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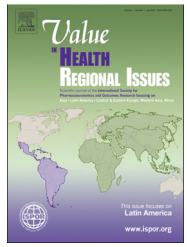

Managed Entry Agreements for Pharmaceutical Products in Middle East and North African countries: Payer and Manufacturer Experience and Outlook

*Christiane Maskineh, MBA, eDBAc, Soumana C. Nasser, PharmD, MHE**

Centre of Clinical, Health Economics, and Outcome Research (CCHO), Beirut, Lebanon; Pharmacy Practice Department, Lebanese American University, Blat, Lebanon

ABSTRACT

Objectives: The first objective is to describe current managed entry agreement (MEA) activity in the Middle East and North African (MENA) region and the pharmaceutical decision makers' perception and use of these agreements; The second objective is to describe the challenges as well as to reflect on the uncertainty related to MEAs implementation and the future outlook for MEAs activities in the region. **Study Design:** A prospective cross-sectional survey. **Methods:** A questionnaire was sent to several pharmaceutical manufacturers and public officials involved in pricing and reimbursement of pharmaceuticals in the region. **Results:** Of the 62% of total respondents, 25% were from the public sector, with the remainder from the pharmaceutical (pharma) industry. Only 42% of participants reported having MEAs running in their institutions, the majority representing Lebanon. All respondents reported the use of financial-based agreements, most referring to "discounted treatment" and, to a lesser extent, a "price volume agreement." Financial-based agreements were reported as either the only type of MEA (71.4%) being used or as being used with outcomes-based agreements (28.6%). The majority of participants ranked challenges in identifying and measuring relevant data as well as the lack of expertise in assessing health economics data. The majority of respondents projected an increase in the use of MEAs to address budget impact while improving access to innovative care. **Conclusions:** Few MENA countries are implementing MEAs, which could be due to lack of data infrastructure as well as a shortage of experts in health economics. Health care stakeholders continue to be optimistic regarding the potential of MEA implementation.

Keywords: financial-based agreements, health economics, managed entry agreement, MENA, outcome-based agreements, performance-based risk-sharing arrangements.

Background

Globally, over the last decade, there has been enough growing interest in health care systems to introduce managed entry agreements (MEAs) to provide improved access to costly, innovative medicines at a time when governments worldwide have been struggling with health care budget constraints due in part to an aging population with increasing health care demands. To provide patients with more rapid access to these innovative technologies that provide value for money, new reimbursement decisions and tools, such as MEAs, are being adopted [1–3]. An MEA is defined as an arrangement between a manufacturer and payer that enables access to new technologies in health care. These arrangements can exist in a variety of forms, such as outcome–based agreements or financial-based agreements as well as a combination of both agreements. Regardless of the form MEAs take, they all aim to distribute the financial risk of investing in new technologies between the manufacturer and payer, while at the same time addressing uncertainty around these new technologies [1–3].

In recent years, various types of conditional coverage decisions have emerged. By tracking the performance of a product in a given population, manufacturers and payers have been able to facilitate the entrance of new technologies into the market by allowing the basis of reimbursement to be dependent on and determined by outcomes [2].

There are three broad categories characterizing the major forms of MEAs which handle payer-provider arrangements [4–7]. Financial-based agreements, which address cost-sharing efforts, facilitate manufacturer contributions to the cost of a new health drug, product, or technology (e.g., discounts or rebates, price-volume agreements, utilization caps) for a particular patient or population without linking reimbursement to health outcomes [5,7]. These types of arrangements have been implemented globally (i.e., United Kingdon [UK], Italy), and each type has unique mechanics, including the set of contract parameters that

* Address correspondence to: Soumana C. Nasser, PharmD, MHE, Clinical Associate Professor, Pharmacy Practice Department, Lebanese American University, P. O. Box 36S, Blat, Lebanon. Mobile: +961 3 489860.

