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Transforming clinical practice guidelines and clinical pathways into fast-and-frugal decision trees to improve clinical care strategies

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Abstract

Background: Contemporary delivery of health care is inappropriate in many ways, largely due to suboptimal Q5 decision-making. A typical approach to improve practitioners' decision-making is to develop evidence-based clinical practice guidelines (CPG) by guidelines panels, who are instructed to use their judgments to derive practice recommendations. However, mechanisms for the formulation of guideline judgments remains a "black-box" operation—a process with defined inputs and outputs but without sufficient knowledge of its internal workings.

Methods: Increased explicitness and transparency in the process can be achieved by implementing CPG as clinical pathways (CPs) (also known as clinical algorithms or flow-charts). However, clinical recommendations thus derived are typically ad hoc and developed by experts in a theory-free environment. As any recommendation can be right (true positive or negative), or wrong (false positive or negative), the lack of theoretical structure precludes the quantitative assessment of the management strategies recommended by CPGs/CPs.

Results: To realize the full potential of CPGs/CPs, they need to be placed on more solid theoretical grounds. We believe this potential can be best realized by converting CPGs/CPs within the heuristic theory of decision-making, often implemented as fast-and-frugal (FFT) decision trees. This is possible because FFT heuristic strategy of decision-making can be linked to signal detection theory, evidence accumulation theory, and a threshold model of decision-making, which, in turn, allows quantitative analysis of the accuracy of clinical management strategies.

Conclusions: Fast-and-frugal provides a simple and transparent, yet solid and robust, methodological framework connecting decision science to clinical care, a sorely needed missing link between CPGs/CPs and patient outcomes. We therefore advocate that all guidelines panels express their recommendations as CPs, which in turn should be converted into FFTs to guide clinical care.

KEYWORDS

clinical recommendations, decision theory, evidence based medicine, fast-and-frugal trees, heuristics, practice guidelines

1 | INTRODUCTION

Currently, most societies worldwide devote an enormous amount of resources to health care, yet patient health outcomes remain relatively poor.[1,2] For example, the United States spends nearly 18% ($3.2 trillion) of its gross domestic product (GDP) on health care; however, it is estimated that only 55% of needed services are delivered while more than 30% health services result in wasteful "care."[3] In the final analysis, the observed (suboptimal) care relates to the quality of medical decisions.[2,3] It has been proposed that personal decisions are the leading cause of death,[4] and that 80% of health care expenditures can be linked to physicians' decisions.[5,6]

1.1 | Evidence-based guidelines as a key approach to improving clinical decision-making

If decision-making can largely explain the relatively poor state of affairs of current health care utilization, how can it be improved? Current approaches to improving clinical decision-making mostly reside in the application of the principles of evidence-based medicine (EBM) to development of "trustworthy" clinical practice guidelines (CPG).[7-9]

Originally defined as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances," CPGs were introduced in 1990 as a way to improve what had been increasingly perceived as low-quality health care, resulting in poor patient outcomes.[10] Research during the last 2 decades has convincingly documented that inadequate adherence to CPGs represents the third leading cause of preventable patient deaths and one third of unnecessary health care spending.[5,11] As a result, the efforts to improve decision-making by uptake of CPG was also sanctioned in the US Merit-based Incentive System law,[12] which considers evidence-based CPGs a key way to improve practitioners' decision-making, and, in turn, the quality of care. Indeed, measuring adherence to CPGs is at the heart of the science of quality improvement[5] and the merit-based financing of health care.[12]

However, as highlighted by the Institute of Medicine (IOM) report *Guidelines We Can Trust*,[8] not all CPGs are "created equal," if CPGs are to improve health care and outcomes, they should be developed using rigorous and sound methodological principles. The IOM has provided an impetus to embark on further methodological work to develop "standards for trustworthy CPGs."[8,13] During the last 15 years, several new systems for developing CPGs have arisen, chief among them Agency for Health Research and Quality,[14] Strength of Recommendation Taxonomy,[15] Scottish Intercollegiate Guidelines Network,[16] US Preventive Services Task Force,[17] National Institute for Health and Clinical Excellence,[18] and GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) systems.[19] Similarly, the Guidelines International Network has called for establishing international standards for guidelines development.[20] Guidelines International Network[20] has defined key components for guideline development and an international group of leading methodologists has developed a checklist covering 18 topics and 146 items to serve as a resource for guideline developers ("Guidelines 2.0").[21] Although differences between these systems are often small or even "cosmetic," due to methodological developmental rigour, GRADE has become today's dominant system for generation of CPGs[22] endorsed by over 100 professional organizations to date.

