two independent reviewers (MM, MK) using the Critical Appraisal Skills Programme (CASP) appraisal tool from the centre for Evidence-Based Medicine (CASP, 2003), as this tool allows for the direct comparison of the quality of studies with heterogeneous methodologies.

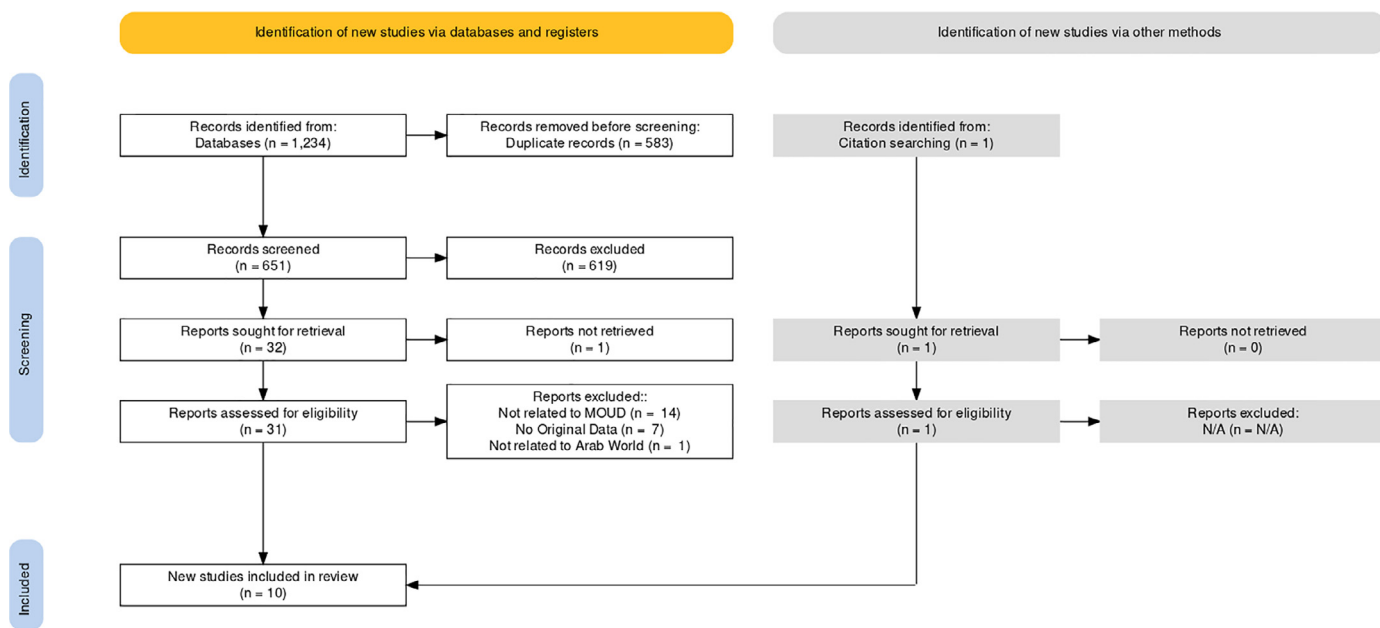
## Results

### Search results

After removing duplicates, our search strategy yielded 651 research articles. Title and abstract screening narrowed the number

