more effort to the role. Although the reporting structure varied, 12 of 21 CWOs (57.1%) reported directly to the dean, chief executive officer, provost, vice-chancellor, or vice-dean. An additional 7 (33.3%) reported to the chief medical officer, chief clinical officer, or chief physician executive. Sixteen CWOs (76.2%) reported managing an independent budget. The median full-time equivalent of direct reports to the CWO was 1.8 (interquartile range [IQR], 1.0-4.0). All 21 CWOs indicated that the source of support for their time and program was institutional operational funds.

With respect to scope, CWOs were responsible for overseeing organizational efforts to support the well-being of a median of 5000 (IQR, 2150-13,500) individuals including a median of 2100 (IQR, 1400-4000) physicians. Twenty CWOs (95.2%) were responsible for efforts to advance well-being for practicing physicians, 16 (76.2%) for residents/fellows, 9 (42.9%) for medical students, and 9 (42.9%) for biomedical scientist faculty. With respect to non-physicians/nonfaculty, most CWOs (n=16 [76.2%]) were responsible for efforts to advance well-being for advanced practice providers (nurse practitioners and physician assistants) whereas less than half were responsible for nurses (n=8 [38.1%]), graduate students (n=6 [28.6%]), other clinicians (eg, pharmacists, physical therapists, and respiratory technicians; n=8 [38.1%]), or nonclinical employees (information technology, administrative staff, and custodial staff; n=6 [28.6%]). Common topic areas of CWO responsibility are summarized in the Table.

In summary, leading organizations have begun to take substantive action to mitigate occupational distress in physicians and other health care professionals. The CWO plays a pivotal role in leading organizational efforts to improve professional well-being. We believe that the information presented here may be helpful to other organizations creating CWO positions, particularly in the wake of the coronavirus disease 2019 pandemic. Organizational efforts to improve well-being should center on addressing problems in the practice environment and organizational culture, rather than attempting to make individuals better equipped to endure broken systems.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at: http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

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Potential Competing Interests: Dr Shanafelt is a coinventor of the Well-being Index instruments and the Participatory Management Leadership Index. Mayo Clinic holds the copyright of these instruments and has licensed them for use outside Mayo Clinic. Dr Shanafelt receives a portion of any royalties paid to Mayo Clinic. As an expert on the well-being of health care providers, Dr Shanafelt frequently gives ground rounds/key note lecture presentations and advises health care organizations. He receives honoraria for some of these activities.

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https://doi.org/10.1016/j.mayocp.2020.09.004

Patient-Centered, Physician-Investigator Friendly Pragmatic Phase I/II Trial Designs—The 4P Model

To the Editor: Traditional dose finding studies designed around safety and toxicity offer no flexibility for physician-investigators or patients. With the recent advent of targeted and immunotherapy, a few early-phase trials in oncology have started opening up physician-investigators' flexibility to exercise their clinical judgment in the evaluation and care of their enrolled patients. For example, immunotherapy trials may allow treatment past progression for investigator-perceived clinical benefit. Yet still most trials mandate that patients come off trial based on RECIST measures, and only a few are flexible to continue beyond clinical progression for