Decision-making, however, remains a complex endeavour. Many factors are known to affect how people, including clinicians, make their decisions. Following the key principle of EBM,[7] GRADE has acknowledged that evidence is necessary, but not sufficient, for effective decision-making.[22,23] GRADE (within its Evidence to Decision Framework) has codified key normative factors that CPG panels *ought to* take into consideration in producing practice guidelines.[21] After considering the key factors (quality of evidence, typically based on systematic review of all available evidence, the health intervention's balance of benefit and harms, use of resources, ie, whether the intervention constitutes a significant burden on resources/patient, and patients' value and preference along with consideration of feasibility, equity, and accessibility), the guidelines panels are instructed to use their *judgments* to either reach consensus (or use formal voting via GRADE so-called grid process, or alternative voting method[24]) to issue CPG recommendations that can be either "strong" or "weak," for or against a health intervention (diagnostic, therapeutic, or public health intervention).[25,26]

1.2 | Developing recommendations according to practice guidelines remains a "black-box" operation

In spite of this tremendous progress in the development of the methodology for generating trustworthy recommendations,[7] how exactly the guidelines panel members judgments operate, or should operate, remains unclear both at the practical and theoretical level. In what Mercuri and colleagues call "the integration problem,"[27] neither GRADE nor any guidelines system gives specific instructions or propose a theoretical framework for how CPG panel members should integrate evidence grades with other important factors, such as patient preferences, and trade-offs between costs, benefits, and harms when proposing a clinical practice recommendation. Thus, even though GRADE and other CPG systems attempts to inform CPG development by specifying factors that guidelines panel members should take into consideration, mechanisms for formulation of their judgments remain essentially a "black-box" operation—the process with defined inputs and outputs, but without any understanding of its internal workings. Importantly, this contradicts the goals of EBM methods, which strive to achieve explicitness and transparency for decision-making.[7] As noted by Mercuri et al,[27] transparency in any process is not a function of what is judged but rather how the basis for the decision is articulated. As a result, the current guidelines process often seems arbitrary, vague, and potentially logically inconsistent.[27]

1.3 | Practice guidelines as a decision-theory problem

The judgments made by the guidelines panels are rendered in a largely "theory-free" environment, which precludes evaluation of the accuracy of CPGs and their impact on patients' outcomes. Manski[28,29] has recently proposed that by reformulating CPG as a problem of decision-making under uncertainty can lead to improved individualized decision-making over uniformly following CPGs. He demonstrated that adherence to guidelines is theoretically inferior to treating clinical judgement as decision-making under uncertainty using expected utility theoretical framework (EUT).[28,29] This, in fact, could be one of the reasons why CPGs are often not followed.[30,31]

However, the problem with advocating for a EUT decision-theoretical framework is that it ignores that practicing physicians are under increasingly severe time pressures, and it assumes that they have instant access to all relevant knowledge, including all alternatives, consequences, and probabilities (this is known as the "small world" theoretical approach to decision-making[32,33]). In a real, "large" world context, however, doctors have limited time available, are often working in different clinical settings, are overwhelmed by new information, and have limited knowledge about the complete set of alternatives, consequences, and probabilities available.[32,33] To make more optimal decisions, one of the core principles of rational decision-making stipulates that decision-making should take into account *context*, as well as the epistemological, environmental, and computational *constraints* of human brains.[34,35] This calls for the application of "large" world theories to decision-making of which a prototype is the heuristic theory of decision-making.[32,33]

1.4 | Application of heuristic theory of decision-making to the development of practice guidelines

