Health-related utility is a quantitative expression of individuals’ or societies’ preference for a particular state of health under the condition of uncertainty [1]. It is typically assessed on a scale of which 0 represents a state of being dead, and 1 represents full health. In cost-effectiveness analysis or clinical decision analysis, utility is commonly used to compute quality-adjusted survivals to measure the effectiveness of healthcare programs or medical interventions. Joint health-states utility represents the utility of individuals with a combination of several health conditions, for example, patients with both hypertension and diabetes. Predicting joint health-states utility has become an increasingly significant research topic due to the ageing of the general population and the increasing prevalence of comorbid conditions [2].

Strictly speaking, a state represents an individual at one point in time whereas a condition refers to a diagnosis. People with the same diagnosis may have different states while a person in a particular state may have multiple conditions. Practically, the methods of predicting utilities for joint conditions versus joint health-states are used interchangeably. In conformity with the literature [3, 4], we use the term “joint health-states” to represent scenarios that include joint conditions.

Utility catalogs for single health states or disease conditions have been developed at a population level and are readily available [5, 6]. As for the utilities for joint health-states, the off-the-shelf list is lacking. Direct sampling from the population is impractical due to the huge number of possible combinations of joint health-states or comorbid conditions. In practice, estimation of the joint health-states utility has primarily relied on several predictive models based on the single health-state utilities, while none were considered the gold standard.

MULTIPLICATIVE MODEL
Given its appealing simplicity, the multiplicative model (\(U_{ij} = U_i \times U_j\)) is probably the one most commonly used in clinical decision analysis. For example, if the utilities for hypertension and diabetes are 0.85 and 0.71, respectively, the joint health-states utility for individuals with both hypertension and diabetes would be estimated as 0.85 × 0.71 = 0.60 based on the multiplicative model.

The multiplicative model has been empirically examined using the preference-based scores derived from Health Utility Index Mark 3 within a Canadian community population [7]. The findings supported the use of the multiplicative model. Nevertheless, it is worth noting that an extra step of rescaling, or “purification” as referred to in the study, was applied. This step to achieve the purified utilities was conducted by dividing the observed utilities by the average utility of subjects who reported no disease conditions. Rescaling adjusts for health problems other than the disease conditions being studied, which may include loss of functional health attributable to unknown factors. However, a difficulty with rescaling in clinical decision analysis is that the utility of persons reporting no disease conditions may likely differ between a specified sample and the general population. That utility may also be unavailable for clinical investigators or decision analysts, which would render the rescaling approach inapplicable.

COMPARE MULTIPLICATIVE MODEL WITH SEVERAL OTHER MODELS
More recent research using United States samples identified that the multiplicative model is not the preferred method [3, 8]. Fu and Kattan examined the multiplicative model using the preference-based scores derived from EQ-5D (EuroQol) within a United States national representative community-dwelling sample [8]. Their results show that multiplying the two single condition utilities results in a numerically large and statistically significant difference from the utility of those subjects who actually had both conditions. Such a difference is larger than most of the other commonly used models regardless if rescaling is included or not. In their study, the multiplicative model was compared to several other models, which included minimum, additive, maximum, average, and the utility of the single condition with smaller prevalence [8]. Dale and his colleagues tested the multiplicative model and compared it with minimum and additive models using the time trade-off scores of patients from two university-based prostate biopsy clinics in the US [3]. They found that for prostate cancer patients, the multiplicative model is not preferred due to larger bias and less efficiency than the minimum model.

The minimum model \(U_{ij} = \min(U_i, U_j)\) is another common method of predicting joint health-states utility based on single-state utilities. For example, if the utilities for hypertension and diabetes are 0.85 and 0.71, respectively, the joint health-states utility for individuals with both hypertension and diabetes would be 0.71, based on the minimum model. Both aforementioned studies [3, 8] identified the minimum model as the preferred choice amongst the existing commonly used models, although it still cannot accurately predict the utility for joint health-states.

Reasons why the multiplicative model does not empirically work were discussed [8]. In reality, it is almost impossible for individual patients to report all their comorbid conditions during a questionnaire survey, in part, due to recall bias and disease under-diagnosis. Therefore, even though a list of conditions is reported for a certain individual, it does not suggest that such a list is comprehensive and exhaustive. Subsequently, when multiplying two utilities, researchers are likely using utilities of patients with more than one condition, and comorbid conditions are likely correlated. Thus, multiplying two utilities is, to some extent, double-counting, because not all patients have only one condition. A difficulty with any study in this context is the impossibility of being sure that a patient has no other conditions beyond those queried, and that those queried are measured without error. In other words, there is no strong reason to expect the inherent independence assumption in the joint health-states where the multiplicative model is assumed true.