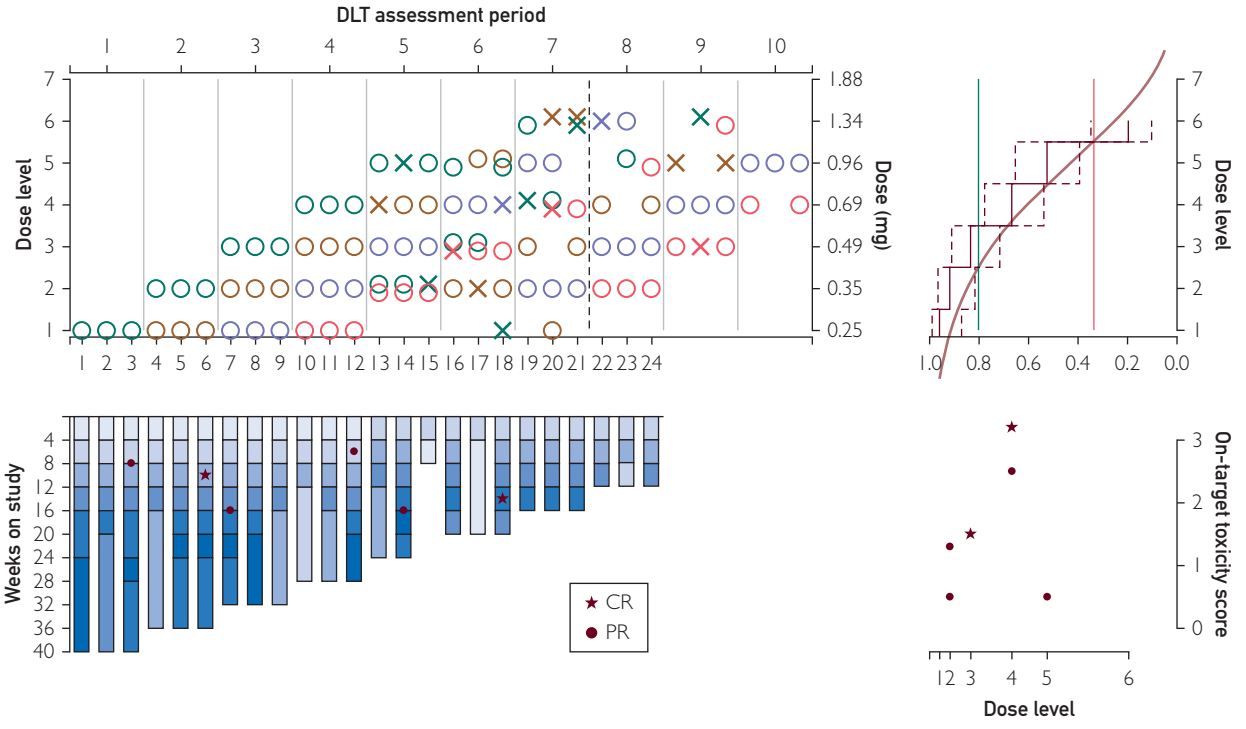

FIGURE. The dose-titration diagram (A) and "dose-survival curve" (B) introduced in reference 4 constitute the upper half of our 4P dashboard. The bottom half represents extensions motivated by our 3 use cases. A vertical "swimmer plot" (C) hangs downward from the dose-titration plot, depicting dose titration by color saturation, and key clinical events by markers. A "titration heuristic" plot (D) aligns likewise with the dose-survival curve above it, thereby scaling doses according to population level tolerability. Consequently, the trial population will tend toward uniform distribution horizontally when titration to final dosing is complete, rendering this plot more directly useful as a starting point for inference. CR = complete response; DLT = dose-limiting toxicity; PR = partial response.

clinical benefit. With respect to the crucial question of *drug dosing*,[1] early-phase trials still impose algorithmic rigidities or statistical formalities on us, hampering our clinical judgment. Even when dose reductions or intrapatient dose escalation are permitted, these occur neither by a clinically coherent[2] design nor with adequate formal supports.

The recent advent of pragmatic phase 1 dose-titration designs,[3,4] however, facilitates extending such support to *clinical judgment* in matters of dose individualization. By generalizing one such design[4] to incorporate measures of therapeutic response, we wish to exemplify a "4P" concept of *p*atient-centered, *p*hysician-investigator friendly *p*ragmatic *p*hase I/II trial design.

During on-trial follow-up, early-phase trial participants ask their oncologists several characteristic questions:

1. Have you found signs my cancer is or isn't responding to the study drug?
2. How does my experience compare with other patients in this trial?
3. Should I keep taking the drug at my current dose, or should we change the dose—or even stop it?

Current phase I/II trial designs offer us no rational support for meeting these valid and urgent questions. To this end, we propose a synoptic graphical "trial dashboard" (Figure).

Building on a previously described phase 1 dose-titration graphic,[4] we see questions 1 and 2 as use cases for a swimmer plot[5] linked to the dose-titration diagram. Question 3 underscores the imperative to maintain an up-to-date *titration heuristic*, incorporating emerging evidence that links drug-exposure measures (including on-target toxicities) with clinical response. This latter consideration prompts addition of response-vs-exposure plots in which both absolute dose and grade of on-target toxicity appear as covariates.