Given the immense amount of information now available and the myriad factors that affect the way we make decisions,[36,37] we must account for the brain's limited capacity for information processing, memory limitations, and storage capability.[38] Simon's *Theory of Bounded Rationality* posits that rational decision-making depends on context and should respect the epistemological, environmental, and computational constraints of human brains.[34,35,39,41] This means that rational behaviour requires adaptation to the environment; this is known as *adaptive or ecological rationality*, a variant of the *Theory of Bounded Rationality*.[32] Because finding the optimum solution to a given problem can be resource and computationally intensive, individuals often use adaptive behaviours that rely on "satisficing" (finding a "good enough" solution) rather than optimizing/maximizing behaviour (striving to find a "perfect" solution).[40] The principle behind satisficing is that there must exist a point (threshold) at which obtaining more information or engaging in more computation becomes overly costly and thereby detrimental. Identifying this threshold at which a decision maker should stop searching for more information is often accomplished via the use of "heuristics."[32] Thus, the *heuristic approach* to decision-making is the mechanism for implementing bounded rationality.[42] A heuristic is a "strategy that ignores part of the information, with the goal of making decisions more quickly, frugally, and/or accurately than more complex, resource-intensive methods."[41] Heuristics often outperform more complex statistical models (the phenomenon known as "less-is-more")[32] and are widely used in medical education as "mental shortcuts," or "rules of thumb." In fact, one approach that exploits a heuristics approach to decision-making is the development of EBM[43] and evidence-based CPGs, the latter often expressed as easy-to-follow algorithms, flow-charts and clinical pathways (CPs).[11,44-47] Clinical pathways are considered a highly effective way to manage today's clinical information overload and the brain's limited storage/processing capacity (eg, 300 pages of text in 500 articles describing management of urinary tract infection was reduced to 3 CPs displayed as clinical algorithms).[44] While at the conceptual heart of the Merit-based Incentive System law is measurement of adherence to evidence-based CPGs, at the operational level, it is care concordance with CPs that is increasingly defining how health care is delivered and financed.[5,48-50] As a result, many payers have begun negotiating with health care organizations about using CPs to standardize practice and help monitor quality of care, with the aim of reducing inappropriate practice variation, decreasing costs, and improving health outcomes.[51,52] Thus, CPs offer a potential way to reduce inappropriate clinical variability by harmonizing EBM with improved medical decisions. However, despite the promise and rapidly increasing use of CPs, no theoretical framework has been developed to guide their development; in addition, there is no standardized definition of CPs. Indeed, the literature contains more than 84 different terms indicating a CP.[47,53] The terms clinical algorithms, CPs, and flow-charts are often used interchangeably. Although they can be informed by evidence-based guidelines, CPs are typically developed ad hoc, by experts in an unsystematic, "theory-free" environment. As any recommendation can be either right (true positive or negative), or wrong (false positive or negative), the lack of theoretical structure precludes the quantitative evaluation of the outcomes of the management strategies that are recommended by CPGs and CPs. As a result, we are left with little idea of how accurate are our decision-making strategies, regardless of whether guidelines/pathways are followed. What is needed is to place CPs (clinical algorithms, flow-charts) within a firm theoretical decision framework. This can be accomplished by converting CPs into fast-and-frugal tree (FFT) heuristics.

1.5 | FFT heuristics: a theoretical framework for constructing clinical pathways

Fast-and-frugals represent a particularly effective class of heuristic strategies, which rely on limited information to reduce estimation error and facilitate fast decisions.[32,41,54] It provides practical implementation of the *satisficing principle*—there must exist a point (threshold) at which obtaining more information or performing another computation becomes detrimental and costly; the application of FFT heuristics helps decision-makers stop searching before this threshold has been crossed.[32] Fast-and-frugals are highly effective, simple decision trees composed of sequentially ordered cues (tests) and binary (yes/no) decisions formulated via a series of if-then statements.[55] Fast-and-frugals are very efficient for solving binary decision tasks such as making diagnosis, prediction, or deciding whether to order tests or initiate treatment.[55] Decision-making strategies based on FFTs have been found to be superior to other strategies, including those using complex multivariate regression models.[55] FFT provide a potentially fundamental link between evidence and action.

Although on the surface CPs (flow charts, clinical algorithms) resemble FFTs, they are different. It is the latter that has in-built theoretical structure that allows quantitative analysis of the accuracy of clinical management strategies. This is possible because the FFT heuristic strategy of decision-making can be conceptually linked to signal detection theory, evidence accumulation theory, and the threshold model to improve decision-making.[33,55] Thus, metrics of signal detection theory (true and false positives, true and false negatives), effect of sequential accumulation of evidence and the consequences of our actions expressed via evidence accumulation theory and threshold model, respectively, become metrics that can be used by FFTs to calculate the accuracy of our clinical decisions. Given that CPs are increasingly developed to address the entire spectrum of care and follow the patients from diagnosis all the way to recovery or demise on the trajectory of clinical management,[47] FFT can enable the quantitative analysis of the accuracy of individual decisions, or the evaluation of an entire management strategy. The latter allows comparisons and statistical analysis of the competing management strategies.