E-mail: soumana.nasser@lau.edu.lb

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generate specific dynamics for that agreement [5]. The second category is what we call outcomes-based agreements, which can be seen as a subset of what has been called performance-based risk-sharing arrangements. The third category is coverage with evidence development (CED), which has been used in the United States and Sweden [7]. CED arrangements, in which a positive coverage decision is based on the collection of additional evidence (only with research or only in research), might result in continued, expanded, or withdrawn coverage [7]. Moreover, interest in MEAs is growing due to increasing cost pressures, the need to balance the interests of patients, clinicians, manufacturers, and other stakeholders, as well as the need for addressing uncertainties and incomplete information at the time of decision making [6].

Despite the potential advantages of MEAs, several studies have addressed challenges of MEA implementation related to high cost of administration, lengthy negotiations, unclear success metrics, and overly complex agreements [8]. Other concerns and limitations are due to lack of transparency of MEA objectives and evaluations, limiting the ability of patients to engage with MEA processes, and limiting the transferability of MEA experiences due to the variability across settings and countries. Major concerns in implementing MEAs surround the uncertainty involving management of budget impact for optimal performance as well as concerns for different stakeholders linked with development of registries, data collection, patient response, and streamlined implementation of MEAs [2]. Financial-based schemes are more commonly used than outcomes-based schemes. For instance, Italy's drug registries have enabled the use of advanced agreements in improving patient access to technologies, although The Netherland's experience with MEAs has been limited due to lack of data collection and registries and Poland's current agreements are mainly financial-based, involving simple discounts to make products more affordable [8].

Although some information on MEAs exists in a European context, little is known about experiences with MEAs in Middle East and North African (MENA) countries, where lengthy registration processes for product market entry from foreign pharmaceutical companies have been frequently addressed. In addition, the frequent use of external price referencing to control pharmaceutical prices has been studied in MENA countries, and a recent survey analysis revealed that such a practice has been leading to higher pharmaceutical prices in lower income countries compared to nonpharmaceutical services [9].

This study had two major objectives. The first is to describe current MEA activity in the MENA region as well as pharmaceutical decision-makers' perception and use of these agreements. The second is to describe the challenges and reflect the uncertainty related to MEA implementation as well as the future outlook for MENA activity in the region.

Methods

A prospective cross-sectional survey was conducted between December 2015 and April 2016 in the MENA region. A questionnaire was sent via SurveyMonkey to several pharmaceutical manufacturers and public officials involved in pricing and reimbursement of pharmaceuticals in the MENA region, namely Algeria, Egypt, Lebanon, Jordan, United Arab Emirates (UAE), and Kingdom of Saudi Arabia (KSA). The taxonomy of performance-based schemes introduced by Carlson et al. [4] was adapted for this study. This research utilizes financial-based agreements to refer to cost-containment schemes (although respondents most commonly used cost sharing to refer to financial-based cost-containment schemes) and outcomes-based agreement or arrangement schemes to refer to those that measure real-world clinical outcomes. This research also addresses reimbursement conditional to real-world patients' outcome schemes [4].

In order to address and answer this study's two main objectives, the survey was tailored to collect data on MEA current activities in the MENA region, such as the numbers and types of agreements by therapeutic area, data on both payer and pharmaceutical manufacturer decision makers' perceptions on the impacts, data on the major barriers and challenges when conducting MEAs, and data on predicted future outlook of MEA projects in some MENA countries. Furthermore, the survey gathered information on matters addressed by MEAs related to diminishing uncertainties surrounding new health technologies, such as budget impact, clinical impact, and cost-effectiveness impact. The survey included the different forms and names of MEAs, i.e., risk-sharing agreements, performance-based agreements, and patient access schemes. Participants were identified from the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Arab Network and were then contacted to inquire about their willingness to fill out the survey. A cover letter was sent by email to participants, detailing the purpose of the survey, the estimated time commitment required for survey completion, and reassurance regarding confidentiality policies. This study has been approved by the Lebanese American University Institutional Review Board.