**Table 1**  
Search strategy.

Search Strategy	
1	[opioid use]
2	substance-related disorders/ or opioid-related disorders/ or heroin dependence/ or morphine dependence/ or opium dependence/ or substance abuse, intravenous/ or substance abuse, oral/ or substance withdrawal syndrome/
3	((opioid* or opiate*) adj3 (abus* or dependen* or disorder* or addict* or misus* or "use" or "user" or "users" or "usage" or "using")).mp.
4	exp Narcotics/po
5	(OUD or IDU or PWID).mp.
6	("injection drug use" or "intravenous drug use").mp.
7	or/2-6
8	[MOUD]
9	((medication-assisted or opiate-agonist or maintenance or replacement or substitution) adj1 (treatment* or therap*)) or methadone or buprenorphine or suboxone or subutex or naltrexone or vivitrol or pharmacotherapy).mp.
10	buprenorphine, naloxone drug combination/ or naltrexone/ or Buprenorphine/ or exp Methadone/ or Opiate Substitution Treatment/ or substance-related disorders/dt or exp opioid-related disorders/dt or substance abuse, intravenous/dt or substance abuse, oral/dt or substance withdrawal syndrome/dt or substance-related disorders/rh or exp opioid-related disorders/rh or substance abuse, intravenous/rh or substance abuse, oral/rh or substance withdrawal syndrome/rh
11	or/9-10
12	7 and 11
13	[MENA region]
14	exp middle east/ or exp africa, eastern/ or exp africa,northern/ or arabs/
15	(algeria* or bahrain* or djibouti* or egypt* or iraq* or jordan* or kuwait* or lebanon or lebanese or libya* or mauritania* or morocco or moroccan* or oman* or palestine* or qatar* or saudi arabia* or saudi* or somalia* or sudan* or syria* or tunisia* or united arab emirates or emirati* or yemen* or middle east* or north africa* or west bank or gaza* or mena or maghreb* or arab* or druze).mp.
16	(Algiers or Manama or Djibouti or Cairo or Baghdad or Amman or Kuwait City or Beirut or Tripoli or Nouakchott or Rabat or Muscat or Ramallah or Doha or Riyadh or Mogadishu or Khartoum or Damascus or Tunis or Abu Dhabi or Sana'a or Sanaa).mp.
17	or/14-16
18	12 and 17



**Fig. 1.** PRISMA flow diagram of study.

of included articles to 32 studies, and full-text review further narrowed the number of included studies to nine studies (Ghaddar, Khandaqji, & Abbass, 2018; Khalaf, Hayek, Bakhos, & Abou-Mrad, 2019; El-Khoury, Abbas, Nakhle, & Matar, 2016; Ghaddar et al., 2017; Hren & Milanic, 2017; Samlali, Azzaoui, & Ahami, 2015; Rawson, Rieckmann, & Gust, 2013; Mawgoud & Al-Haddad, 1996; Tahboub-Schulte, Ali, & Khafaji, 2009). One additional study (Idrissi, Ahami, Ghaihlan, Azaoui, & Mammad, 2018) was identified through a citation analysis, bringing our total number of included studies to 10. Without full-text versions available, two of the 10 studies were included as abstracts. Fig. 1 displays a 2020 PRISMA flow diagram that provides an overview of our search and selection process of included studies for this review.

*Study characteristics*

Characteristics of included studies used for final review are shown in Table 2. The studies included in this review spanned a timeframe from 1980 to 2017. Represented study designs included qualitative studies (n = 1), cohort studies (n = 3), economic evaluations (n = 1), case studies (n = 1), cross-sectional studies (n = 1), and policy analyses (n = 3). Countries included are Lebanon (n = 5), Kuwait (n = 1), Morocco (n = 2), Bahrain (n = 1), and the United Arab Emirates (UAE; n = 2). Four papers considered health-systems aspects of MOUD administration, such as its economic cost-effectiveness compared to other treatment modalities, the motivations for and impact of changes to national MOUD policies, the types of social, political, and scientific advocacy that led to

