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\textbf{Abstract}

\textbf{Background}: Adequate access to essential medicines for cardiovascular disease is necessary to address the high cardiovascular disease burden in countries of the Eastern Mediterranean Region of the World Health Organization (WHO).

\textbf{Aims}: This study compared the cardiovascular disease medicines included in the WHO Model Essential Medicines List with those in the national essential medicines lists of 19 countries of the Region.

\textbf{Methods}: Data were extracted on the number of cardiovascular medicines and dosage forms in the national lists and compared with those on the WHO Model List (24 medicines in total and 48 dosage forms). Factors associated with the number of essential cardiovascular medicines on the national lists (burden of cardiovascular diseases and health expenditure per capita) were assessed. The number of medicines from 6 therapeutic groups of cardiovascular medicines listed in the national lists but not in the core WHO Model List were evaluated.

\textbf{Results}: Countries with the lowest percentage of medicines from the WHO Model List out of the total cardiovascular disease medicines in the national lists were Djibouti (21\%), Tunisia (22\%), Saudi Arabia and Iraq (31\% each), and Bahrain and Libya (32\% each). The most common medicine dosage form in the national lists was tablets while some that needed oral liquid forms were not listed by any country. Tunisia (8\%), Jordan (14\%), Bahrain and Saudi Arabia (15\% each) had the lowest alignment of dosage forms from the WHO model list.
Conclusions: Countries should improve the selection of essential medicines for cardiovascular diseases to promote access to therapy.

Keywords: Drugs, Essential, Cardiovascular diseases; World Health Organization, Eastern Mediterranean region

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Introduction

In 2011, the United Nations (UN) launched a global campaign to reduce deaths from noncommunicable diseases (NCDs) (1). The summit declaration highlighted that about 9 million deaths caused by NCDs occur before the age of 60 years, with nearly 80% of those in low- and middle-income countries. To tackle the burden of NCDs, the UN recommended strengthening national policies and health systems through a multisectoral approach to implement policies and plans, taking into account the World Health Organization (WHO) global strategy for the prevention and control of NCDs (2).

WHO released a briefing document following the 2011 UN meeting which stated that the burden of disease related to NCDs could not be reduced without equitable access to essential medicines (3). While primary prevention of NCDs is a key objective, treatment of existing cases (secondary prevention) is also needed. Medicines are an essential component of the treatment of NCDs such as cardiovascular diseases, diabetes, chronic obstructive pulmonary disease
including asthma, many cancers (including palliative pain treatment) and depression (3).

WHO defines essential medicines as, “medicines that satisfy the priority health care needs of the population. Essential medicines are intended to be available in the context of functioning national health systems in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford” (4).

The WHO Model Essential Medicines List plays a key role in defining the criteria for medicines, including public-health relevance, efficacy, safety and cost–effectiveness, and it is an important tool for promoting health equity (5). The list is a guide for countries in developing their national essential medicine lists, and most countries around the world have developed their own lists in order to best meet the needs of their communities (6).

In order to achieve good health outcomes, access to medicines needs to be combined with the provision of quality care and services. One critical step to achieving better access to medicines at the national level is defining those medicines required to tackle the burden of NCDs in the country. The WHO Model List can help guide countries in their priority setting exercise.

The Eastern Mediterranean Region (EMR) of WHO has one of the highest burdens of disease, and NCDs have been among the top causes of death since 1997 (7). It is estimated that 54% of deaths from NCDs in the Region are caused by cardiovascular diseases (8). Deaths attributed to cardiovascular diseases (of total deaths) range from 512 per 100,000 in Afghanistan to 157 in Qatar (9).

The objective of this study was to compare the WHO Model Essential Medicines List for cardiovascular disease medicines with available national essential medicines lists of EMR countries. Three countries were omitted because their lists were unavailable online. The study aimed to identify differences between countries of different economic and developmental status, and highlight the need for EMR countries to prioritize the selection of medicines for NCDs given their great burden in the Region.