Participants were asked to voluntarily and anonymously fill out the predesigned survey, which included 22 questions to mostly capture 1) types and number of agreements implemented by therapeutics areas and 2) information on matters addressed by MEAs related to uncertainty, such as budget impact, clinical impact, and cost-effectiveness impact. In addition to the primary objectives, the survey addressed the challenges and barriers to implementing MEAs as well as stakeholders' perspectives and outlooks. The scale adopted to measure the study's objective on matters addressed by MEAs as they relate to uncertainty ranged from "most valuable" to "least valuable." Variables were summarized using frequencies and percentages. The survey, followed by several reminders, was sent to 70 potential participants, and then results were generated from completed surveys.

Results

A total of 44 participants (62%) responded to the mailed survey, of which 25% were from the public sector, with the remainder from the pharmaceutical industry. The public sector represented five countries from the region and the pharmaceutical sector represented all countries from the MENA region. Only 42% of participants reported having an MEA running in their institution, the majority representing Lebanon (8 out of 11 respondents). All respondents reported the use of financial-based agreements, most referring to "discounted treatment" and, to a lesser extent, a "price volume agreement." These financial-based agreements were reported as either the only type of MEA (71.4%) being used or as being used with outcomes-based agreements (28.6%). None of the participants reported the use of the latter as the only MEA type. Fifty percent of participants reported one year of experience in MEA implementation. These agreements were considered exceptions by 54.5% of institutions and as general rules, when needed, by 36.4%. Furthermore, the findings showed that agreements are mainly conducted for severe diseases (58.3%), chronic diseases (41.7%), and orphan drugs (25%), and are mostly being initiated by pharmaceutical industries or along with payers (53.8%) (Table 1).

The most favorable financial-based agreement was discounted treatment, and the most favorable outcomes-based agreement was coverage with evidence development or evidence with research. The majority of manufacturer participants

Table 1 – General information on MEA activities (first part of the survey questions).

Are you working for:	N = 44
Public sector*	25.0% (11)
Pharmaceutical industry†	75.0% (33)
Do you have MEA running in your institution:	N = 31
Yes	41.9% (13)
No	54.8% (17)
No opinion	3.2% (1)
Respondents who answered "yes" to the above question were asked to answer the following questions (N = 13)	
Please specify which type of MEA:	
Cost-sharing arrangements	77% (10)
Performance-based arrangement	0.0%
Both	23% (3)
For cost-sharing agreement, please specify which type:	
Discounted treatment/treatment cycle, i.e., first doses or last doses	77% (10)
Patient utilization cap	7.7% (1)
Price volume agreement with budget cap	23% (3)
Simple discount	31% (4)
Patient cost cap	7.7% (1)
How many years do you have experience in MEA implementation:	
1	46% (6)
2	15.4% (2)
3	7.7% (1)
> 4	23% (3)
Are these agreements considered general rule/exception:	
Exception	46% (6)
Quite frequent when needed	31% (4)
Systematic practice	7.7% (1)
These MEA agreements are conducted for:	
Severe diseases	54% (7)
Chronic diseases	38.5% (5)
Orphan drugs	23% (3)
All diseases	23% (3)
These agreements are initiated by:	
Pharmaceutical industry	38.5% (5)
Payers	7.7% (1)
Both	54% (7)

* Representing countries from Lebanon, Jordan, UAE, Egypt, Saudi Arabia.
† Representing all countries in the MENA region.

Table 2 – MEA objectives and CSA schemes from the manufacturer and payer perspectives.