**Table 2**  
Characteristics of included studies.

Author (Year)	Title	Period of Study	Study Design	Main Findings
Ghaddar et al. (2018)	Challenges in implementing opioid agonist therapy in Lebanon: a qualitative study from a user's perspective	June - July 2016	Qualitative study using a semi-structured interview among 81 male buprenorphine therapy (BT) patients at an OAT dispensary in Beirut, Lebanon. Questions concerned access to treatment, satisfaction with treatment rules, patient-provider relationship, perceived benefits and side effects of buprenorphine, as well as buprenorphine misuse and diversion.	Access mediates experiences of BT among patients, with higher satisfaction reported among people with fewer financial & logistical barriers to access. Major concerns about BT expressed by people with OUD include buprenorphine dependence, financial and geographic access to treatment. 15% of participants reported accessing buprenorphine through diversion.
Ghaddar et al. (2017)	Opiate agonist treatment to improve health of individuals with opioid use disorder in Lebanon	January 2013 - December 2014	Cohort study among male patients receiving OAT at the SKOUN Addiction Center in Beirut, Lebanon. Outcome variables were measured at follow-up 3 and 12 months after baseline.	OAT associated with (i) significantly higher employment, quality of life, lower anxiety and depression, fewer recent arrests and overdoses, and less heroin, cocaine and marijuana use at 3-month follow up and (ii) fewer recent arrests and overdoses, and less heroin, cocaine and marijuana use at 12-month follow up.
Hren and Milanic (2017)	Cost-effectiveness Comparison of Opioid Substitution Therapy Vs. Non-Pharmacologic Therapy in the State of Kuwait	N/A	Economic evaluation comparing buprenorphine/naloxone OAT to non-pharmacologic treatment in Kuwait using two microsimulation decision models.	OAT therapy "was at least highly cost-effective, if not cost-saving", compared to non-pharmacologic therapy
Samlali et al. (2015)	Methadone substitution treatment and its impact on quality of life among Moroccan patients	N/A	Cohort study among Moroccan patients receiving methadone OAT in Tangier, Morocco.	49% of patients displayed improved somatic status after therapy, with mixed (and negative) results seen for others. Very large increases (69.56% and 112.5%) seen in the number of patients reporting part-time and full employment, respectively.
Mawgoud and Al-Haddad (1996)	Heroin Addiction in Bahrain: 15 Years Experience	1980-1994	Policy Analysis. A historical perspective on management of OUD in Bahrain.	Bahrain's initial response to a 1983 opioid use epidemic was the use of widespread outpatient maintenance OAT. In 1987, Bahrain switched to a detoxification- and rehabilitation-based approach, only providing opioid and other antagonist therapies to patients with withdrawal symptoms identified by the OOWMS. The latter approach has seen considerable decreases in the number of patients receiving care for substance use (from 2978 in 1986 to 382 in 1994), and the total amount of medicine dispensed for substance use disorders (from 94,896 doses of any kind in 1986 to 621 in 1994, and 13,696 doses of methadone in 1986 to 81 in 1994)
Khalaf et al. (2019)	Comparative study between prison- and community-based treatment satisfaction for opioid use disorder in Lebanon	September - November 2017	Cross-sectional study comparing satisfaction with and general perceptions of OUD treatment among 30 patients in community receiving OAT and 30 under incarceration for opioid use receiving non-OAT symptomatic therapy.	Significantly lower satisfaction with treatment was reported among patients in incarceration than among those in the community (18.67 vs 34.73, respectively)
El-Khoury et al. (2016)	Implementing opioid substitution in Lebanon: Inception and challenges	2011 - 2014	Policy Analysis. Historical perspective and policy analysis of Lebanon's BT program for OUD, considering the system's structure, patient demographics and major challenges.	In Lebanon, OAT patients enter treatment through referral from psychiatrists authorized to prescribe buprenorphine. Between 2011 and 2014, 1244 patients were referred to the BT program. Six-month retention was calculated at 71%, 15% of which had been lost to follow up and re-enrolled within the study period, with higher retention for patients on higher-dose BT. Hepatitis C prevalence among Lebanese people with OUD decreased from 27% to 16% in 2014, though whether this is due to BT is not known
Rawson et al. (2013)	Addiction Science: A Rationale and Tools for a Public Health Response to Drug Abuse	N/A	Policy Analysis. Policy paper considering ways to create evidence-based public health responses to substance use disorder, with case-studies from Vietnam, Lebanon and the UAE.	OAT therapy in Lebanon was explicitly legalized in 2011, with the roll-out of a national OAT system in 2012, due to the persistence of clinician advocates and their allies in NGOs and international organizations. A major expansion of Abu Dhabi's National Rehabilitation Center saw the importation of Suboxone for OAT.
Tahboub-Schulte et al. (2009)	Treating Substance Dependency in the UAE: A Case Study	~2009	Case Study of a 35 y/o patient with OUD detoxified using an unspecified agent and maintained on 25 mg of buprenorphine a day, prescribed by Abu Dhabi's NRC.	N/A
Idrissi et al. (2018)	The Evolution of the Health Status and Quality of Life of Heroin Addicts Treated with Methadone in the City of Tangier, Morocco	March - August 2013	A cohort study evaluating somatic status and quality of life among 101 OUD patients receiving MT in Tangier/ Morocco.	MT was associated with improved somatic status, lower unemployment and improved occupational status, as well as increased family cohabitation.

the adoption of MOUD in Arab countries, and what challenges limit the wide-scale adoption of MOUD (El-Khoury et al., 2016; Hren & Milanic, 2017; Rawson et al., 2013; Mawgoud & Al-Haddad, 1996). Six other papers considered MOUD at the level of individual patients and patient groups, evaluating outcomes such as patient quality of life, addiction severity, patient satisfaction, and patient perspectives about comparing opioid agonist therapy (OAT) (Ghaddar et al., 2018; Idrissi et al., 2018; Khalaf et al., 2019; Ghaddar et al., 2017; Samlali et al., 2015; Tahboub-Schulte et al., 2009).