**Methods**

All 22 EMR countries were eligible for inclusion, 19 of which had a national essential medicines
lists available online. The countries were classified according to the World Bank income levels (Table 1). We used the most recent WHO Model Essential Medicines List at the time of our study (2015) (10) and the national essential medicines lists available online. The section on cardiovascular medicines (section 12) of the WHO Model Essential Medicines List has 24 medicines in its core list and 4 medicines (amiodarone, streptokinase, dopamine and sodium nitroprusside) as complementary. Complementary essential medicines are for diseases for which specialized diagnostic or monitoring facilities, and/or specialist medical care, and/or specialist training are needed. Core essential medicines satisfy the basic needs of a health care system, and consist of safe and cost-effective medicines for priority conditions.

**Cardiovascular medicines and dosage forms**

We extracted data on the following for each country:

- number of cardiovascular medicines in the national list that are listed in the WHO Model List (24 medicines in total).

- total number of cardiovascular medicines listed in the national list. The percentage of WHO medicines out of the total number of cardiovascular medicines listed in the national list was calculated.

- number of WHO cardiovascular medicine dosage forms (48 product forms) listed in the national list.

- total number of cardiovascular medicine dosage forms listed in the national lists. The percentage of WHO cardiovascular medicine dosage forms out of the total number of cardiovascular dosage forms listed in the national list was calculated.

The dosage form is relevant because solid forms of medicines (e.g. tablets, pills, capsules) may not be appropriate and other forms (e.g. syrups, injections, sublingual dosage forms) may be needed to ensure treatment access for patients of different age groups (e.g. the elderly) or different disease severities.

**Medicines not listed in the WHO Model List**
Medicines for which the WHO Model List selects an example of one out of a class of medicines are denoted by a square box symbol (11). Any other medicine from the same pharmacological class, which has similar clinical effects, can replace medicines with this symbol with a medicine of the appropriate anatomical therapeutic classification code (10). These can be substituted by medicines that are recommended in the WHO Technical Series Reports (http://www.who.int/biologicals/technical_report_series/en/).

WHO indicates substituted medicines for the following 6 groups: thiazides and sulfonamides (diuretics), selective beta blockers and alpha blockers, dihydropyridil derivatives, angiotensin-converting enzyme inhibitors, HMG CoA reductase inhibitors, and organic nitrates (vasodilators).

A matrix was used to identify those countries with either no medicine listed in each of the 6 therapeutic groups or more than 2. No medicine listed would indicate a gap in the selection, while more than 2 would indicate that selection is not restricted to the most essential medicines.

**Statistical analysis**

Univariable linear regression analysis was used to examine the associations between continuous variables (burden of cardiovascular disease and overall health expenditure per capita of the countries) and the total number of essential medicines for cardiovascular medicines on the national lists of the studied countries. The burden of disease for cardiovascular disease (age-standardized mortality rates) was obtained for each country from the WHO Global Health Observatory (11). World Bank data on health expenditure per capita for the countries were used (12).

SAS software was used for all statistical analyses. A P-value ≤ 0.05 was considered statistically significant.

**Ethics statement**

This study did not need Ethics Review Board approval/review as it used publicly available data which did not involve people or animals.

**Results**

Table 1 shows the national essential medicines lists available in EMR countries by income.
group. Nineteen countries had national list or formulary guides accessible online, which included information on the medicine, or the medicine and the dosage form. For 3 countries (Kuwait, Qatar, United Arab Emirates), no national essential medicines list was publicly available electronically (Table 1). None of the 19 countries only included medicines from the WHO Model List.

Comparison of medicines on the WHO Model List and national lists

Table 2 shows the number of medicines from the WHO Model List for cardiovascular diseases included in the national lists for the 19 EMR countries. Bahrain had all 24 medicines in the WHO Model List in their national list, Sudan had 23, Oman and Saudi Arabia each had 22, and Libya had 21. Dijbouti and Somalia, each with 9 medicines, and Yemen with 12 had the fewest number of the medicines for cardiovascular diseases from the WHO Model List.

