

Original Research Article

Health Dynamics through Composite Index of Health Status

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Abstract: Background: Improved health is positively associated with economic benefits and improved societal Quality of life (QOL). Health can be measured by a composite index combining relevant dimensions and indicators pertaining to activities of daily living, physical and cognitive functions, emotional well-being, feelings, etc. This involves appropriate biomarkers, patient-reported questionnaires and performance-based scales giving rise to ratio scale data, count data, ordinal data and categorical confounders. **Method:** The paper transforms scores of biomarkers, item scores of scales to form normally distribution resulting in meaningful addition of ratio level data and ordinal data and derivation of an index reflecting overall health status (I_{Health}) which follows normal distribution, satisfies desired properties and facilitates assessment of changes over time, better evaluation of psychometric qualities. **Results:** Dimensions of I_{Health} can be ranked by $\frac{\text{Change in } I_{Health}}{\text{Unit change in a dimension}}$. Health dynamics is reflected by changes in I_{Health} of one patient or sample of patients across time along a disease continuum across categorical variables like gender, income, educational levels, stages of disease, etc. Normally distributed index can help to test equality across groups, using χ^2 –test. Computation of separate index is recommended for vulnerable groups like old aged citizens, postpartum women running the risk of maternal mortality, economically backward class, etc. **Conclusions:** The proposed index I_{Health_i} contributes to improve evaluation of tests and QOL, undertaking parametric analysis for better comparisons, stratification, and integration is recommended.

Keywords: Outcome measure, Ratio scale, Ordinal data, Normal distribution, Theoretical reliability, Factorial validity.

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INTRODUCTION

Improved health outcomes with reduced morbidity and disability positively influence human capital that drives job creation, increased productivity, higher female labour force participation (FLPR), broader economic benefits and improved societal well-being. Strategic investment of each dollar in health gives return of \$23 [1]. The World Bank has decided to support developing countries by providing affordable, quality health services to 1.5 billion people by 2030 for global economic development through IDA and IBRD financing. The complex dynamic relationship between economic growth and public health depends on (i) country's demographic stage, (ii) improvements of health at different stages affecting productivity, (iii) quality of the instrument and suggested policy approach integrating health considerations into economic strategies [2]. Sound Index of Health for a country or region facilitates such empirical relationships. The index needs to indicate physical, psychological, and social

well-being of citizens covering positive and negative health indicators like life expectancy, mortality rate, etc. and patient-reported outcomes (PROs) regarding functional status on health [3]. Importance of health has been identified in the Sustainable Development Goals like SDG-3, SDG-8 etc. for achieving economic growth and well-being. Researchers have identified health as one of the important factor influencing economic growth in the long run [4 – 7]. However, well defined index of Health status can help to relate public health and economic growth at national or regional levels.

Measurement of multidimensional concept of health combining relevant dimensions and indicators pertaining to physical and cognitive functions, emotional well-being, activities of daily living, feelings, etc. is problematic. One important objective of health care is to assess interactions of an individual or a group of individuals responding to treatments and interventions for a disease or condition and to measure progress with

time. This is achieved by use of appropriate biomarkers and treatment efficacy by standard tests or scales. While biomarkers play critical roles in diagnosis of patients and decide appropriate treatment plans influencing prognosis, and health status of patients receiving treatments for various diseases, scales and PROs are often used to find efficacy of treatment plans for patients suffering from chronic diseases resulting in disability in terms of cognitive impairments like memory loss, difficulty in information processing, poor executive functions, etc. [8]. Epidemiological studies (descriptive, analytic, and experimental) quantify rates of occurrence of disease, identify risk factors and develop effective measures for control in addition to tracking disease trends [9]. Health outcomes researches evaluate healthcare interventions and the outcomes, to promote quality of life (QOL) of patients and to guide health professionals, clinicians, and policy makers [10]. Synergy of biomarkers and clinical practices was discussed in depth by [11] who recommended rigorous testing with standardized assays, and reliability, validity, predicting values of biomarkers for better patient outcomes and progress.