Of the 10 studies included in this review, seven were assessed for quality using CASP appraisal tools (Ghaddar et al., 2018; Idrissi et al., 2018; Khalaf et al., 2019; Ghaddar et al., 2017; Hren & Milanic, 2017; Mawgoud & Al-Haddad, 1996; Samlali et al., 2015). Two policy analyses and one case study were not assessed because of a lack of methodological requirements for these study types. Additionally, two of these ten studies (Hren & Milanic, 2017; Samlali et al., 2015) were abstracts, and therefore, were not able to be appraised in full. Overall, of the studies appraised, four were at a high risk of bias. Detailed assessments of the risk of bias across the studies are presented in **Supplementary File 1**.

### Study findings

Articles utilizing a health-systems approach provide a variety of perspectives on MOUD in the Arab World. Hren and Milanic (2017) used two microsimulation models to perform a cost-effectiveness analysis of OAT to non-pharmacological therapy for OUD treatment in Kuwait and found OAT to be “highly cost-effective, if not cost-saving,” compared to non-pharmacological treatment. Mawgoud and Al-Haddad (1996) gave an overview of OUD management in Bahrain, outlining the country’s transition from widespread use of OAT for outpatient maintenance therapy to a new detoxification- and rehabilitation-based approach in 1987, and the strict use of OAT only in response to signs and symptoms of opioid withdrawal reflected by the Opioid Objective Withdrawal Manifestations Scale. This new regime saw substantial decreases in the number of patients receiving care for substance use and the number of medications dispensed. This study attributes this transition to the over-prescription of OAT under the initial maintenance-based approach and cites increased patient responsibility for treatment success using approaches such as treatment contracts and stronger enforcement of substance use and trafficking laws by the Bahraini police.

El-Khoury et al. (2016) takes a similar approach and provides a historical perspective and policy analysis of Lebanon’s buprenorphine therapy (BT) program for OUD, considering the system’s structure, patient demographics, and major challenges. In Lebanon, patients enter BT through referral from psychiatrists authorized to prescribe buprenorphine and are required to also register with one of four NGOs focusing on substance use disorders. Treatment is offered at a variety of sites, from heavily subsidized programs at community centers to more expensive options at private clinics. Between 2011 and 2014, 1244 patients were referred to the BT program, with half of all patients enrolled during 2012, the first full year of the program. Six-month retention in the program was calculated at 71%, 15% of which had been lost to follow-up and subsequently re-enrolled within the study period. High correlations were found between early poor attendance and treatment discontinuation. Other common causes for discontinuation included legal and financial issues. Though 6% of all patients were women, it is uncertain whether this reflects overall patterns of opioid use and OUD in Lebanon because some treatment locations may be male-dominated. Higher retention was seen for patients on higher-dose BT, with patients receiving BT of 16 mg/day and above showing higher 36-month retention than those receiving lower-dose regimens. Hepatitis C prevalence among Lebanese people with OUD decreased from 27% to 16% in 2014, but the authors note it is unclear whether this can be attributed to increased availability of BT. Major challenges discussed include a lack of communication between MOUD prescribers and dispensers involved in the program, an absence of local prescribing guidelines, a lack of su-

pervised dose dispensing, limited patient and family education, drug diversion and trafficking, and limited coordination with security agencies and the legal justice system.

Rawson et al. (2013) used the Lebanese example alongside two others from Vietnam and the UAE to consider how, across a variety of contexts, advocates for MOUD and other medical services for substance use disorders can collaborate to create evidence-based public health initiatives to support patients with these conditions. In the Lebanon example, this study demonstrates how persistent advocacy on the part of clinicians providing care to people with substance use disorders, along with their allies in NGOs and international organizations, were able to achieve the explicit legalization of OAT in Lebanon in 2011, and the roll-out of a national OAT system in 2012. The article’s discussion of MOUD in the UAE was limited to a mention that, as part of a major expansion of Abu Dhabi’s National Rehabilitation Center (NRC), the UAE imported doses of Suboxone to provide OAT to patients with opioid use disorder.