For cost-sharing agreements, the following schemes were reported to be favorable to most favorable (N = 11):	
Discounted treatment/treatment cycle (last or first cycles/doses)	11
Patient utilization cap	4
Patient cost cap	4
Price-volume agreement	5
Discount†	3
As a manufacturer, when going for MEA, the following objectives were reported to be important to most important (N = 9):	
Improve level of access	9
Increase revenue	7
Reduce uncertainty for payers	8
Gain competitive advantage	7
Fostering better partnership with payers	9
Preserving price across markets	6
Fitting into a particular payer's framework	5
Moving discussion on value vs. cost	6
As a back-up strategy	2
As a payer, when implementing MEA, which of the following objectives were reported to be important to most important (N = 3):	
Limit total budget impact	3
Reduce uncertainty about products	2
Provide a technology in such a way that it demonstrates value	2
Early access to patients	3
Share risk with manufacturer if product not performing	2

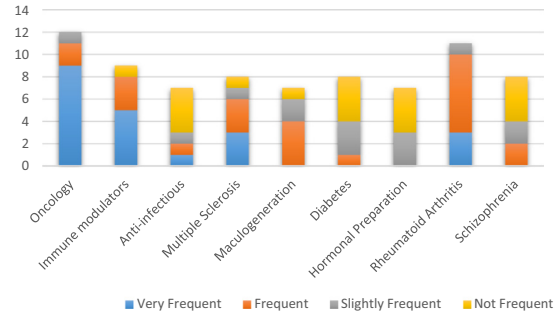
reported the most important objective for MEA access was to improve level of access as well as to foster better partnership with payers, to reduce uncertainty for payers, to gain competitive advantage, and to increase revenues. Serving as a back-up strategy was the least important objective in MEA implementation, as reported by manufacturer participants (Table 2).

The most important objectives reported by payers for MEA implementation were to limit total budget impact, to provide early access for patients, to reduce uncertainty about product performance, and to provide a technology that demonstrates value. The most frequently targeted therapeutic areas for MEA agreements were oncology, rheumatoid arthritis, and immunomodulators, followed by multiple sclerosis (Graph 1, Graph 2).

Although cost-effectiveness and budget impact analyses are lacking in the MENA region, participants reported the frequent use of certain instruments for addressing uncertainty, i.e., by limiting prescribing and reimbursement for either specific therapeutic indications or patient subgroups or by assessing the adopted budget agreement. Nevertheless, granting reimbursement for a limited time period until further evidence of cost-effectiveness was made available, was not frequently used in addressing the uncertainty of certain technologies.

When conducting MEAs in their respective countries or institutions, the majority of participants ranked challenges in measuring relevant data and outcomes, identifying or defining meaningful outcomes, and in using the limited data infrastructure available for measuring relevant outcomes as important. This was, followed by the significant additional effort required to establish/execute MEAs, as well as lack of expertise in assessing pharmacoeconomic and health outcome data, and challenges in assessing risk up front due to the complexity of real-world data. On the other hand, payers' concerns about adverse patient selection (31%), lack of control of how the product will be used (43%), and difficulty in reaching contractual agreements (56%) were not ranked as top challenges in conducting MEAs (Table 3).

For a successful MEA, all responders ranked having experts in pharmacoeconomic and outcome research as well as having data infrastructure and registries as the most important capabilities needed. Other important to most important factors included having experts in modeling MEA design, building local or national MEA pragmatic frameworks, and having human resources experts in partnership programs (Table 3). The majority of respondents expressed their positive perception of the future of MEAs in the MENA region by stating that MEAs, in relation to cost containment measures, price pressure, and budget constraints at the payer level, are helping to accelerate patient access to innovative life-saving therapy and are becoming very important for both payers and manufacturers due to the pressures on health care budgets.



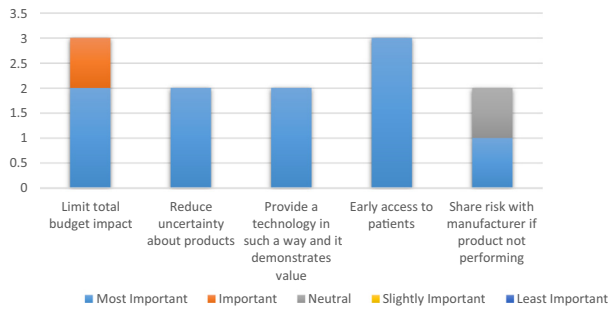
Graph. 1 – MEA implementation per therapeutic areas.