Clinical set up considers among others, patient reported outcomes (PROs) from generic or disease specific questionnaires (ordinal scores), performance-based tools where patients are evaluated through different tasks and assign scores in ratio scale (time taken for completing a task) or count data like number of errors. Different types of PROs are being used for the same disease. For Myotonic Dystrophy type-1 (DM1), popular PROs are:

- Muscle impairment rating scale (MIRS) consisting of 5-point items measures 11 muscle groups to decide stages of DM1 and corresponding progress [12].
- Performance based outcome like Six-Minute Walk Test (6-MWT) (ability to walk longer distances); 10-meter Walk Test (short distance walking speed); chair-stand test for 30 seconds (30-sCST) (dynamic balance and strength of lower limbs); Nine-Hole Peg Test (9-HPT), etc. [13].
- Gait alterations in ambulant patients by severity indices *SI-1* and *SI-2* considering plot of time taken for negative- angles (plantar-flexion) as well as positive – angles (dorsi-flexion) and “narrow” time interval [14].

Choice of proper PROs are extremely important for better understanding of stages of diseases, progress if any, or development of infection, with passages of time [15].

Meaningful aggregation of data on biomarkers in ratio scale with ordinal scale data from questionnaires/scales and confounders in categorical scale is problematic due to different nature of data and unknown distributions of the variables. Distribution of

item scores are different for different forms of items like binary items (Yes-No type), k-point Likert items for $k=3,4,5,6$, etc. Aggregations without knowledge of distribution of item scores fail to facilitate parametric analysis for meaningful evaluation of patients and the chosen PROs [16]. Other methodological issues for categorical and ordinal data are non-satisfaction of equidistant property (construct/trait distance between levels are different) [17], non-admissibility of arithmetic averages [18-19] implying non-meaningful statistics like mean, variance, correlation, Cronbach α , etc. which may distort results of correlation-regression, Principal component analysis (PCA), Factor analysis (FA), etc. with ordinal scores. Test scores as sum of dimensions (or items) treating items and dimensions with equal importance fail to justify different values of correlations between items, item-total correlations and factor loadings or eigenvalues [20]. For independent dimensions or factors, addition is not meaningful. The manual of the 36-Item Short Form Health Survey questionnaire (SF-36) does not support overall score (<http://www.webcitation.org/6cfeefPkf>), since several independent factors are being measured as emerged from analysis like confirmatory factor analysis (CFA) [21]; factor analysis [22], structural equation model [23]. Mean, SD, reliability (Cronbach α), etc. increase with increase in number of items (scale length), number of levels per item (scale width) [24].

Usual criterion validity of multidimensional health status may not be relevant due to absence of a criterion showing specific, directly observable measure of health. To overcome this problem, factorial validity (FV) of multidimensional test defined as
$$\frac{\text{First eigenvalue } (\lambda_1)}{\text{Sum of all eigenvalues } (\sum \lambda_i)}$$
 was preferred [25] from single administration of the scale avoiding the problems of selection of criterion scale with similar factor structures. FV reflects validity of the main factor for which the test was developed. Similarly, reliability of multidimensional tools for health measures ignores theoretical definition of test reliability or even verification of assumptions of Cronbach alpha like tau-equivalence of the items implying unidimensional test, etc. However, alpha has been reported for scales with two or more independent factors. For example, Cronbach alpha = 0.92 was reported for two-factor solution of Repeatable Battery for Assessment of Neuropsychological Status (RBANS) with 12 sub-tests [26]. Battery reliability ($r_{tt\text{Battery}}$) $\neq$ average of reliability of sub-tests. Reliability (Cronbach alpha) for the battery of Wechsler adult intelligence scale–Fourth Edition (WAIS-IV) was 0.98 where alpha for the component scales ranged from 0.90 to 0.96 [27]. Avoiding assumptions of Cronbach alpha and complex McDonald's omega (ω), [28] proposed theoretical reliability ($r_{tt\text{Theoretical}}$) of a test by splitting the test into g -th and h -th subtests which are parallel, as

$$r_{tt-Theoretical} = \frac{\text{True score variance } (S_T^2)}{\text{Observed score variance } (S_X^2)} = 1 - \frac{S_E^2}{S_X^2} = 1 - \frac{\frac{1}{N}[\|X_g\|^2 + \|X_h\|^2 - 2\|X_g\|\|X_h\|\cos\theta_{gh}]}{NS_X^2} \quad \text{where } N:$$

sample size; $\|X_g\| = \sqrt{\sum_{i=1}^N X_{ig}^2}$ and $\|X_h\| = \sqrt{\sum_{i=1}^N X_{ih}^2}$

are the length of g -th and h -th sub-test vector, and $\cos\theta_{gh}$ is the cosine of the angle between the sub-test vectors. For a battery consisting of K -subscales, the authors derived battery reliability ($r_{tt\text{Battery}}$) as functions of sub-test reliabilities (r_{tti}) where battery score is the unweighted sum of sub-test scores.

