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EDITORIAL COMMENT

# Clinical Decision Support Tools for Optimizing Guideline-Directed Medical Therapy for Heart Failure

## Computing the Possibilities*

Tien M.H. Ng, PharmD

Guideline-directed medical therapy (GDMT) for heart failure (HF) with a reduced ejection fraction confers a substantial benefit by reducing the risk for hospitalizations and mortality by more than 75%,[1,2] in addition to positive effects on ventricular function and quality of life. Importantly, the impressive benefits are based on several key evidence-based tenets. First, GDMT need to be used in combination with the benefit proportional to the number of therapies and the greatest benefit seen when the 4 pillars of renin-angiotensin-aldosterone system (RAAS) inhibitor, beta-blocker, mineralocorticoid receptor antagonist, and sodium-glucose cotransporter-2 inhibitor comprise the regimen.[3,4] Second, the magnitude of benefit exhibits some dose-dependency. Therefore, the guidelines clearly indicate the need for continuous assessment of opportunities to optimize GDMT regimens.[2]

In reality, prescribing of GDMT remains suboptimal. Real-world data consistently demonstrate an underutilization of GDMT, and when prescribed, the minority are at target doses shown to confer maximal benefits.[5,6] There are many reasons, however, clinical inertia is a major contributor. An analysis of outpatient HF registry data found the majority of patients fail to have GDMT added or doses uptitrated despite a lack of obvious contraindications.[7]

Efforts to improve GDMT optimization have included a variety of modalities and interventions. One relatively naïve area of investigation is the development of clinical decision support (CDS) tools specifically for GDMT optimization. Literature of CDS tools in HF is limited with only 2 recent studies targeting greater use of GDMT,[8-10] while others focused on selecting patients for advanced HF therapies[11] and diagnosis in primary care.[12] Application of CDS for cardiovascular disease in general has been limited and with variable success.[13] Barriers to CDS design and implementation have been reviewed extensively elsewhere.[13-16]

In this issue of *JACC: Advances*, Dorsch et al[17] describe the validation of an application programming interface computational algorithm for the identification and provision of recommendations for GDMT optimization for HF with reduced ejection fraction. The algorithm also calculates a medication optimization score (MOS), providing a percentage of how closely a regimen includes all evidence-based, first-line GDMT and proximity to target doses. The decision-tree utilizes medication name and dose, New York Heart Association functional classification, race, allergies, and select readily available clinical data (systolic blood pressure, heart rate, serum creatinine, and potassium levels). The algorithm was tested by applying data from 2 clinical trials (GUIDE-IT [Guiding Evidence-Based Therapy Using Biomarker Intensified Treatment in Heart Failure] and ACTION-HF [Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training]). Major findings were: 1) the algorithm correctly identified non-optimized medication regimens at any specific visit with high specificity (very few cases of failure to identify a particular drug class); 2) the algorithm identified a significant number of potential opportunities to optimize GDMT (initiating new therapies or uptitrating doses); and 3) the MOS was prognostic of the risk of HF hospitalizations and cardiovascular death at

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From the University of Southern California, Los Angeles, California, USA. The author attests they are in compliance with human studies committees and animal welfare regulations of the author's institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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baseline and as a time-dependent covariate. Analyses of the MOS also confirmed incremental benefit of GDMT by number of medications and proximity of dosing to evidence-based target doses. Of note, the MOS suggested substantial room for improvement in GDMT prescribing despite high rates of baseline use in prospective studies specifically designed to improve HF care.

The algorithm developed by these authors is noteworthy as it satisfies many of the desired characteristics of effective CDS tools. Inputs utilize individual patient-level data easily gathered automatically through electronic health records (EHRs), it can be embedded into an EHR system, it not only provides assessment-based prompts but also specific recommendations, and recommendations are tied to well-accepted evidence-based guidelines. The outputs appear modifiable for different stakeholders, including providers, patients, or health systems for benchmarking and continuous quality improvement. Since the MOS is associated with clinical outcomes, this tool may also have utility for population health if adaptable to other populations.

As currently constructed, the algorithm was indeed effective at identifying shortcomings in medication regimens, however, there are limitations. As acknowledged by the investigators, validation with more contemporary clinical trial data that includes angiotensin receptor neprilysin inhibitor and sodium-glucose cotransporter-2 inhibitor use and with real-world data is needed. The algorithm itself has limitations that may hinder implementation. It uses select clinical factors with fixed thresholds and appears to handle inputs as static values. Trends or directional changes of lab values and vital statistics that may affect clinical decision-making are not accounted for. Taken further, clinical decision-making is much more complex than the factors currently included in the tool. Other factors remain unaccounted for that may influence the decision not to optimize certain therapies during certain visits (logistical, patient, other clinical factors). As such, the algorithm recommendations may not reflect real-world clinical complexity which could contribute to lack of provider trust, alert fatigue, and other identified barriers to successful CDS system implementation.[13,14] Importantly, the algorithm currently does not incorporate a determination of safety where de-escalation of therapy may be required (eg, high potassium does not trigger advice about lowering or discontinuing RAASi therapy).

The MOS was associated with patient outcome, potentially making this metric a useful tool for benchmarking and improving outcomes. However, the relationship between MOS and the relative magnitude of outcome improvement was not examined by specific drug class. Thus, it may be less helpful in differentiating between multiple GDMT recommendations when a step-wise approach to optimization is desired. Refining the MOS, allowing each therapy decision to be quantified, may aid in shared decision-making discussions with patients.

The authors should be commended in developing an application programming interface algorithm with much potential value. In the time of digital health, the development of effective tools that utilize EHR and can be easily integrated into CDS systems remains a high priority. To encourage adoption of these tools, their functionality must be efficient, precise, and recommendations accurate. For optimization of HF GDMT, incorporation of other clinical, patient, and health system factors would be important to improve precision and accuracy. Utilizing artificial intelligence and machine learning has advantages over regression-based computational approaches as many more factors can be incorporated.[18] Addition of predictive analytics, such as using EHR data to select patients that would benefit or be at risk from further optimization steps, could also enhance accuracy. These computational techniques could allow for more individualized recommendations. These technologies could then be tailored to different populations and care settings more easily.

As the care of patients with cardiovascular diseases becomes more complex, integration of digital health technologies continues to be increasingly relevant. Achieving optimal GDMT remains a major challenge. The demonstration of a simple EHR computational approach to systematically improving HF medication optimization is step in the right direction. More research is needed to define best practices for the design and implementation of computational tools for HF, but the possibilities are within reach.

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**ADDRESS FOR CORRESPONDENCE:** Dr Tien M.H. Ng, Clinical Pharmacy and Medicine, Titus Department of Clinical Pharmacy, USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences, Keck School of Medicine, University of Southern California, 1985 Zonal Avenue, Los Angeles, California 90089-9121, USA. E-mail: tienng@usc.edu.

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**KEY WORDS** clinical decision support, health technology, heart failure, medications