In addition, among participants who replied to the question addressing impacts from MEA implementation (N = 9), clinical impact and cost-effectiveness impact were ranked the highest (96% and 88.5%, respectively), followed by budget impact (81%). Finally, 81% of respondents agreed that the use of MEAs is likely to increase in the future.

Discussion

MEAs between payers and manufacturers are becoming a more common practice for the improvement of patients' access to innovative medication in European countries and the US. As reported in this survey, MEAs between payers and manufacturers are taking place, but only in some MENA countries. Fourty pecent of respondents reported having implemented MEA in their institutions, with the majority running the financial-based arrangements. This highlights the need to facilitate MEAs as well as Health Technology Assessment (HTA) integration in the pricing and reimbursement decisions and policies in MENA countries. In the UK, the National Institute for Health and Care Excellence (NICE) Decision Support Unit was commissioned to develop a framework that could potentially be used for assessing proposed MEAs within NICE technology appraisals [3,10]. In other European countries (France, Italy, Germany, Sweden), MEAs are an integral part of the pricing and reimbursement policies [6]. It is worth noting that Egypt has recently developed an HTA unit as part of that country's drugs committee, and there is a continuous request from payers in Egypt to implement MEAs and HTA as part of decision-making policies [11]. In addition, the Algerian Social Security Fund established new legislation called pay-per-performance contract with pharmaceutical companies for the reimbursement of innovative medicines, where there will be a conditional reimbursement for innovative drugs if the Marketing Authorization Holder (MAH) is committed to a payback in case of therapeutic failure [12].

In terms of MEA types, this study's survey revealed that financial-based schemes account for the majority of MEAs



Graph. 2 – Objectives of MEA implementation.

Table 3 – Challenges ranked as important to most important when conducting MEA and for successful MEA building in the future (N [%]):.

Total respondents to this survey section out of the 44 respondents	16 (36%)
When conducting MEA in your country/institution:	
A significant additional effort required to establish/execute MEA (compared to traditional rebates, discounts)/internal organizational structure	14 (87.5%)
Negotiation complexity	10 (62.5%)
Challenges in identifying/defining meaningful outcome	14 (87.5%)
Challenges in measuring relevant real world data/outcome	15 (94%)
Limited data infrastructure inadequate for measuring relevant outcome	14 (87.5%)
Difficulty in reaching contractual agreement (on the selection of outcome, patients, data collection methods)	9 (56%)
Payer concern about adverse patient selection	5 (31%)
Fragmented, multipayer health insurance market with significant patient switching	9 (56%)
Challenges in assessing risk upfront due to complexity of real word data	12 (75%)
Lack of control of how product will be used	7 (44%)
Lack of expertise in assessing pharmacoeconomic and health outcome data	13 (81%)
Significant cost or resources associated with ongoing adjudication	11 (69%)
For successful MEA building in the future:	
Experts in pharmacoeconomic and outcome research	16 (100%)
Experts in modeling MEA design	13 (81%)
Building local or national pragmatic MEA implementation frameworks	14 (87.5%)
Data infrastructure and registries	16 (100%)
Human resources experts in partnership programs	13 (81%)

(specifically in the form of simple discount arrangements) in the region. A similar proportion of both financial and outcome-based types of MEAs across seven European countries has been reported in some studies [3,13], although other studies reported that the trend has been moving toward more financial schemes due to the administrative burden of outcome-based agreements [4,6]. For instance, such MEAs have become more regularly used in the UK, where simple discounts have been mostly used [3,10]. This could be explained by a report on a 10-year outcome-based agreement on multiple sclerosis drugs showing that the administrative burden was very much underestimated, and this poses a threat for successful MEA implementation [14]. On the other hand, the practice of establishing MEAs between manufacturers and private payers in the US and in Europe has demonstrated the limited use of outcome-based schemes due to the challenges of data collection and the fragmented, pluralistic health care system, coupled with the absence of integrated data collection infrastructure [3,7,15].