Many countries had considerably more medicines for cardiovascular diseases in their national lists than the WHO Model List. Bahrain had the most cardiovascular disease medicines in its national list (74 medicines), followed by Saudi Arabia with 72 medicines, Libya with 66, Iraq with 64, and Tunisia and Djibouti each with 63 medicines listed. The countries with the lowest percentage of medicines from the WHO Model List out of the total cardiovascular medicines in the national lists were Djibouti (21%), Tunisia (22%), Saudi Arabia and Iraq (each 31%), and Bahrain and Libya (each 32%).

Comparison of dosage forms on the WHO Model List and national lists

The WHO Model List gives 48 dosages forms for the cardiovascular medicines listed. Table 3 shows the dosage forms included in the national lists of the EMR countries. The average number of medicine dosage forms for cardiovascular diseases from the WHO Model List was 19. Sudan with 33 dosage forms included the highest number of WHO dosage forms in its national list, Pakistan had 32 WHO dosage forms, Islamic Republic of Iran had 25, and Lebanon and Iraq each included 24 WHO dosage forms. Somalia with 7 WHO dosage forms, Yemen with 8, Djibouti with 10 and Tunisia with 11 included the fewest WHO dosage forms in their national lists.

The countries with the lowest percentage of dosage forms from the WHO Model List out of the total dosage forms for cardiovascular diseases medicines in the national lists were Tunisia (8%), Jordan (14%), and Bahrain and Saudi Arabia (each 15%).
Factors associated with the selection of essential medicines

Table 4 shows the association between the burden of cardiovascular disease and per capita health expenditure and the number of cardiovascular medicines in a national list. Per capita health expenditure was significantly associated with the number of medicines on the national list ($\beta = 0.00456, P = 0.00463$). The data suggest that an increase in health expenditure per capita of US$ 100 would on average result in the addition of 5 medicines for cardiovascular diseases on the national list. The relative burden of cardiovascular diseases, based on deaths from cardiovascular diseases, was not associated with the total number of essential medicines for cardiovascular disease on the national list ($\beta = -0.0352, P = 0.571$).

Complementary groups of medicines

Table 5 shows the number of medicines from the 6 therapeutic groups of cardiovascular medicines listed in the core WHO Model List and others that are not on the WHO Model List but which are in the national essential medicine lists of the different countries. Most of the countries listed more than 2 medicines from each therapeutic group in their national lists, one of which was usually a medicine on the WHO Model List. Other countries such as Bahrain, Iraq, Islamic Republic of Iran, Jordan, Saudi Arabia and Syrian Arab Republic had more than the 1 WHO-recommended model list medicine listed for all 6 therapeutic groups in their national lists. Pakistan and Sudan were most aligned with only 1 medicine per therapeutic category. Yemen, Somalia, Afghanistan and Djibouti had the biggest gaps in their national lists with no medicines listed for some therapeutic groups.

Discussion

Our results indicate that there is room for improvement in the selection of essential medicines for cardiovascular diseases in EMR countries. Several countries (e.g. Yemen, Somalia, Afghanistan and Djibouti) have no medicines listed in certain therapeutic areas which are necessary to treat cardiovascular diseases. Moreover, in some other countries such as Tunisia and Saudi Arabia, the percentage of cardiovascular medicines and corresponding dosage forms from the WHO Model List in their national lists is low, which could limit access for certain populations. Previous studies that compared national lists for cancer and diabetes treatment in countries also found several areas needing improvement (13–15).

A higher burden of cardiovascular diseases was not associated with a more essential cardiovascular disease medicines in the national list, which suggests a more rational selection procedure is needed in EMR countries (Table 4). Each country should develop its national list, not only according to the WHO Model List, but taking account of the country’s specific political, social, financial, economic and epidemiological context. The listing of medicines should be in line with the burden of disease (16). National essential medicines lists are the foundation to
ensure public health delivery of essential medicines, including consistent supply and management (17).

In the past few years, EMR countries have experienced a growing number of conflicts. These include Afghanistan, Iraq, Somalia, Yemen, Syrian Arab Republic and Libya. After communicable diseases, cardiovascular diseases are the second most common cause of death in the Syrian Arab Republic (28%), Yemen (21%) and Libya (43%) (11). Countries with very limited resources need to ensure that the selection of medicines is guided by the disease burden and standard treatment guidelines, among other factors (18).