The paper transforms scores of biomarkers, item scores of scales to follow normal distribution so as to make addition of ratio level data and ordinal data meaningful and derives indices reflecting overall health status (I_{Health}) for an individual and $\bar{I}_{Health}$ for a sample. Each index follows normal distributions and facilitate assessment of health dynamics by assessing changes over time and also better evaluation of reliability and validity.

LITERATURE SURVEY

Confounders are factors, which are not directly considered in research questions but can alter an outcome. In other words, if X : exposure, Y : outcome and Z : possible confounder, then if X is related with Z , and Y is related with Z but Z may not be caused due to X or Y or both. For example, observed difference on renal failure between the two groups of hypertension could be the result of the uncontrolled confounding variable called diabetes since diabetes may also affects kidney functions. Similarly, age is a confounder in association between smoking and lung cancer. Thus, consideration of all potential confounders associated with the outcomes other than the treatments need to be measured during study design [29]. Theoretically identified confounders need to be adjusted for irrespective of evidences derived empirically [30], but if a confounder affects both exposure and outcome, it should not be adjusted for.

Integrated algorithm was developed [31] based on decision tree model (a popular tool in machine learning) combining plasma based biomarkers and cognitive impairments along with categorical variables like *APOE* genotypes and key demographic variables for prediction of brain β -amyloid pathology. However, plasma biomarkers for diagnosis of Alzheimer's disease (AD) may be affected by factors like age, gender, family history, comorbidities, etc. [32]. Diagnosis of AD with blood based biomarkers needs to address challenges like pre-analytical and analytical harmonization and standardization. Moreover, decision tree approach split data into binary subsets based on the input variables and can introduce large change in the decision tree structure due to a small change in data by creating biased learned trees in case of dominating classes.

The Expanded Disability Status Scale (EDSS) scores reflecting brain functions for tracking progression of Multiple Sclerosis (MS), [33] suggested use of *EDSS_{Basal}* and *EDSS_{Modified}* scores from the Brief International Cognitive Assessment Scale (BICAMS) [34]. But, different distributions of *EDSS_{Basal}* and *EDSS_{Modified}* fail to compare their means by t -statistic which assumes normally distributed scores is not justified. Typically, distribution of EDSS score shows two modes. Number of MS relapses decreases as the patients register progress with time [35]. However, concepts of number of MS relapses and severity of relapse are different and relapses did not show reliable impact on progression on the EDSS [36]. Moreover, MS relapse was weakly or moderately associated with long-term disability [37].

Risks of cardiovascular disease (CVD) are often assessed involving questionnaires covering items on risk factors like age, gender, family history, lifestyle habits etc. (Categorical or Ordinal data) and laboratory based indicators like blood pressures, cholesterol (HDL, LDL, Total), body mass index (BMI); ventricular hypertrophy (both left and right); diabetes; triglycerides; new CVD-risk markers evaluated through Systematic Coronary Risk Evaluation (SCORE2), AHA Predicting Risk of CVD Events (PREVENT), lipoprotein(a) (Lp[a]) risk calculator, etc. (cardinal data in different units). Challenges remain on effective cardiovascular risk stratification and finding clinically meaningful risk thresholds for different age-groups across genders especially for pharmacotherapy of hypertension and hyperlipidemia. In addition, directions of the scales vary. Low score in Mini-Mental State Examination (MMSE) [38], Montreal Cognitive Assessment (MoCA) [39] indicate severity, the reverse is true for Activities of Daily Living (ADL) [40]. Most health outcome measures are influenced by different number of levels of variables which are categorical like gender, age, education, etc.

PROPOSED METHOD

Ensuring positive relationship of each item to the construct and assigning 1, 2, 3, 4, 5, etc. to the levels of items avoiding zero, [41] suggested to convert discrete ordinal score of i -th item to continuous equidistant scores (E_i) using weights ($W_{ij} > 0$) to j -th level of the i -th item.