How do FFTs work? In an FFT, clinical information ("cues") for a series of binary decisions (yes/no) are assembled. The relation among the cues is framed as a series of *if-then* statements (eg, *if* risk for a cardiovascular event is high [cue], *then* administer statins [decision]). If the condition is met, the decision is made and the FFT is exited. Otherwise, the FFT sequentially considers additional cues until the exit condition of a cue is met. If the exit occurs after a positive cue ("yes"), an intervention is enacted. If the exit occurs after a negative cue ("no"), no intervention is administered. The last cue of an FFT has 2 exits, to avoid indefinite loops, and to ensure that a decision is ultimately made.[55] The FFT is typically identified by the sequence of the cue exits before the final one. For example, FFT's with 3 cues can be arranged in 24 possible combinations ($3!\cdot2^2$), and one writes FTTyy, FFTyn, FFTny, FFTnn to denote that the exit sequence before the last cue was "yes" (y) or "no" (n), respectively.

To summarize, FFTs powerfully link several established decision science features.[4] They have been linked to signal detection theory, as every cue in an FFT either correctly or incorrectly classifies "signal" (eg, disease) (true positive [TP)], true negative) and "noise" (false positives [FP] and false negatives [FN]) (eg, absence of disease), respectively.[33,55] An essential feature of FFT is that the structure of the exits from the cues (yes/no) determines the ratio between false negatives vs false positives.[33,55] Thus, FFTs where all cues in a fixed order have all their exits on the "yes" side of each cue (eg, FFTyy … y) has a high true positive rate at the expense of a large number of false alarms. In contrast, FFTnn … n reduces false alarms at the expense of large false negative rates.[55] Most importantly, these features of FFTs allow the application of Bayesian approaches to calculate the accuracy of the entire FFT[55]—and the entire clinical management strategy.[33]

1.6 | An illustrative example—statins for primary prevention

By proposing that clinical management strategies expressed via CPGs or CPs be converted into FFTs, we provide a theoretical and practical platform for assessing and improving CPGs and CP-based clinical management strategies. We illustrate the approach by converting a flowchart developed by the American College of Cardiology and American Heart Association (ACC/AHA) for the use of statins for primary prevention of cardiovascular diseases (Figure 1), a vigorously debated topic central to the underuse vs overuse of statins.[56] We used the Framingham Data Set (n = 3715) to illustrate the concept. However, we believe these methods can be readily used in any setting in need of the assessment of the impact of the guidelines on patient outcomes.

Fast-and-frugals allow an assessment of the accuracy for both the individual patients who meet the given decision criteria, and the evaluation of the entire management strategies, at the population level. For example, the figure shows the conversion of the ACC/AHA statins guidelines (A) into an FFT with 5 cues (B); C shows the performance of the FFT at individual patient levels with the answer "yes" to all cues (FFTyyyy). The overall accuracy of this FFT expressed as a positive predictive value = 11.4%, indicating that 11.4% of our treated patients will be appropriately given statins, but 88.6% will not, suggesting there is a better FFT sequence. One of the powerful features of FFT methodology is that it allows us to evaluate the performance of *all possible* clinical strategies by changing the orders in which we collect (and act upon) available clinical information (cues). Figure 1D shows the performance characteristics for all 1920 combinations that it is possible to generate with 5 cues. The analysis can help identify the most sensitive and specific clinical management strategies; in addition, if data on the benefits and harms of statins are used, the various consequences of actions can be incorporated into the analysis to generate the FFT with the most optimal trade-offs between TPs and FPs.[33]

It is also valuable to know which clinical management strategies are useless or less informative. For example, the FFT shown in Figure 1 generates 384 combinations with TP = 0 and FP = 0; 1795 FFTs resulted in TP ≥ 90%, and 768 FFTs had FP ≤ 5%. No combination had TP ≥ 90% and FP ≤ 5%.

Note that in this example, only classification accuracy as per ACC/AHA guidelines was done. That is, we did not explicitly model the effects of benefits and harms of statins. However, as mentioned earlier, extension of the FFT known as FFT with the threshold (FFTT) to take the consequences of treatment into account is available.[33] Depending on the magnitude of benefits and harms of treatment, FFT and FFTT can yield substantially different classification patterns (see Hozo et al for details[33]).