Per a recent report prepared by the Center for Evidence-based Policy in 2016 in the context of the State Medicaid Alternative Reimbursement and Purchasing Test for High-cost Drugs (SMART-D) program, the decision on the schemes' type is potentially linked to the health authorities' different goals [3,16]. For instance, the goal of an MEA in the UK is to take a drug that is deemed not cost-effective and make it cost-effective. The easiest way to accomplish this is to reduce the price of the drug. In Italy, these MEAs allow the Italian health care system, with the use of

outcome-based schemes, to achieve goals such as facilitating faster access to drugs and ensuring that patients do not continue ineffective treatments [2,17]. Another study has revealed that three-quarters (75%) of all the agreements in selected European countries aimed to address budget impact either alone (42%) or in combination with cost-effectiveness (16%) [6]. Budget impact, cost-effectiveness impact, and improvement of access to innovate health technologies have been the major reasons for payers to engage in MEAs in the MENA region. Nevertheless, it is believed that the situation in the MENA region involving the dominance of financial schemes is due mainly to the limited expertise in designing and implementing outcome-based schemes and to the lack of data collection infrastructure, not a clear strategy, as is the case in Italy and the UK [2]. Whether the trend changes in the MENA region remains to be seen.

As for MEAs' therapeutic focus, the survey findings indicate that the largest proportion of MEAs across all countries involve oncologic and immune-modulating products. This is consistent with the European picture and reinforces payers' reported rationale behind entering MEAs, which is reducing budget impact and improving patients' access to costly drugs [17].

MEAs have been recognized as having numerous benefits on health care systems. They limit the growth of pharmaceutical expenditures and ensure efficiency by maximizing health gain within finite budgets. Several EU markets have reported the return of revenue back to the health system from these MEAs. In 2004, France reported total rebates that amounted to €670 million, around 3% of total pharmaceutical expenditure, and in 2006, the payback in Hungary was approximately €90 million, or 5.69% of the budget [5].

Although there is a consensus about the potential importance of MEA agreements and their positive role in access to medicine, many challenges and barriers are inherent in MEAs, mainly due to the high cost of administration, lengthy negotiations, and overly complex agreements [2,8]. A limitation in performance based schemes with payback for nonresponders lie in the collection framework from the MAH, which has been a challenge for the health care system in Italy. In some instances, patients interrupt treatment for reasons not cited in the MEA contract, which could lead to a disagreement on the payback by the MAH. Financial agreements offer better financial security for payers at a lower cost. Nevertheless, the administrative workload can still be a challenge, and these schemes do not address the uncertainties related to drug effectiveness, thus showing the least opportunities for sharing risk between MAH and payers [17]. This has led countries such as the UK, Sweden, and France to shift toward more simple financial-based agreements rather than outcome-based agreements, although they do recognize that these schemes do not address fundamental uncertainties about value, which is an important factor for pricing and reimbursement [7,12,17]. Health outcome-based MEAs have been more successfully used in Italy, with cost sharing and price reduction making up the largest proportion of the schemes (50%), followed by payment per effective response or reimbursement for nonresponders (43%) [18]. The existence of infrastructure for collecting necessary data for performance-based schemes helped Italian health authorities with the implementation of these agreements and was recognized as a public-private partnership (PPP) best practice [7,8,16].

Despite these numerous challenges, MEAs are still considered instruments for facilitating access to new high-cost technologies [2,17]. Globally, forecasts estimate that spending on new oncologic and biologic agents will outpace overall spending growth on medicines and will represent a high percentage of the estimated $1.5 trillion total pharmaceutical market in the US by 2021 [19]. Such a situation is similar and potentially more serious in the MENA region. A recent study published in 2016 revealed that the total spending on oncologic drugs by the Lebanese Ministry of Public Health has witnessed a compound annual growth rate of 15.6% between 2008 and 2013 [20]. Financial-based agreements are mainly used in several European countries, ensuring access to highly priced oncologic drugs [16]. These agreements are further developed by different stakeholders to better meet the specific needs and requirements of health care systems in different countries. Therefore, payers have an incentive to develop strategies that can help control costs, while ensuring patient access to medical products that benefit health. Similarly, manufacturers consider MEAs a platform for negotiation with payers and a tool to keep the real reimbursement prices confidential, allowing them to tier prices by markets without the threat of external reference pricing [13].

