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Editorial: you bet your life – medication risk taking by gastroparesis patients in a hypothetical exercise

Two thirds of gastroparesis patients rate their health as fair to poor or are dissatisfied with available treatments, reflecting impaired quality of life (QOL).[1] Generic surveys (eg SF-36) quantify impact of health status on physical and mental activities and permit QOL comparisons with other disorders.[2] Disease-specific questionnaires (eg PAGI-QOL) query effects of food on functioning possibly offering more sensitive detection of reduced QOL.[2]

Such observations do not describe sacrifices patients make for better health. Risk taking is another component of QOL. Clinicians already know gastroparesis patients take risks when choosing therapies with possible irreversible or fatal consequences (eg metoclopramide, domperidone, gastric surgeries). Navas et al employed standard gamble methodology to quantify gastroparesis patients' acceptance of medication risks.[3] One hundred and three patients with moderate to severe symptoms stated they would accept a 13.4% risk of immediate death to ensure cure of gastroparesis with one dose of a hypothetical drug. Those with severe symptoms or psychosocial dysfunction were willing to assume greater risks. Nearly half expressed hopelessness their symptoms would ever resolve.

The standard gamble was described in 1953 to define the risk of death a person would accept to achieve perfect health when offered curative therapy.[4] Standard gambles define a value called utility that ranges from 0 (dead) to 1.0 (perfect health) (Figure 1). Conditions with bleak outcomes have lower utilities while chronic illnesses with little mortality risk score higher. In this study, willingness to accept a 13.4% mortality risk translates into a utility of 0.866 (1–0.134). Functional dyspepsia patients assume a similar 12.7% possibility of death—an expected finding given the overlap of functional dyspepsia with gastroparesis and the lack of impact of gastric emptying delays on QOL in diabetics with dyspeptic symptoms.[5,6] However, IBS patients accept a 1% mortality risk for immediate cure suggesting lesser QOL impairments than gastroparesis.[7]

Quantitative findings of standard gambles should not be overinterpreted. Binary standard gamble choices rarely mimic standard management options offered in clinical practice.[8] No medication cures gastroparesis in one dose and mortality from gastroparesis unrelated to comorbid illness is rare. Thus, absolute risk percentages based on artificial premises of this standard gamble might not reflect accurate risk considerations when traditional treatments are advocated. Study design factors known to influence standard gamble utility include changing risk wording from death to survival and modifying ordering of the survey mortality probabilities from a sequential profile as in this study to a "ping pong" pattern where risks of death from 0% to 100% are ordered randomly.[9,10]

These limitations do not diminish the importance of this study or conclusions of the willingness of gastroparesis patients to consider risks when making treatment decisions. These findings complement the emerging literature on QOL deficits in gastroparesis. One hopes