Articles considering individual patients and patient groups provided insight at a more granular level. Three such articles considered patients and populations in Lebanon. Ghaddar et al. (2017), a cohort study among male patients receiving OAT in Beirut, associated OAT with significantly higher employment and quality of life, lower anxiety and depression, fewer recent arrests and overdoses, and less heroin, cocaine, and marijuana use at 3-month follow up. Ghaddar et al. (2018), a qualitative study of 81 semi-structured interviews with BT patients at one of Beirut’s two OAT dispensaries, identified access as a key mediator of experiences of BT, with higher satisfaction reported among people with fewer financial and logistical barriers. Interviewees’ major concerns about BT included worries about buprenorphine dependence, as well as concerns about financial and geographic access to treatment. Khalaf et al. (2019) used the Treatment Perceptions Questionnaire in a cross-sectional study design to compare satisfaction with OUD treatment between a group of 30 patients receiving BT and 30 people in prison for OUD receiving non-OAT symptomatic therapy and found higher satisfaction among the OAT group.

Three additional considered patient experiences outside of Lebanon. Samlali et al. (2015), a cohort study among OUD patients receiving methadone therapy (MT) in Tangier, Morocco, associates MT with improved somatic status, decreased solitary living, increased cohabitation with family, and improved employment status. Idrissi et al. (2018), another Tangier-based cohort study, also associated MT with improved somatic status. Outside of Morocco, Tahboub-Schulte et al. (2009), a clinical case study, describes the experience of a 35-year-old patient with OUD at Abu Dhabi’s NRC receiving detoxification treatment using an unspecified agent and maintenance on 25 mg of buprenorphine a day.

### RE-AIM

The RE-AIM framework was used to organize our interpretation of these results and to consider the implications of these findings on MOUD implementation in the Arab world. We mapped our findings to RE-AIM criteria in Table 3. Mawgoud and Haddad (1996) and El-Khoury et al. (2016) considered R-REACH and demonstrated that systems of MOUD administration have been successfully established and scaled up to the national level in Arab contexts. Ghaddar et al. (2017), Hren and Milanic (2017), Samlali et al. (2015), Tahboub-Schulte et al. (2009), and Khalaf et al. (2019) each addressed E-EFFECTIVENESS, and collectively made the case that MOUD in Arab Countries was cost-effective and associated with positive outcomes for OUD patients.

A-ADOPTION was considered in Rawson et al. (2013), which showed that strong coalitions consisting of clinical practitioners that provided care to patients with OUD, as well as their allies, can successfully lobby to establish MOUD programs in Arab countries. I-IMPLEMENTATION was most directly addressed by Ghaddar et al. (2018), which highlighted the importance of access in influencing OAT outcomes, and El-Khoury et al. (2016), which outlined key challenges that limit MOUD

**Table 3**  
Evidence mapped to RE-AIM criteria.

RE-AIM framework	Pertinent Articles	Summarized Findings
<b>R-Reach</b>	Mawgoud and Haddad (1996) and El-Khoury et al. (2016)	Systems of MOUD administration have been successfully established and scaled-up to the national level in Bahrain and Lebanon.
<b>E-Effectiveness</b>	Ghaddar et al. (2017), Hren and Milanic (2017), Idrissi et al. (2018), Samlali et al. (2015), Tahboub-Schulte et al. (2009) and Khalaf et al. (2019)	MOUD in Arab Countries is cost-effective (Kuwait) and associated with positive outcomes for OUD patients (Lebanon, Morocco, UAE).
<b>A-Adoption</b>	Rawson et al. (2013)	Strong coalitions consisting of clinical practitioners that provide care to patients with OUD, as well as their allies, can successfully lobby to establish MOUD programs in Arab countries (Lebanon).
<b>I-Implementation</b>	Ghaddar et al. (2018) and El-Khoury et al. (2016)	Highlight the importance of access in influencing OAT outcomes and outline key challenges that limit MOUD (Lebanon).
<b>M-Maintenance</b>	Mawgoud and Al-Haddad (1996)	In Bahrain, concerns around over-prescription and under-regulation led to a shift in the dominant OUD management paradigm, from outpatient maintenance therapy to strict use for detoxification purposes only.

implementation in Lebanon. Of the articles included in our final review, Mawgoud and Al-Haddad (1996) addressed M-MAINTENANCE by showing how, in one Arab context, concerns around over-prescription and under-regulation led to a shift in the dominant OUD management paradigm, from outpatient maintenance therapy to strict use for detoxification purposes only.