Somalia had the lowest number of cardiovascular medicines from the WHO Model List and also the lowest number in total cardiovascular medicines in its national list. However, the list we found was old and did not include a specific cardiovascular medicine section. There is a need therefore to update the current list. In the current edition of Somalia’s national health strategic plan, the country’s service provision ranked “less than adequate” (19) and the supply of essential medicines to the country relies on diseases kits provided by the UN and nongovernmental organizations (20). Capacity building is a key component of WHO’s intervention for essential medicines (20). Updating the national essential medicines list and addressing gaps in the selection of cardiovascular medicines should form part of Somalia’s health systems strengthening activities.

Although the current Syrian crisis has limited many of the country’s public health activities, WHO prioritized the provision of essential medicines for primary care and chronic illness, and the country’s 2014 national essential medicines list incorporated priority medicines, including those for cardiovascular diseases (21,22).

Collective action to deliver health services in countries affected by conflict is needed, which includes the provision of essential medicines, in order to increase the resilience of the health systems in the face of emergencies, and ensure effective public health responses during crises (23). A national essential medicines list can help countries, both in conflict and with limited income, use their resources to procure and make available the most appropriate treatments in relation to their burden of disease (17).

Jordan and Tunisia selected many medicines out of the same therapeutic group, including ACE inhibitors, dihydropyridil derivatives and HMG CoA reductase inhibitors. For better efficiency, a maximum of 2 of each class should be selected. WHO has highlighted that “careful selection of
a limited range of essential medicines” will improve the quality of care, management of medicines and cost-effective use of resources (18). Jordan’s national formulary guide (national list) includes medicines specified by international nonproprietary names or specific brands of generic medicines. This influences the public sector market to procure from a particular manufacturer (24). It is recommended that Jordan follows best practices to procure medicines by generic names and specify quality standards, not specific brands, for its products (24).

Medicines that had been on the WHO Model List for longer (e.g. digoxin, isosorbide dinitrate and glyceryl trinitrate) were more likely to be in the national lists, including medicines that may have been removed from the Model List. The April 2015 WHO Model Essential Medicines List was used for comparison with the national essential medicines lists while most of the national lists were last updated and notified to WHO 3–6 years ago. Countries need to update their lists every 2 years as is done with the WHO Model List (18). However, there are some medicines, such as sodium nitroprossuide, that have been on the WHO Model List for over 25 years but only 6 countries had this medicine in their national list. Even though there is strong evidence about the effectiveness of sodium nitroprossuide, countries may avoid its use because of its potential toxicity and treatment management compared with other medicines.

Non-solid dosage forms, such as liquids, suspensions, suppositories and injection forms of medicines, are important for certain patient groups (e.g. geriatric or paediatric patients) (25). Children and the elderly may have difficulty in swallowing solid dosage forms for oral use. In both patient groups, small tablets or liquid dosage forms are more appropriate. We found that the most frequently listed medicine dosage forms in the national lists were tablet form. Furosemide oral liquid solution and hydrochlorothiazide oral liquid solution 50 mg were not listed by any country as a form of drug intake. This creates access barriers for patient groups who need to take the required medicines in a liquid form.

Limitations

We did not examine the budget allocation for medicines and standard treatment guidelines. The WHO formulary guide was last updated in 2008 (19). There is a disparity between the medicines listed for cardiovascular diseases in the formulary guide compared with the WHO Model List that is updated frequently. For 3 of the countries (Bahrain, Jordan, Tunisia) we retrieved the cardiovascular essential medicines selection from their national formulary guide. It is unclear, therefore, whether they had used the WHO Model List or formulary guide to select their medicines.

The relatively small sample size (19 countries) could have affected the analyses on the association between per capita health expenditure and burden of disease and the number of
essential cardiovascular medicines; the statistical power might have been too low to detect small differences.

Finally, we did not look at the procedures for procurement and reimbursement which would highlight the actual availability of medicines. As previously noted, national lists serve as the first step to achieving access to medicines (26).