This clinically realistic dashboard illuminates a 4P concept that

bolsters patient-centered decision making in early-phase oncology trials. Moreover, by accentuating crucial decision problems faced by early-phase cancer trial participants and their oncologists, this model should help trial methodologists to propose useful adjunctive formal decision supports.

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Potential Competing Interests: Dr Norris operates a scientific and statistical consultancy focused on precision medicine methodologies such as those advanced in this letter. Dr Sen reports research funding for clinical trials (paid in full to his institution) from Loxo, Jacobio, Exelixis, GlaxoSmithKline, BioAtla, Xencor, Epizyme, Abbisko Therapeutics, Fujifilm, Synthorx, Turning Point Therapeutics, Daiichi-Sankyo, and Tesaro. Dr Groisberg reports consultancy/advisory board fees from Regeneron. Dr Subbiah reports research funding/grant support for clinical trials from Roche/Genentech, Novartis, Bayer, GlaxoSmithKline, NanoCarrier, Vegenics, Celgene, Northwest Biotherapeutics, Berg Health, Incyte, Fujifilm, PharmaMar, D3, Pfizer, MultiVir, Amgen, AbbVie, Alfasigma, Agensys, Boston Biomedical, Idera Pharmaceuticals, Inhibrx, Exelixis, Blueprint Medicines, Loxo Oncology, MedImmune, Altum, Dragonfly Therapeutics, Takeda, National Comprehensive Cancer Network, National Cancer Institute Cancer Therapy Evaluation Program, The University of Texas MD Anderson Cancer Center, Turning Point Therapeutics, and Boston Pharmaceuticals as well as travel support from Novartis, Pharma Mar, American Society of Clinical Oncology, European Society for Medical Oncology, Helsinn, and Incyte. He reports consultant/advisory board fess from Helsinn, Loxo Oncology/Eli Lilly, R-PHARM US, Incyte, QED Pharmaceutical Services, MedImmune, and Novartis. He also reports support from Medscape.

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https://doi.org/10.1016/j.mayocp.2020.09.009

Risk Framing in Cardiovascular Medicine I

To the Editor: We applaud the work of Drs Alkhouli and Rihal[1] in examining the important topic of risk/benefit framing in patient-centered decision making. However, we disagree with the choice of a sodium-glucose cotransporter 2 inhibitor (SGLT2i), canagliflozin, as an example in their arguments and that "the other 98% [of treated patients] would see no incremental benefit from the treatment."(p.1316) First, to clarify, the primary outcome in Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation was not a composite major adverse cardiovascular event outcome as stated, but rather a composite of end-stage kidney disease, doubling of the serum creatinine level from baseline sustained for at least 30 days, or death from renal or cardiovascular disease. Patients who received canagliflozin 100 mg/d had a 30% relative risk reduction (4.3% absolute risk reduction) for this primary outcome.[2] Reduction of hospitalization for heart failure (a secondary end point) was profound, with a 39% relative risk reduction (2.4% absolute risk reduction) seen in patients receiving canagliflozin. This is in addition to the major adverse cardiovascular event outcome data quoted by the authors.[3]

Sodium-glucose cotransporter 2 inhibitors continue to show promise as one of the most important and pluripotent cardiovascular medications of a generation, recently exhibiting groundbreaking efficacy in heart failure with reduced ejection fraction with and without diabetes[4,5] and dramatic renoprotective effects in patients with chronic kidney disease with and without diabetes, including markedly lowering mortality.[6] Many of these effects are thought to be classwide, and the use of these agents often targets multiple cardiovascular protective end points in an individual patient. Studies have also reported the cost-effectiveness of this class.[7] Therefore, although again we agree with the central message of the commentary, we disagree with the authors' selection of an SGLT2i as an example and recommend against limiting SGLT2i benefit to a single end point.

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Potential Competing Interests: Dr Modarressi is on the speakers' bureau for AstraZeneca. Dr Derakhshan reports no competing interests.