**Discussion**

To the best of our knowledge, this study is the first to systematically review the literature surrounding MOUD in the Arab World through an implementation science framework. Despite its well-established effectiveness and the rise of substance use disorders across the Arab World, MOUD remains unavailable in a large majority of Arab World countries (Bassiony, 2013; Cheikh, Rousseau, & Mekki-Berrada, 2011; Fawzui, 2011). This review reveals that the published literature surrounding MOUD in this context is limited, with only 10 peer-reviewed publications qualifying for inclusion in this review. That being said, this review demonstrates that within Arab contexts, MOUD is an extremely cost-effective treatment modality and is associated with improved treatment outcomes and increases in patient responsibility, satisfaction, and quality of life. Using the RE-AIM framework, which ultimately serves as an established tool for stakeholders to improve implementation of evidence-based interventions, this review also identifies contextual factors that are associated with MOUD uptake in the Arab World and that can be leveraged to further scale MOUD implementation in this context (Glasgow et al., 2019).

Among the studies included in this review, only five of 22 Arab World countries, including Lebanon, Morocco, the United Arab Emirates, Bahrain, and Kuwait, were represented, reinforcing the notion that a paucity of literature exists to address MOUD across the Arab World countries (ElKashef et al., 2019; Khalsa & Mathur, 2021). In addition, following evaluation by standardized appraisal tools, most of the studies were determined to be at a high risk of bias. Of Arab World countries, OAT is knowingly provided in Morocco, Bahrain, the United Arab Emirates, Palestine, and Lebanon. However, the research output on OAT in these countries stands in stark counterpart to that of neighboring, non-Arab countries, namely Israel, Turkey, and Iran. Iran, for example, has been a worldwide leader in evaluating treatments for OUD, adopting OAT in its national policy, creating strong outpatient programs with over 4000 dispensing centers, and developing a robust literature base on substance use disorder treatments (Ghaddar et al., 2017; Noori, Narenjiha, Aghabakhshi, Habibi, & Khoshkrood Mansoori, 2012). The disparity in quality research output among Arab countries reflects a need for both increased research on MOUD in Arab contexts and a need for methodologically rigorous research. When considering the R-Reach and A-Adoption of MOUD implementation, this disparity highlights the limited availability and reach of MOUD in the Arab World. To address this,

Rawson et al. (2013) provides evidence that clinical practitioners can work together to not only provide care to patients with OUD but also to lobby, along with other healthcare workers, to establish effective MOUD programs in Arab countries. Similarly, in Lebanon and Bahrain, Mawgoud and Haddad (1996) and El-Khoury et al. (2016) demonstrate how MOUD administration can be established and scaled to national levels. Therefore, to strengthen the literature base surrounding harm reduction and MOUD in the Arab World, researchers and policymakers must work collectively to prioritize the development of quality research studies that provide the evidence necessary to inform effective policy and programming. Then, to improve the reach and adoption of MOUD in the Arab World, stakeholders and constituent countries must consider the development of a national strategy for the delivery of OUD care involving OAT. Such a strategy should be based on clinical evidence and outline a clear standard of treatment and measurable goals that stakeholders can monitor and work toward and monitor regularly.

Furthermore, the findings of this review relating to the effectiveness and impact of MOUD in Arab World countries are consistent with those found in the literature of other countries and regions across the globe. Ghaddar et al. (2017), Hren and Milanic (2017), Idrissi et al. (2018), Samlali et al. (2015), Tahboub-Schulte et al. (2009), and Khalaf et al. (2019) provide evidence that MOUD is cost-effective for OUD patients in Arab countries and is correlated with decreased dependence on illicit substances, decreased Hepatitis C prevalence, improved somatic status, and improved quality of life measures, including higher employment and fewer depressive symptoms. As such, when considering the RE-AIM framework, this review provides substantial evidence to support MOUD's E-Effectiveness in the Arab World. Half of the studies included in this review were conducted in Lebanon, which is likely reflective of the impact of advocacy efforts done by Lebanese NGOs working in harm reduction. For example, the Middle East and North Africa Harm Reduction Association (MENAHRA) is a regional network based in Beirut that strives to improve the lives of drug users through advocacy, capacity building, and technical assistance. Evidence from other regions, including Europe and the United States, further emphasize the importance of increasing access to integrated treatment programs with OAT (Dematteis et al., 2017; ElKashef et al., 2019; Kampman & Jarvis, 2015). A WHO collaborative study found that OAT reduced illegal opioid use, HIV-associated risky behaviors, and criminality, as well as improved physical and mental health among patients dependent on opioids (Lawrinson et al., 2008). In line with the findings of this review, other studies have also demonstrated that OAT can have consistent positive outcomes across a diversity of cultural contexts and in both low- and middle-income and high-income countries, reinforcing findings of substantial improvements in quality of life, family relations, criminality, decreased drug use, decreased risky behaviors, and improved psychological and social well-being (Armstrong, Kermode, Sharma, Langkham, & Crofts, 2010; Feelemyer, Des Jarlais, Arasteh, Phillips, & Hagan, 2014;

