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The Rational Use of Medicines (RUM) in Coronavirus Disease 2019 (COVID-19)

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The Rational Use of Medicines (RUM) is defined as prescribing / administering the right medicine for the appropriate medical indication to the right patient (clinical need) with the correct dose via the right route, and for an adequate duration of time that is cost-effective for the individual and the health care system (1).

According to the World Health Organization (WHO), the irrational use of medicines is a global concern, since "more than half of all medicines are prescribed, dispensed, or sold inappropriately, and half of all patients fail to take them correctly"(2). This is while the proportion of national budget spent on medicines in developing countries alone is estimated between 20% – 40%, which in addition to poor health outcomes, results in considerable waste of resources (3).

Since the outbreak of the COVID-19 Pandemic in December 2019, the practice and implementation of RUM has globally become compounded by a lack of proven treatments for the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) that are safe, effective, and affordable. This is especially concerning developing countries where in resources scarce and the availability, accessibility, and affordability of medicines are among pressing issues faced by health regulators and policymakers.

As of June 2021, there are over 2,100 clinical trials investigating potential treatments for COVID-19 worldwide (4), while to date, corticosteroids remain to be the only effective treatment recommended for severe and critical stages of the infection (5).

The interim results from the Solidarity Trial - an international clinical trial launched by the WHO to find an effective treatment for COVID-19 - which was published in October 2020, found that all four investigated treatments (remdesivir, hydroxychloroquine, lopinavir/ritonavir and interferon) had little to no effect on important COVID-19 outcomes: including overall mortality, initiation of ventilation and duration of hospital stay (6).

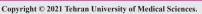
In addition to inadequate effectiveness, many of these agents have raised major safety concerns. Reports of increased QT interval and liver enzymes with hydroxychloroquine (7), high rates of potential and major drug-drug interactions between lopinavir / ritonavir and concomitant medications (8), as well as significant increase in the risk of arrhythmia (serious bradycardia) with remdesivir (9) are a few such safety warnings

Despite all the efficacy and safety concerns noted above, some of these medicines are still being prescribed for the treatment of COVID-19 in certain countries, which do not only go against the most recently updated pharmacotherapy recommendations for the management of COVID-19 (5,10), but are also at odds with RUM as a cornerstone of pharmacotherapy principles and practice. The WHO recommends a list of 12 core interventions to promote RUM (table 1) (11), of which following appear to bear additional importance in the context of an emerging disease, such as the novel coronavirus (2019-nCoV):

1. Use of evidence-based clinical guidelines - Clinical practice guidelines are crucial to promoting RUM. Currently, most countries refer to internationally credible

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guidelines (e.g., the living guideline by the WHO for therapeutics and clinical management of COVID-19) as their reference for developing and adopting national pharmacotherapy guidelines that are appropriate given their resources and population needs. However, important considerations in developing national pharmacotherapy guidelines are to (a) use an interdisciplinary approach in devising feasible pharmacotherapy recommendations, (b) ensure that they are regularly updated (as new evidence becomes available) and promptly communicated to health care professionals. Otherwise, certain medicines will continue to be prescribed long after they have been proven ineffective or unsafe Moreover, (c) guidelines recommendations should be developed using an organized structure and language that is clear, concise, easy to understand and follow.

2. Supervision, audit and feedback – Supportive and positive supervision along with audit and feedback of prescriptions are effective methods and strategies employed for quality improvement in health care practice. It is most beneficial when prescribers are aware that their prescriptions will be compared to acceptable guidelines in their specialty / field of practice, or to that of their colleagues using a peerreview approach. The latter has shown to be particularly

effective in helping physicians take corrective action in their practice and prescribing habits.

3. Use of appropriate and enforced regulations — The regulation of all professionals involved in the prescribing, dispensing and administration of medicines, and enforcing those regulations through legal avenues is key to ensuring RUM in practice. It is equally important to closely oversee and monitor the licensing of health professionals and medicine outlets, as well as the accreditation of educational institutions and medical facilities. Finally, it is imperative for health regulators to ensure that only safe and effective medicines are registered and available in the national market, and that all promotional material / claims used to advertise pharmaceutical products are accurate, informative, up-to-date and unbiased.

RUM remains a national and global health priority. However, adhering to RUM principles has become more challenging ever since the outbreak of the COVID-19 Pandemic. Paying special attention to the core interventions noted above, while keeping in mind the evolving nature of treatment information for the 2019-nCoV could help improve RUM and in return, enhance the provision and quality of healthcare.

Table 1. World Health Organization (WHO) Core Interventions and Policies to Promote Rational Use of Medicines (RUM) (11)

#	Core Interventions / Policies to Promote Rational Use of Medicines
1	An established, multidisciplinary, national body to devise and coordinate policies relevant to medicine use
2	Use of evidence-based clinical guidelines and treatment protocols
3	Development and use of national Essential Medicine List (EML)
4	Drug and therapeutics committee in hospitals / medical facilities
5	Incorporation of problem-based pharmacotherapy cases in undergraduate health science curricula
6	Requiring Continuing Medical Education (CME) for licensure of medical professionals
7	Supportive supervision, audit and feedback of physician prescribing
8	Use of independent (unbiased and accurate) medicine information
9	Public education pertaining to medicines
10	Avoiding perverse financial incentives
11	Use of appropriate regulations and their enforcement
12	Allocation of sufficient resources to ensure availability of medicines and health care personnel

^{*}Note: This table contains the full / complete list of interventions and policies recommended by the WHO to promote RUM. It is included in this editorial for the readers' reference

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