2 | DISCUSSION

In the current healthcare environment, CPGs and CPs are touted as one of the main approaches that should be undertaken to reduce both errors and costs, while simultaneously improving health outcomes and raising patient satisfaction.[1,11] Consequently, they are being widely adopted. However, to realize their full potential, they need to be placed on more solid theoretical grounds than is currently the case. We believe this potential can be best realized by converting CPGs/CPs into FFTs; this provides a simple and transparent, yet solid and robust, methodological framework connecting decision science to clinical care, a sorely needed missing link between CPGs/CPs and patient outcomes. We therefore advocate that all guidelines panels and CPs developers express their recommendations as flow-charts or clinical algorithms, which in turn should be converted into FFTs to guide clinical care. The methods proposed have strong theoretical foundations in decision science, for which user-friendly software already exist to allow their widespread dissemination.[33,55,57] Finally, and consistent with the IOM's "Learning Health Care Systems" recommendations,[58] the panels, guidelines-users, and policy-makers could assess the impact of CPGs and CPs in data sets collected in the real-world settings where the recommendations will be applied.

It is important to note that the construction of FFTs does not obviate the need for considerations the quality of evidence and all other GRADE factors. Rather, it assumes that once all these factors are taken into consideration, the process requires the guidelines panels to make the decisions explicit. This may also refers to their assessment of patients' values and preferences that are typically believed not to work well with clinical algorithms and flow-charts. However, the patients values and preferences can be explicitly modelled in FFT, and, in fact, the explicitness of the approach may help patients better clarify their preferences and subsequently the choices they wish to make. But, to assess how well FFT works, individual patient data (that may include data on patient values and preferences) need to be collected. (NB, as explained in the legend, we did not have data on patient' values and preferences to integrate them in the FFT statin model. The statin FFT example only illustrates how clinical algorithms [derived from guidelines] are to be converted into FFT). Therefore, one of the main usefulness of FFT is probably in the implementation phase of the guidelines development, where the approach can allow assessment

