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The PRIMER study: Nudging patients with liver disease toward healthier habits, one step at a time

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Frailty is exceedingly common in individuals with cirrhosis, is associated with a variety of poor outcomes, and is often a barrier for many patients seeking transplant. In this population, physical exercise can improve aerobic capacity, muscle mass and function, and quality of life.^[1] The concept of “prehabilitation” to improve physical function prior to transplant surgery has therefore become popular as a method to facilitate transplant for frail patients.^[2] There are challenges, however, in delivering exercise interventions to this population. Most transplant hepatology care is provided in large medical centers far from the patients’ homes, where logistical barriers limit the impact of hospital-based supervised exercise. Unsupervised home-based exercise in cirrhosis lacks the structure and accountability required to maintain adherence.^[3] Similarly, novel app-based, self-directed programs also suffer from poor adherence.^[4,5] These failures of behavioral interventions reflect lack of readiness and significant barriers to lifestyle change in chronic liver disease, underscoring the importance of developing targeted behavioral interventions for cirrhosis.

In this edition of *Liver Transplantation*, Serper and colleagues report the findings of a pilot randomized trial assessing the feasibility and efficacy of an incentivized physical activity program as compared with a more limited lifestyle intervention in individuals pursuing liver transplant.^[6] All participants received personalized physical activity and diet handouts. Additionally, those in the intervention arm received a more formal at-home exercise program including (1) financial incentives for meeting step goals and for participating in weekly phone check-ins and (2) twice daily text-based reminders to support medication adherence. This multipronged intervention leverages the psychology of decision-making. Behavioral scientists have developed theories of how humans make decisions, with most describing 2 cognitive systems that guide real-world decision-making (“system 1” and “system 2”). This theory and the field of behavioral economics were popularized by Daniel Kahneman in his book *Thinking, Fast and Slow*.^[7] “System 1” thinking is fast, automatic, and intuitive, while “system 2” thinking is effortful, analytic, and, thus, slower. With time and attention becoming increasingly at a premium in our day-to-day lives, many decisions (including those that have a tremendous impact on our health) are made using system 1. Importantly,

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system 1 relies on heuristics (shortcuts or rules of thumb) to produce fast decisions and is heavily influenced by the environment (mental, social, and physical) in which the decision is being made.^[7,8] Behavioral economics has shown that we can take advantage of this feature by modifying the decision-making environment to support healthier choices.^[8] The modifications are known as nudges. Examples of nudges include changing the default choice (eg, requiring an “opt-out” for organ donation) and placing the desired choices in prominent areas (eg, healthier food earlier in the cafeteria food line or on the most accessible grocery store shelf). Through small changes in the environment, nudges can allow an individual to effortlessly overcome old habits without adding cognitive burden or requiring intentionality.

The PRIMER (Prehabilitation Intervention to Maximize Early Recovery) study leverages several such nudges to modify the environment of the study participants to facilitate physical activity. Specific to the physical activity goal, the study employs financial loss aversion (\$3 was deducted for each day the step goal was not met). Loss aversion nudges capitalize on the tendency of most individuals to prefer avoiding loss over making gain (ie, not losing \$3 is more attractive than gaining \$3). In addition, participants experience nudges via text message–based reminders and education via personalized diet and exercise recommendations, which target system 2 thinking. In fact, the study interventions focus on several of the most common influential forces driving human behavior as described in the MINDSPACE framework (Table 1).^[9]

Through their complex intervention, largely within the patient’s home, their early results show great promise. Participants found the interventions acceptable, with 93% adherence to wearing the fitness tracker and 51% adherence to step goals. Importantly, those receiving the intervention walked nearly 1000 steps more per day than controls at the end of the study period (after adjusting for baseline steps). The study is not without limitations. With only 20 patients in the intervention arm, the study has limited ability to show changes in clinical outcomes. Acceptability and adherence in larger, diverse cohorts remain to be seen. The costs of the program were significant, and, as the authors acknowledge, it remains to be seen who will bear these costs if moved to real-world practice. Finally, it remains unclear which of the components of the PRIMER interventions were truly beneficial. For example, it is possible that improved adherence to and achievement of step count goals were seen due to the incentivized weekly check-ins with trained staff who could actively address the barriers and provide motivation and support with less impact of daily reminders or step tracking.

Despite these limitations, the PRIMER study authors should be commended on testing novel health care interventions within the complex home environment and day-to-day journey of our patients. This study tackles two major barriers faced by patients pursuing liver transplant—frailty and behavioral change—and it is a step in the right direction to promote improved health in a scalable, sustainable way for our patients. Future studies can learn much from the lessons provided by the PRIMER study. Subsequent studies may also benefit from patient participation in the program design and agile implementation methodology to embed evidence-based nudges into clinical practice.^[10,11]

In conclusion, the management of chronic liver disease at all stages requires significant changes in an individual’s behavior. Thus far, there are few proven methods to successfully

promote behavioral change in the pretransplant setting. The PRIMER study provides the transplant hepatology community a nudge in the right direction.

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Abbreviations:

PRIMER study	Prehabilitation Intervention to Maximize Early Recovery study
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TABLE 1 MINDSPACE framework describes some of the most influential forces behind decision-making^[9]

Influence	Description	Example from PRIMER study
Messenger	We are heavily influenced by who is communicating information	Transplant team members advocating for physical activity
Incentives	Our responses to incentives are shaped by predictable mental shortcuts, such as the strong desire to avoid losses	Losing \$3 for not meeting step goal; losing \$9 for not completing phone check-in
Norms	We are heavily influenced by what others do	Being told physical activity is part of cirrhosis care
Defaults	We “go with the flow” of preset options	Participants received step-tracker and personalized physical activity recommendations, likely creating a default expectation of increased walking
Saliency	Our attention is drawn to novel things that seem relevant to us	Text-based reminders, weekly phone calls
Priming	Our actions are often influenced by subconscious cues	Participation in a study focused on physical activity likely impacted the subconscious of participants
Affect	Our actions can be powerfully shaped by our emotional associations	—
Commitments	We seek to be consistent with our public promises and to reciprocate actions	Signing informed consent to participate in a physical activity-based study
Ego	We act in ways that make us feel better about ourselves	Receiving congratulatory text messages for meeting goals