E_i -scores were standardized as $Z_i = \frac{E_i - \bar{E}}{SD(E)} \sim N(0, 1)$ which were further transformed to proposed scores $\mathcal{P}_i = 99\left[\frac{Z_i - \text{Min}.Z_i}{\text{Max}.Z_i - \text{Min}.Z_i}\right] + 1$ where $1 \leq \mathcal{P}_i \leq 100$, irrespective of number of levels of items. Score of j -th dimension ($\mathbb{D}_j$) = $\sum \mathcal{P}_i$ and scale score ($\mathbb{S}_i$) is defined as $\sum \mathbb{D}_j = \sum \mathcal{P}_i$. Each of $\mathbb{D}_j$ and $\mathbb{S}_i$ follows Normal distribution. Variables measured in ratio scale like biomarkers, count data, Number of errors, time taken to complete tasks, etc. can be straight-away standardized to Z -scores and normally distributed $\mathcal{P}$ -scores. For the i -th patient, the index I_{Health_i} is sum of all corresponding $\mathbb{S}_i$'s of ordinal

scores and ratio scale scores. The index $\overline{I_{Health_i}}$ is the sample average of all I_{Health_i} 's. Parameters of normally distributed I_{Health_i} and $\overline{I_{Health}}$ can be estimated from the data.

Properties:

- I_{Health_i} combines meaningfully scores of biomarkers and several scale scores, even when formats of the scales differ. Each of the indices I_{Health_i} and $\overline{I_{Health}}$ is unit free and is differentiable. Can be computed separately for each region (say states and Union Territories (UTs) and different socio-economic-demographic groups. I_{Health_i} can be decomposed into $I_{Health_{pathological}}$ for pathological characteristics and $I_{Health_{Tests}}$ evaluating overall cognitive impairments through tests.

Benefits

- Relative importance (RI) of a dimension is given by $\frac{\text{Change in } \overline{I_{Health}}}{\text{Unit change in } i\text{-th Dimension}} \times 100$ showing how scores of an input dimension or a scale influences the index. IR helps to rank the dimensions of $\overline{I_{Health}}$. Similarly, IR of a factor/indicators assessed by $\frac{\text{Change in } \overline{I_{Health}}}{\text{Unit change in } i\text{-th indicator}} \times 100$ can also be used to rank them and decide priorities of Public health. RI is positively correlated with the conditional expectation $E(\overline{I_{Health}}|S_i)$ and can be estimated by regressing $\overline{I_{Health}}$ on S_i 's or on $\mathbb{D}_j$'s.

- Progress made by i -th patient in two consecutive time-periods can be evaluated by

$$\frac{I_{Health_i(t)} - I_{Health_i(t-1)}}{I_{Health_i(t-1)}} \times 100 \text{ and can be plotted}$$

across time to get Progress path. The progress also reflects how effective was the adopted treatment plans. Progress of $\overline{I_{Health}}$ can be assessed similarly. Progress will be significant in case of rejection of hypothesis

$$H_0: \frac{I_{Health_i(t)} - I_{Health_i(t-1)}}{I_{Health_i(t-1)}} = 0 \text{ or}$$

$$\frac{I_{Health(t-1)} - I_{Health(t)}}{I_{Health(t-1)}} = 0 \text{ by } \chi^2 \text{ test since ratio of}$$

two normally distributed variables $\sim \chi^2$ distribution.

- Point bi-serial (r_{pbs}) correlation between categorical variable (X) (say gender) and the continuous variable I_{Health_i} (Y) can be computed by $r_{pbs} =$

$$\frac{M_1 - M_0}{S_n} \sqrt{\frac{n_1 n_2}{n}}$$

where $M_1: \bar{Y}$ for the sub-group with $X=1$ (with sample size n_1)

$M_0: \bar{Y}$ for the sub-group with $X=0$ (with sample size n_2); $n = n_1 + n_2$

$$S_n = \sqrt{\frac{1}{n} \sum (Y_i - \bar{Y})^2} \text{ and } -1 \leq r_{pbs} \leq 1$$

- Significance of r_{pbs} can be tested using t-statistics

where $t = \frac{r_{pbs}}{\sqrt{\frac{n_1 - n_2 - 2}{1 - r_{pbs}^2}}}$ which follows t -distribution with $(n_1 - n_2 - 2)$ df.

- Normality of I_{Health_i} and $\overline{I_{Health}}$ facilitate:

Testing $H_0: \overline{I_{Health_{Group A}}} = \overline{I_{Health_{Group B}}}$ using cross-sectional data or $H_0:$

$$\overline{I_{Health_{Group A_{Time period t}}}} =$$

$\overline{I_{Health_{Group A_{Time period (t-1)}}}}$ using longitudinal data by t -ratios or ANOVA.