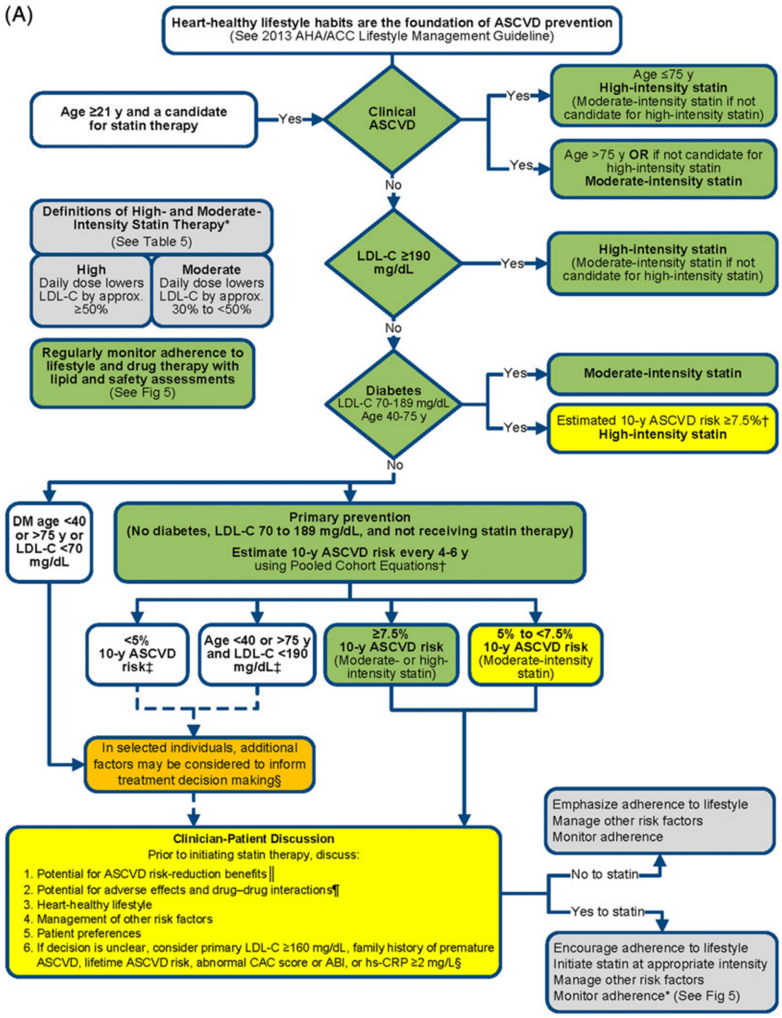

FIGURE 1 A, American College of Cardiology and American Heart Association (ACC/AHA) flow-chart for the use of statins for primary prevention of cardiovascular disease.[59] B, Five cues fast-and-frugal tree (FFT) for prescribing statins for primary prevention of heart disease (generated by conversion of the ACC/AHA flow chart into FFT shown in A. This tree generates 1920 different FFTs. If all contextual factors are taken into account (yellow box in A), an FFT is composed of 10 cues. Such a tree can generate $1.858 * 10^9$ different FFTs (possible clinical strategies). (Note that we did not have data on patient preferences. For the last cue, we used the data on smoking (yes/no). Because our main goal was to classify the accuracy of decision to use statins (yes/no) and not the consequences of benefits and harms of the various statins, we did not distinguish between effects of the various doses of statins.) C, The performance of FFTyyyy shown in Figure 1B (based on exit structure for cues as "yes"). Calculation for individual paths and the overall FFT is shown. The boxes shows values for TP, FP, TN, FN, P(D + |T+), and P(D + |T−). Calculation follows classic Bayesian statistics. For example, "positive" answer to cue 1 (ASCVD) was calculated as P(D + |T+) = [p*TP/(TP + FN)]/[p*TP/(TP + FN) + FP/(FP + TN)*(1-p)] = [0.075*339/(339 + 322)]/ [0.075*339/(339 + 322) + 572/(572 + 2482)*(1-0.075)] = 18.2%, while "negative" answer to cue 1 will result in P(D + |T-) = [p*FN/(TP + FN)]/[p*FN/(TP + FN) + TN/(TN + FP)*(1-p)] = 4.63%. The latter number is then used to calculate P(D + |T+) for cue 2 (LDL C ≥ 190 mg/dl) as per P(D + |T+) = [p*TP/(TP + FN)]/[p*TP/(TP + FN) + FP/(FP + TN)*(1-p)] = (0.0463* 0.04969)/[(0.0463*0. 04969) + (0.02216)*(1-0.0463)] = 0.0982 and so on to calculate the accuracy statistics for remaining cues. By summing all values across all paths, we can calculate the accuracy statistics for the entire FFTyyyy. From the figure, we see that total number of TP = 78 + 158 + 16 + 339 = 591. Similarly: total FP = 1726, total FN = 70, and total TN = 1328. Total TP rate = TP/(TP + FN) = 591/(591 + 70) = 89.5%; Total TN rate = TN/(TN + FP) = 1328/(1328 + 1726) = 43.5%; total FN rate = FN/(FN + TP) = 70/(70 + 591) = 10.5%; total FP rate = FP/(FP + TN) = 1726/(1726 + 1328) = 56.5%. Applying Bayes formula as per above, P(D + |T+) for the entire FFTyyyyy = 11.4%. (Above calculations take into consideration conditional dependency of cues; assuming independence among the cues often provide similar results.[33]) D, Receiver operating characteristic (ROC) analysis of a 5-cue FFT for decision to use statins for prevention of heart disease. The performance of 1920 permutations is illustrated. The FFTs with the highest sensitivity (true positive rate), specificity (lowest false positive rate), and the one with the most optimal trade-offs in the accuracy of classification (TPs vs FPs) are written out on the graph. If a clinician or health plan wants to minimize overuse, then they should gather clinical information ("cues") or identify patients according to the FFT with the sequence of cues as 54321: NNNNN; if the goal is to minimize underuse, then the FFT with cue sequence 12345:YYYYY should be applied. Fast-and-frugal with cues arranged as 31425:YYNY will result in clinical use of statins with optimal trade-offs. All calculations were performed using publicly available Framingham Data Set from the National Heart, Lung and Blood Institute; we used mortality as the main outcome and according to the methods described in Hozo et al.[33] Abbreviations: FP, false positives; FN, false negative; P(D + |T+), Positive Predictive Value, post-test probability of outcome (death) if the test (cue) was "positive"; P(D + |T-), post-test probability of outcome (death) if the test (cue) was "negative"; p, prior probability of outcome (condition) of interest; in our case, it was set at 7.5% to correspond to the ACC/AHA guidelines; ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; CAC, coronary artery calcium; hs-CRP, high-sensitivity C-reactive protein; MI, myocardial infarction; TN, true negative; TP, true positive