The use of MEAs is expected to grow with the aim to address uncertainties around the value of new innovative heath technologies [2,4,13,15]. Although our survey respondents consider MEAs highly challenging, with numerous barriers in the design and implementation, the outlook for future growth is very optimistic, with 80% of respondents reflecting a perceived increase in MEA implementation in the near future. Although it is not clear whether they are referring to outcome-based or financial-based schemes, their replies highlight the need for MEAs in accelerating patients' access to innovative life-saving therapy as well as the importance of MEAs for both payers and manufacturers due to the budget impact on health care systems. This could be a limitation related to the impact of socioeconomic situations on health care systems in the MENA region, prohibiting effective implementation of MEAs, resulting in unfair differential pricing across countries based on income, and favoring schemes that are financial in nature over outcome-based schemes. The study has several other limitations that are common to surveys. The survey targeted stakeholders from public payers, academia, and private manufacturers in key MENA countries (Egypt, KSA, Lebanon, Jordan, UAE, and Algeria). Nevertheless, the response rate from some countries (Egypt and KSA), and from the public, was low. Thus, the study has a limited number of examples from each payer and pharmaceutical manufacturer. This, in turn, limited the opportunity to analyze separately public and industry perspectives as well as generalize data to the MENA region.

Given the sensitive nature of contractual agreements in the MENA region in this field, it is likely that information on schemes remains confidential and manufacturers will be reluctant to disclose details about patient access schemes. We thus are likely to have underestimated the total number of MEA schemes in the MENA region (only 42% of participants reported having MEAs running in their institutions). Finally, the data collection was done through SurveyMonkey, with the inherent limitations of online surveys. Nevertheless, this study provides insights into what types of agreements and therapeutic lines are common targets for MEA schemes as well as recent experiences in the MENA region that may inform the development of future, triangular, and explorative research.

Conclusion

MEAs in the MENA region represent a potentially important tool for both payers and manufacturers for optimizing access to innovative medications for patients, while managing the budget impact on health care expenditures. Although financial-based schemes are most common, some countries, such as Lebanon and Egypt, tend to couple outcome-based with financial-based arrangements. The main disease indication targets for MEAs are immunomodulators, biological therapies for cancer, and chronic diseases. In contrast to Europe and the US, MEAs are still in the

early stage of use in the MENA region due to several challenges, such as limited expertise in health economics and outcome research, limited data collection instruments, and the absence of patient and disease registries. Despite the challenges encountered and projected in our survey, health care stakeholders in the MENA region continue to be optimistic about the increase in the utilization and implementation of MEAs because they are viewed as a valuable financial, quality improvement, and management mechanism, as well as a negotiation tool for use between payers and drug manufacturers.