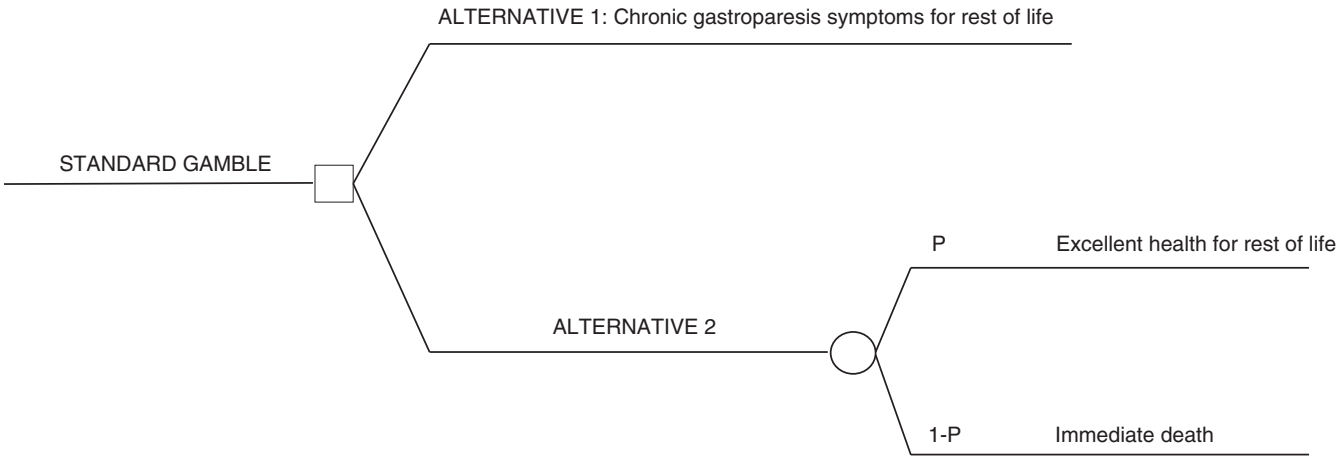

FIGURE 1 The standard gamble for the study [3] in gastroparesis is shown. A patient is offered a choice between alternative 1 (living the rest of his/her life with chronic stable gastroparesis symptoms) or alternative 2 (accepting a risk of "gambling" between excellent health for the rest of his/her life vs immediate death). The probability of excellent health (*P*) is varied until the patient is indifferent between the chronic gastroparesis health state and the gamble. Figure adapted from Reference [2]

that future studies will contrast standard gamble findings concurrently with other functional and motility disorders to clarify the extra illness burden assumed in gastroparesis and correlate standard gamble utilities with other QOL surveys to inform caregivers when considering treatments for refractory symptoms.

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Editorial: should we abandon HCV genotype testing? Maybe

Hepatitis C virus (HCV) genotype testing has been one of the mainstays of HCV management since the 1990s as it was the strongest predictor of treatment outcome with Interferon-based regimens, and was associated with the velocity of progression to cirrhosis if left untreated.[1,2] Its role was not diminished by the introduction of directly acting anti-virals (DAAs) as first- and second-generation DAAs were genotype specific in their activity and had different treatment schedules based on HCV genotype and subtype.[3] The availability of pan-genotypic DAA combinations however, calls for an evaluation of the need for HCV genotype testing before treatment initiation. The recent EASL guidelines eliminate HCV genotype testing only in the setting of resource-limited countries where a simplified treatment algorithm could increase access to treatment and favor HCV elimination.[4] Whether this recommendation should be extended to all treatment settings is still a matter of debate. In this scenario, the study by Mettikanont *et al*[5] is of relevance as it is the first systematic review to address the epidemiology and treatment options for genotype 6 infections. Genotype 6 (GT6) chronic hepatitis C virus infection accounts for less than 5% of the global prevalence of HCV and is particularly rare in western countries. However, it is responsible for a significant proportion of HCV infections in Asia where among the 1 000 000 HCV-infected patients, genotype 6 has a prevalence of 20%-50% in South-East Asia and Southern China respectively.[6] When looking at the efficacy of the pan-genotypic combinations of sofobuvir/velpatasvir (SOF/VEL) and glecaprevir/pibrentasvir (G/P), the SVR rates were 100% (135/135) and 99% (107/108) respectively. However, the efficacy was lower when analysing SVR rates obtained with sofosbuvir/ledipasvir (SOF/LDV), as a 64% SVR rate (25/39) was reported in a study conducted in Myanmar. Interestingly, the majority of the patients treated in Myanmar were infected by GT6c-i subtypes, whereas patients participating in studies conducted in other countries, where SVR rates to SOF/LDV reached the 95% rate, were infected mainly by GT6a.[7,8] Whether this finding is the consequence of the reduced activity of SOF/LDV in HCV-6, or on the other hand highlights a difficult to cure strain in HCV GT6c-I still needs to be elucidated. Similarly, a recent study by Fourati et al analysing HCV DAA failures in France, identified GT4r as a predictor of treatment failure due to frequent preexistence of both NS5A and NS5B S282 RASs. However, once again all but one of the analysed patients had failed SOF/LDV, making it impossible to