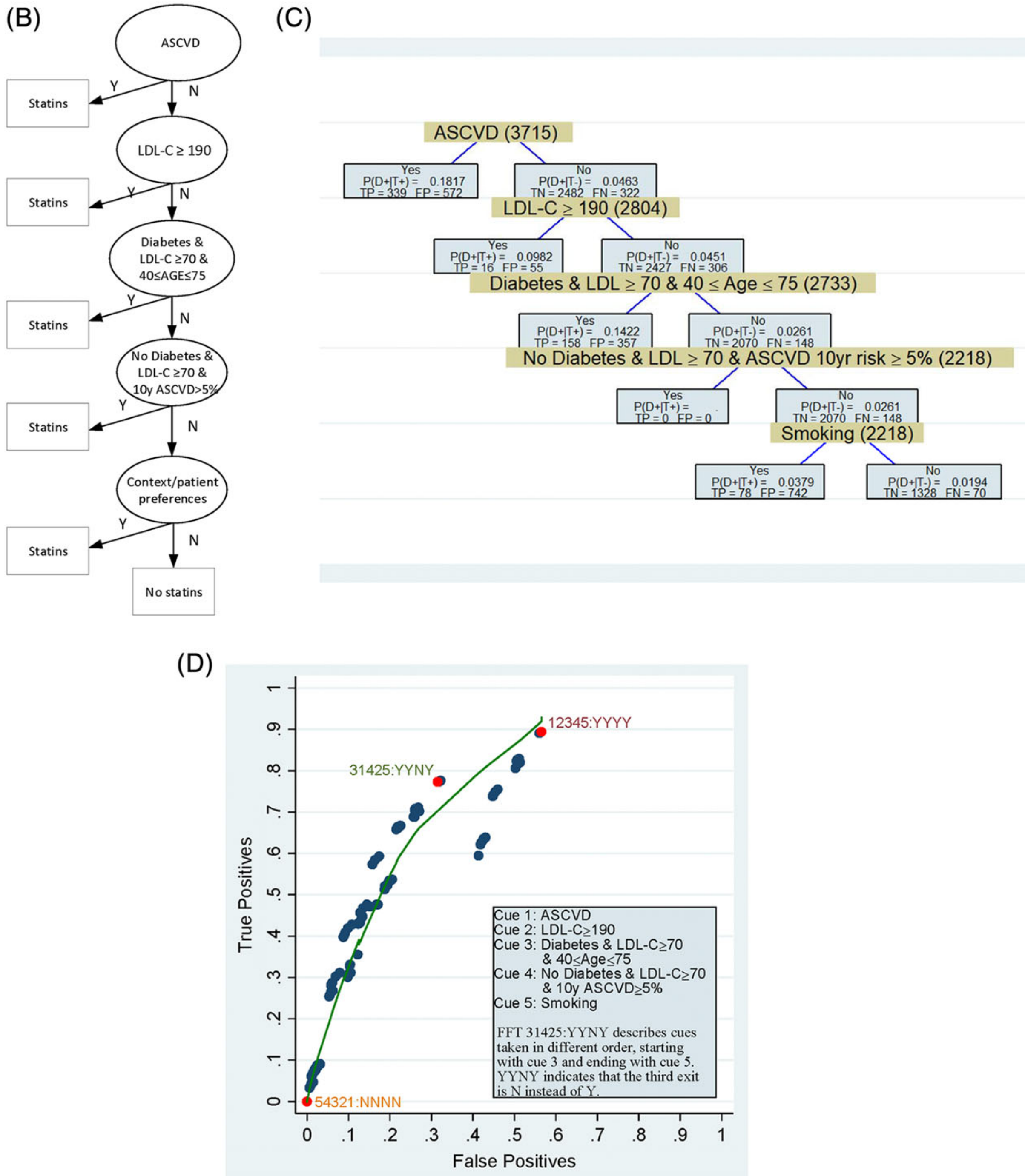

FIGURE 1 Continued

of the accuracy of the recommended management strategies using data actually collected and along with the philosophy of the "Learning Health Care Systems."[58]

In the recent review of the progress of EBM during the last quarter of a century, it was concluded that "the main challenge for EBM remains how to develop a coherent theory of decision-making by relating it to other decision science disciplines."[7] By reformulating theory-free CPG recommendations within a framework of theory-driven FFTs, we believe that we have successfully addressed this challenge and offer one technical solution and a path forward for further improvement of decision-making in clinical medicine.

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