**Conclusion**

EMR countries need to keep up-to-date with the WHO Model List which is revised every 2 years, so that they can keep track of the addition and deletion of medicines on the Model List and link their disease burden to the medicine selection process (26). Countries that have not provided WHO with their national lists need to make them publicly available to be transparent about selection of medicines and increase accountability (18). In addition, a pricing and availability study, similar to a previous study in the EMR, would complement our study and provide the health system perspective on access to medicines (10).

It is important for countries, especially those with limited resources, to select medicines efficiently. This can be done by reducing the number of medicines in therapeutic groups and limiting numerous dosage forms, and by linking public sector procurement with the national essential medicines list.

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**Competing interests:** None declared.

**Analyse comparative des médicaments essentiels pour le traitement des maladies cardio-vasculaires dans les pays de la Région OMS de la Méditerranée orientale**

**Résumé**

**Contexte:** Un accès suffisant aux médicaments essentiels pour le traitement des maladies cardio-vasculaires est nécessaire afin de s’attaquer au problème de la charge de morbidité élevée due à ce type de maladies dans la Région OMS de la Méditerranée orientale.
**Objectifs**: La présente étude a comparé les médicaments pour le traitement des maladies cardio-vasculaires de la liste modèle OMS des médicaments essentiels avec ceux des listes nationales de médicaments essentiels de 19 pays de la Région de la Méditerranée orientale.

**Méthodes**: Des données ont été extraites sur le nombre de médicaments cardio-vasculaires et les formes galéniques inclus aux listes nationales, et ces données ont été comparées avec celles de la liste modèle OMS (24 médicaments au total et 48 formes galéniques). Les facteurs associés au nombre de médicaments essentiels pour le traitement des maladies cardio-vasculaires inclus dans les listes nationales (charge des maladies cardio-vasculaires et dépenses de santé par habitant) ont été étudiés. Le nombre de médicaments issus de six groupes thérapeutiques de médicaments cardio-vasculaires et inclus aux listes nationales, mais absents de la liste modèle OMS principale, a été évalué.

**Résultats**: Djibouti (21 %), la Tunisie (22 %), l’Arabie saoudite et l’Iraq (31 % chacun), et Bahreïn et la Libye (32 % chacun) étaient les pays qui avaient le plus faible pourcentage de médicaments figurant sur la liste modèle de l’OMS par rapport au nombre total de médicaments cardio-vasculaires sur leurs listes nationales. La forme galénique la plus répandue sur les listes nationales était les comprimés, tandis que certains liquides administrables par voie orale n’étaient listés par aucun pays. La Tunisie (8 %), la Jordanie (14 %), Bahreïn et l’Arabie saoudite (15 % chacun) étaient les pays qui alignaient le moins leurs formes galéniques sur la liste modèle de l’OMS.

**Conclusions**: Les pays peuvent améliorer leur sélection de médicaments cardio-vasculaires essentiels afin de promouvoir l’accès au traitement.
The objectives of this study were to compare medicines for cardiovascular diseases listed in the WHO Eastern Mediterranean Region Country Formularies with the WHO Model List of Essential Medicines.

The study aimed to examine the number and types of cardiovascular medicines in the national formularies and compare them with those listed in the WHO Model List of Essential Medicines. The evaluation included a total of 48 medicines and 24 model medicines. The analysis was conducted for 6 countries, and the results showed that 6 countries had a lower percentage of medicines that were consistent with the WHO Model List of Essential Medicines.

The findings were as follows: the countries that had a lower percentage of medicines consistent with the WHO Model List of Essential Medicines were Lebanon (22%) and Jordan (21%). The countries that were consistent with the WHO Model List of Essential Medicines were the Kingdom of Saudi Arabia (32%), the United Arab Emirates (31%), and the United Arab Emirates (14%). The countries that had a lower percentage of medicines consistent with the WHO Model List of Essential Medicines were Nigeria (8%) and Libya (15%).

Conclusions: it is possible for countries to improve the selection of essential medicines for cardiovascular diseases to enhance clinical outcomes.

References

WHO EMRO | Comparative analysis of essential medicines for cardiovascular diseases in countries of the WHO Eastern Mediterranean Region


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