- Finding equivalent scores (x_0) for test-1 with probability density function (pdf) $f(x)$ and (y_0) for test-2 with pdf $g(y)$ by solving $\int_{-\infty}^{x_0} f(x) dx = \int_{-\infty}^{y_0} g(y) dy$, even if scales differ in formats or dimensions. Equivalent scores help to integrate tests by finding equivalent cut-off scores of two or more tests for the purpose of diagnosis and/or classification. [41] solved the equation using $N(0,1)$ table,

- Enables PCA and finding the eigenvalues and computing factorial validity (FV) of a multidimensional test as $\frac{\lambda_1}{\sum \lambda_i}$ from single

administration [25]. For a test containing m -number of standardized items, $FV_{Z-scores} = \frac{\lambda_1}{m}$, relationship

of Max. Cronbach's alpha (α_{PCA}) = $\left(\frac{m}{m-1}\right) \left(1 - \frac{1}{\lambda_1}\right)$ with FV was derived as $\alpha_{PCA} = \left(\frac{m}{m-1}\right) \left(1 - \frac{1}{FV \sum \lambda_i}\right)$ = $\left(\frac{m}{m-1}\right) \left(1 - \frac{1}{m \cdot FV_{Z-scores}}\right)$. [42]. Clearly,

higher $FV_{Z-scores}$ increases α_{PCA} .

- Normality of I_{Health_i} facilitates population estimates of Cronbach's alpha for the battery used to assess health status avoiding complex methods of [43].

- Possible to fit stepwise linear regression equation of I_{Health_i} on different chosen dimensions where ability of the i -th dimension in predicting I_{Health_i} is indicated by the regression coefficient β_i .

- Two-way Analysis of variance (ANOVA) of I_{Health_i} with a number of categorical variables with multiple levels helps to detect significant difference between groups, including effects at the cross-levels or third order cross-levels.

DISCUSSION

Following proposed steps to compute scale scores and I_{Health_i} , one can obtain normally distributed QOL_i score of the chosen QOL-tool, enabling finding of empirical relationship between I_{Health_i} and QOL_i . Normally distributed index can help to test equality across groups, using χ^2 -test. Computation of separate index is recommended for vulnerable groups like old aged citizens, postpartum women running the risk of maternal mortality, economically backward class, etc.

Each of the indices I_{Health_i} and $\overline{I_{Health}}$ is unit free, differentiable and can be computed separately for each region (say states and Union Territories) enabling ranking of the regions and different socio-economic-demographic groups. The index I_{Health} can be decomposed into $I_{HealthPathological}$ for pathological characteristics and $I_{HealthTests}$ evaluating overall cognitive impairments through tests. The sub-indices can be used for diagnosis, and deciding stages of disease and evaluation of progress.

The index I_{Health} considering cognitive impairments and pathological biomarkers may reflect the health dynamics by assessing changes in overall health status of one or a group of individuals along a disease continuum across categorical variables like gender, income, educational levels, stages of disease, etc.

Progress path based on longitudinal data may also help comparisons across regions over time with respect to I_{Health_i} and $\overline{I_{Health}}$ along with feasibility of statistical tests of significance or progress.

Max. Cronbach's alpha (α_{PCA}) and factorial validity of I_{Health} can be found in terms of eigenvalues and estimate theoretical reliability $r_{tt(theoretical)} = \frac{s_T^2}{s_X^2} = \frac{s_T^2}{\frac{\lambda_1 + 2 \sum_{i \neq j=1}^m Cov(X_i, X_j)}{FV}}$. High value of reliability implies rank robustness.

CONCLUSION

The proposed index I_{Health_i} contributes to improve scoring of tests and QOL tools and facilitating analysis under parametric set up for better comparisons, stratification, and integration. Economic indicators like GDP or per capita GDP or suitably chosen social indicators like Active participation in society [44], Comprehensive E-participation index (CEPI) [45], SDGs Index (SDGI) [46], etc. of a country can be regressed on the index $\overline{I_{Health}}$ at different years to see effect of health status on such socio-economic variables. Computation of separate index is recommended for vulnerable groups like old aged citizens, postpartum women running the risk of maternal mortality, economically backward class, nomadic, semi-nomadic and De-Notified tribes, sanitation workers, people with substance use disorder, people living in poverty-stricken areas; etc. Future empirical investigations may explore salient properties of proposed method and robustness of findings including psychometric properties.

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