OTHER METHODS FOR JOINT HEALTH-STATES UTILITY PREDICTION
An alternative approach is to estimate the joint health-states utility by regressing the empirical evidence on the single utilities or the joint health-states utilities estimated from some common nonparametric models. For example, one may use the following linear index model:

\[
    U_{ij} = \alpha_0 + \alpha_i \cdot U_i + \alpha_j \cdot U_j + \beta \cdot \min(U_i, U_j) + \beta_2 \cdot \text{Multiplicative}(U_i, U_j)
    + \beta_3 \cdot \text{Additive}(U_i, U_j)
\]  

where the a and b-coefficients shall be estimated from a large-sample dataset by using the least square method. If any of the a’s and b’s are not statistically significantly different from zero, the corresponding term can be omitted from the equation. A special case of Equation 1 has been used in applications with prostate cancer patient data, where a linear function of the single health-state utilities and the multiplicative joint health-states utility was applied [4]. The parametric models allow combining information from multiple utility measures, which may produce better estimates (e.g., smaller bias) than the nonparametric models.
Another special case of Equation 1 that appeared in the literature is the application of marginal disutility. For example, if the utility for asthma is 0.71 and the marginal disutility for hypertension is -0.03, the joint health-states utility for individuals with both hypertension and diabetes would be 0.71 + (-0.03) = 0.68 based on this model. The idea of marginal disutility associated with each condition is intuitively attractive. Using regression modeling, the marginal disutility of a certain disease condition is the utility difference between patients with and without that condition in the model. A series of related studies have been conducted to identify the marginal utilities for most of the common disease categories using the preference-based scores derived from EQ-5D within a United States national representative community-dwelling population [6, 9]. Additionally, the regression model can provide marginal utilities for not only each condition, but also other covariates that can be included in the model, such as age or gender.

A main disadvantage of the parametric methods, however, is that they would be sensitive to the model form, data source, and the individual health states or conditions, which prevent their popularity of use among clinical investigators. For example, the estimated α and b-coefficients in Equation 1 are likely different for the joint conditions of asthma and diabetes and the joint conditions of hypertension and heart disease. Even for the same group of joint health-states, different datasets could yield different estimates from a same model form. Additionally, it is arguable that a linear model may not be a good choice compared to some alternatives, such as the Tobit model, the censored least absolute deviations (CLAD) model [6, 9], the two-part model [10, 11], and the latent class model [12]. Overall, it is generally difficult to interpret joint health-states utility predicted from a parametric model for clinical investigators. Thus, they have not been commonly used in clinical decision analysis.

FUTURE DEVELOPMENTS
Parametric models may be refined when new patient utility data become available. The modeling is relatively flexible and, hence, can produce accurate predictions of joint health-states utilities. These predictions are limited to the particular available sample, for example, prostate cancer patients [4]. Different parametric models may have to be developed if the study focus switches to another population. Nonparametric models, conversely, are attractive for their simplicity, which is why they are popularly used among clinical investigators.

Rasch Models of Item Response in Health-Related Quality-of-Life (HRQoL) Instruments
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HRQOL CONSTRUCT
The health-related quality-of-life (HRQoL) construct has become increasingly important in health outcome assessment and in resource allocation decision-making [1]. For example, health indices based on the HRQoL construct provided the original basis for quality-adjusted life years (QALYs) [2]. Only later did QALYs gain a basis in decision theory [3].

Currently, widely used HRQoL instruments include the Quality of Well-Being (QWB) scale, Health Utility Indexes (HUI), short-form 6D (SF-6D) and the EuroQol EQ-5D [4]. These are all generic preference-based instruments designed to capture item response, weighted for preference in economic evaluations. While much attention has been devoted to preference-based weighing of HRQoL items, item endorsement underpins the HRQoL score for any respondent and has received less attention.

The underlying assumption of these measures is that fewer problems endorsed indicate better HRQoL. Therefore, when for one or more items, endorsement is not governed by changes in HRQoL, a HRQoL measure may become less sensitive in detecting treatment effects, or HRQoL differences. From a methodological standpoint, this can be problematic when one seeks to demonstrate HRQoL improvements with treatment or HRQoL disparities between groups. In this article, we discuss how to test this fundamental assumption using a Rasch model.

THE EQ-5D
The EQ-5D, a widely used HRQoL measure for clinical and economic evaluations [5], provides a good case for the study of item endorsement properties. From 2000 to 2003, the EQ-5D was included in the Medical Expenditure Panel Survey (MEPS), which is an annual U.S. national survey on health care use and expenditures using a representative sample of the non-institutionalized US civilian population conducted by the US Agency for Healthcare Research and Quality (AHRQ).

The EQ-5D consists of five three-leveled items classifying health in terms of...