Ghaddar et al., 2017; Lua & Talib, 2012; Morozova, Dvoriak, Pykalo, & Altice, 2017; Padaiga, Subata, & Vanagas, 2007; Pang et al., 2007; Wang et al., 2012). Given the demonstrated effectiveness of integrated treatment programs utilizing OAT in improving several health and social outcomes, national governments must make investments that allocate resources to research and relevant centers to make these services available and improve OUD care. To support policymakers and public health officials in developing successful programs, future research may consider further evaluating what factors have enabled the development of successful treatment programs, as well as identifying potential factors that have resulted in programming failures.

This review also highlights structural barriers to MOUD that are of particular relevance to the Arab World and can be targeted to improve MOUD implementation through each of the five metrics characterized by the RE-AIM framework. Ghaddar et al. (2018) describes financial, geographical, and social barriers to access MOUD, and El-Khoury et al. (2016) highlights communication and coordination challenges between prescribers and dispensers, an absence of local prescribing guidelines, a lack of supervised dispensing of medications, a lack of education regarding consumption and cessation of medications, drug diversion and trafficking, and constrained cooperation with security forces as barriers to treatment of patients in Lebanon. Many of these barriers may stem from the criminalization of narcotics in many Arab World countries, as well as the regional stigma associated with OUD patients (Harm Reduction International, 2020). Fear of misuse and diversion risk usually restrict access to OAT and information about treatment needs in the Arab World (ElKashef et al., 2019). To achieve adequate I-Implementation, policymakers and public health authorities must consider adequately addressing these barriers to accelerate and facilitate the development of effective OUD treatment programs in the Arab World. Consistent with our findings, similar studies in other countries have identified the need to improve access to and the quality of primary healthcare services to support patients with substance use disorders and to eliminate barriers to care (Ross et al., 2015). Through a collaborative model of primary care, quality services can be delivered, and education about mental health and substance use disorders can be provided to both patients and service providers (Ross et al., 2015). Similarly, to improve the I-Implementation of MOUD in Arab states, knowledge promotion among patients and health providers and collaboration among clinical experts, researchers, and policymakers have been noted to be strong facilitators of MOUD implementation (ElKashef et al., 2019; Grella, Ostle, Scott, Dennis, & Carnavale, 2020). Other studies have emphasized the importance of patient-centered care with buprenorphine and extended-release naltrexone, as opposed to office-based treatment, in order to address challenges relating to retention and re-engagement with OUD therapy (Tofighi et al., 2019). Patient management protocols, quality of delivery, coordination of interventions, engagement of educated staff, and regular program appraisements must be incorporated to achieve high-quality MOUD treatment programs (Elarabi et al., 2014; Hunter et al., 2018).

At present, the relative newness of MOUD in the Middle East precludes an abundance of research that can be said to fully address MAINTENANCE. Given that the risk of all-cause, overdose, suicide, alcohol, cancer, and cardiovascular-related mortality has been found to be significantly lower for people receiving OAT, increasing retention of patients in treatment programs is of paramount importance (Santo, Clark, & Hickman, 2021). One of the most important factors in the treatment of substance use disorders and prevention of relapses in patients with OUD is the identification of the triggers, motives, objectives, and predispositions of individuals to use drugs. For instance, treatments for mental illnesses such as posttraumatic stress disorder, anxiety, depression, and ADHD can lead to drug addiction (Bizzarri et al., 2007; Kousha, Shahriyar, & Alaghband-Rad, 2012; Mason, Mennis, Russell, Moore, & Brown, 2019; Stewart & Conrad, 2003; Zemestani & Ottaviani, 2016). Similarly, chronic pains, personality traits, and social and familial factors can foster addictive tendencies. Some of the most common causes for relapse