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REFERENCES

1 Klemp M, Fronsdal KB, Facey K. What principles should govern the use of managed entry agreements? Int J Technol Assess Health Care 2011;27:77–83. http://dx.doi.org/10.1017/S0266462310001297.
2 Kanavos P, Ferrario A, Tafuri G, Siviero P. Managing Risk and Uncertainty in Health Technology Introduction: The Role of Managed Entry Agreements. Global Policy 2017;8:84.
3 Wilsdon T, Barron A. Managed Entry Agreements in the context of Medicines Adaptive Pathways to Patients 2016. Available from: http://adaptsmart.eu/wp-content/uploads/2016/12/CRA-MEA-in-the-context-of-MAPPs-Final-Report-16-December-2016-STC.pdf. [Accessed May 30, 2018].
4 Carlson JJ, Garrison LP, Sullivan SD. Paying for outcomes: innovative coverage and reimbursement schemes for pharmaceuticals. J Manag Care Pharm 2009;15:683–7. http://dx.doi.org/10.18553/jmcp.2009.15.8.683.
5 Adamski J, Godman B, Ofierska-Sujkowska G, et al. Risk sharing arrangements for pharmaceuticals: potential considerations and recommendations for European payers. BMC Health Serv Res 2010;10:153.
6 Ferrario A, Kanavos P. Dealing with uncertainty and high prices of new medicines: a comparative analysis of the use of managed entry agreements in Belgium, England, the Netherlands and Sweden. Soc Sci Med 2015;124:39–47.
7 Garrison LP Jr, Towse A, Briggs A, et al. Performance-based risk-sharing arrangements–good practices for design, implementation, and evaluation: report of the ISPOR good practices for performance-based risk-sharing arrangements task force. Value in Health 2013;16:703–19.
8 Aggarwal R. Risk-Sharing Agreements: Country Experiences and Challenges. INSEAD Healthcare Management Initiative 101/2014, http://docplayer.net/6963032-Risk-sharing-agreements-country-experiences-and-challenges.html. [accessed Dec 2017], Ref Type: Online Source.
9 Kaló Z, Alabbadi I, Al Ahdab OG, et al. Implications of external price referencing of pharmaceuticals in Middle East countries. Expert Rev Pharmacoecon Outcomes Res 2015;15:993–8.
10 National Institute for Health and Care Excellence. Proposals for changes to the arrangements for evaluating and funding drugs and other health technologies appraised through NICE's technology appraisal and highly specialized technologies programmes. NICE and NHS England. 1st Version, 2016. Ref Type: Online Source. https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/board-paper-TA-HST-consultation-mar-17-HST-only.pdf.
11 Elsisi G, Kalo Z, Eldessouki R, et al. Recommendations for Reporting Pharmacoeconomic Evaluations in Egypt. Value in Health Regional Issues 2013;2:319–27.
12 Art. 98 published in Journal officiel de la republique algerienne N. 77. Conventions et Accords Internationaux – Lois et Decrets, Arretes, Decisions, Avis, Communications et Annonces. 2016. Available from: https://www.droit-afrique.com/uploads/Algerie-LF-2017.pdf. [Accessed May 30, 2018].
13 Morel T, Arickx F, Befrits G, et al. Reconciling uncertainty of costs and outcomes with the need for access to orphan medicinal products: a comparative study of managed entry agreements across seven European countries. Orphanet J Rare Dis 2013;8:198.
14 Spoors J. Patient Access Schemes in the New NHS. British Journal of Healthcare Management 2012;18:412–8.
15 Garrison LP Jr, Carlson JJ, Bajaj PS, et al. Private sector risk-sharing agreements in the United States: trends, barriers, and prospects. Am J Manag Care 2015;21:632–40.
16 Stuard S, Beyer J, Bonetto M, et al. State Medicaid Alternative Reimbursement and Purchasing Test for High-cost Drugs (SMART-D) 2016. Available from: http://smart-d.org/wp-content/uploads/2016/09/SMART-D-Summary-Report-Final.pdf. [Accessed May 30, 2018].
17 Pauwels K, Huys I, Vogler S, et al. Managed Entry Agreements for Oncology Drugs: Lessons from the European Experience to Inform the Future. Front Pharmacol 2017;8:171. http://dx.doi.org/10.3389/fphar.2017.00171.
18 Garattini L, Curto A, van de Vooren K. Italian risk-sharing agreements on drugs: are they worthwhile? Eur J Health Econ 2015;16:1–3.
19 QuintilesIMS Institute. Outlook for Global Medicines through 2021. 2016. Available from: http://static.correofarmaceutico.com/docs/2016/12/12/qiihi_outlook_for_global_medicines_through_2021.pdf. [Accessed May 30, 2018].
20 Elias F, Khuri FR, Adib SM, et al. Financial Burden of Cancer Drug Treatment in Lebanon. Asian Pac J Cancer Prev 2016;17:3173–7.