include a need to fit in with friends, difficulty dealing with withdrawal symptoms, boredom, loneliness, temptation, and stress (Cloninger, Sigvardsson, Przybeck, & Svrakic, 1995; Darharaj, Habibi, Kelly, Edalati-mehr, & Kazemitabar, 2017; Gruzca et al., 2006; Laudet, Magura, Vogel, & Knight, 2004; Martinotti, Cloninger, & Janiri, 2008; Schuman-Olivier et al., 2010; Vallerand, Fouladbakhsh, & Templin, 2005). In maintaining MOUD programs, healthcare workers should pay close attention to these factors in providing patient-centered treatment and preventing episodes of relapse. Further research is needed to identify best practices in the implementation of OAT follow-up programs, including assessments of baseline opioid tolerance, ongoing monitoring during the induction period, patient education about the risk of overdose, healthcare services coordination, and the incorporation of a patient-centered approach (Bahji, Cheng, Gray, & Stuart, 2019; Cloninger, Zohar, & Cloninger, 2010; Wong & Cloninger, 2010).

Our study findings illustrate deficiencies in the recruitment of specific demographics in assessing MOUD in the Arab World. For instance, women were excluded in several studies included in this review, partly because of cultural circumstances that exacerbate opportunities to collect females' point of views toward OAT (Ghaddar et al., 2017; Ghaddar et al., 2018; Khalaf et al., 2019). Furthermore, some included studies note that confounders were not identified and assessed, while others emphasize how confounders may play an important role in over- or under-estimating effectiveness of MOUD (Mawgoud & Al-Haddad, 1996; Sayuk et al., 2018). Further research is needed to account for the impact of potential confounders and quite importantly, to more adequately represent the experiences of marginalized demographics with MOUD.

Finally, a combination of psychological and pharmacological therapies has been demonstrated to be effective in treating individuals with dual disorders including OUD (Bayanzadeh et al., 2007; Drake, Mercier-McFadden, Mueser, McHugo, & Bond, 1998; Kelly & Daley, 2013). For instance, relapse prevention cognitive-behavioral treatment models in patients with OUD accompanied with methadone maintenance treatment have been effective in decreasing relapse (Pashaei et al., 2013). One systematic review suggested that health services need to integrate contingency management (i.e. a type of behavioral therapy in which individuals are rewarded for evidence of positive behavioral change) with OAT for OUD to improve retention to treatment; this review also recommended the need for high-quality RCTs to establish more definitive conclusions (Rice et al., 2020). Thus, integrating psychological therapies in treatment strategies for patients receiving MOUD has the potential to confer many advantages. However, utilizing psychological therapies was not reported in any of the studies reviewed in this review. Thus, future research conducted in this context should evaluate the integration of psychological therapies with MOUD.

#### Limitations

This review is subject to several limitations. Firstly, two of the ten studies included in this review were abstracts, and therefore, considerable information regarding their methodologies and findings were unable to be assessed (Hren & Milanic, 2017; Samlali et al., 2015). Second, this study only utilized three bibliographic databases and a search strategy written in English. As a result, literature published in other common languages in the Arab World (Arabic or French) and potentially relevant gray literature were excluded. Future research may identify additional findings relevant to this review's objectives by incorporating more expansive search criteria.

#### Conclusion

Illicit drug use, especially in the form of opiates, is on the rise and has become a serious public health problem across the Arab World. In many Arab countries, injection drug users are at the highest risk for blood-borne infections, and there is evidence that there is an HIV epidemic

among this vulnerable population in at least a third of MENA countries (Himmich & Madani, 2016). The current state of harm reduction efforts across the region has been noted to be deficient in both quality and scale of response. Our systematic review of MOUD in the Arab World reveals a small body of literature in only a few countries. However, through an implementation science framework, the available literature indicates that MOUD is cost-effective and associated with significantly positive health and social outcomes. Future rigorous research and work are urgently needed to address the rise of OUD in the Arab World and the development of integrated treatment programs that effectively provide MOUD services. This review provides evidence that stakeholders can work together to establish MOUD programs that can be scaled to a national level in the Arab World. As such, policymakers and governing institutions must invest more in OAT research, making MOUD services readily accessible and addressing barriers to quality provision of services.

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### Ethics approval

The authors declare that the work reported herein did not require ethics approval because it did not involve animal or human participation.

### Declarations of Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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### Supplementary materials

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