Reference Data and Known-GroupsValidity of the EQ-5D-5L for Vietnam

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Abstract

Purpose

This study aims to provide EQ-5D-5L reference data of the general Vietnamese population and to test the EQ-5D-5L’ known-groups validity among people living with hypertension in Vietnam.

Methods

The EQ-5D-5L population norms were obtained via a representative sample from a general population of 1200 adults. Outcomes of the population norms were presented through five dimensions and five levels, EQ-VAS, and EQ-5D-5L indexes. Descriptive statistics of these outcomes were categorised by gender and age groups. Evidence of the known-groups validity was based on a sample of 577 non-hypertensive adults, 242 individuals with undiagnosed and 477 individuals with diagnosed hypertension. A hypothesis was formulated that people with worse health status would have lower EQ-VAS and EQ-5D-5L indexes.

Results

For the EQ-5D-5L population norms, 54.4% of the respondents reported having full health. The mean EQ-VAS and EQ-5D-5L indexes were 81.10 and 0.94, respectively. The EQ-VAS and EQ-5D-5L indexes were higher among males, people at younger ages, those with more education, a paid job, and single. The mean EQ-VAS and EQ-5D-5L indexes of people in the diagnosed hypertension group were statistically significantly lower than they were in the other two groups.

Conclusion

The EQ-5D-5L population norms were derived for the Vietnamese general population. The EQ-5D-5L can distinguish the quality-of-life differences among Vietnamese with hypertension.

Introduction

Vietnam’s life expectancy at birth has been increasing significantly in recent decades [1], yet simultaneously so has the prevalence of chronic illnesses [2]. For instance, the prevalence of people with hypertension among the general population aged 25–64 years was reported to increase from 15.3–20.3% in 2010 and 2015, respectively [3]. The characteristics of people living with such diseases varied among living conditions, sex, and economic status, which were clearly shown in the 2015 national survey on non-communicable disease factors [4]. Vietnam’s Ministry of Health (MOH) is upgrading the healthcare system to provide sufficient healthcare services for people living with long-term illnesses [5]. The MOH has enacted several targeted programmes to prevent non-communicable diseases; nevertheless, efficient measures to monitor and evaluate these programmes are still in need [2]. Intermediate outcomes (e.g. levels of systolic and diastolic blood pressure) and natural measures (e.g. number of deaths / or averted cases) are sometimes not adequate enough to evaluate the effectiveness of a healthcare intervention for people living with chronic illness [6]. For example, health interventions on hypertension may simultaneously exert effects on people with cardiovascular diseases [7]. Hence, multi-dimensional health outcomes are needed to identify the additional health benefits offered by such interventions [8]. A multi-dimensional health outcome, the health-related quality of life (HRQOL), is now getting more attention [6, 9]. The HRQOL, which has been commonly used to investigate the impact of health status on quality of life [10–12], can be described by many different health dimensions and at different levels achieved within each dimension [8]. Several measurement instruments attempt to describe HRQOL, but overall, it can be grouped into either disease specific measures – designed to measure the HRQOL of people with some specific health problems (e.g. EORTC QLC-C30 or EORTC-8D for cancer patients); or generic measures to describe HRQOL of any health status that can be represented by different health dimensions with their respective levels of achievement/severity (e.g. a profile-based measure: 36-Item Short Form Survey - SF-36; index-based measures: EQ-5D, SF-6D, Health Utility Index - HUI) [8]. The disease specific measures are customised according to disease’ characteristics, whereas the generic measures are responsive to overall HRQOL, and are more flexible in their use for comparisons across disease areas [8]. Therefore, utilising a generic measure for HRQOL estimations support consistent policy-making processes, and enable comparisons between the amount of health gained and lost within society [8].
Vietnam’s MOH has taken the first steps in making use of a generic measure for HRQOL in healthcare service's evaluations by enacting the national health technology assessment (HTA) guidelines and upgrading the health insurance benefit package with cost-effective drugs based on HTA evidence [13]. Those facts implied a demand to promote evidence-informed policymaking in the national healthcare system, initially in health insurance. According to the national guideline on HTA submissions, the measure of generic quality adjusted life years (QALY) is a suggested index in Vietnam. Health outcomes as HRQOL and/or QALY have also been requested by other countries when it comes to HTA [14–17].

The number of QALY(s) can be estimated by multiplying the number of years of life with the quality of life during those years [8]. Whilst years of life is an obvious indicator, quality of life can be represented by a generic index-based measure of HRQOL, under the term “utility”. This utility conventionally runs on a scale from 0 - representing “death” to 1 – which is “full health”. Several discussions on negative value of utility (for worse than death states of health) still generate controversy [8, 9]. Utilities are commonly measured by three instruments to quantify HRQOL, including EQ-5D; SF-6D, and HUI [8]. In Vietnam, EQ-5D-5L is currently the only instrument that can produce utility that is based on preferences of the general Vietnamese population [18]. Therefore, EQ-5D-5L has been suggested in the Vietnam's HTA guidelines. The EQ-5D-5L instrument includes five dimensional five-level questions, a visual analogue scale (EQ-VAS), and a value set which was tailored for the Vietnamese people [18]. The application of EQ-5D-5L can be included but not limited in QALY estimations. The instrument itself can reflect people's quality of life via their health status being reported by either the five dimension five-level questions, or the EQ VAS scores, or the health state’ values.

The EQ-5D-5L has already been suggested in the national HTA guidelines, yet there are still two big concerns regarding the instrument. The first one is that Vietnam needs reference data allowing utility comparisons between people with certain health conditions and the general population of the same age/gender. The reference data deriving from EQ-5D-5L is one of such utility reference data, and it is also referred to the name as "EQ-5D-5L population norm data" or "EQ-5D-5L population norms" [19]. The EQ-5D-5L population norms typically provide three outcomes, including the reference data of descriptive five dimensional five levels, EQ-VAS, and EQ-5D indexes. The EQ-5D-5L descriptive reference data is presented in percentages of the general population at each of five levels (from “no problems” to “unable to do/extreme problems”) on each of five health-related dimensions. The EQ-VAS reference data can often yield a table of mean(s)/median(s) EQ-VAS scores by age-sex groups, while the mean(s)/median(s) EQ-5D-5L indexes were derived from the national value set for the EQ-5D-5L indexes reference data [20]. The population norms using the EQ-5D-5L were developed globally, from Western countries [21–30] to Asian countries [31–37]. A hint of population norms using the EQ-5D-5L for the Vietnamese has been done elsewhere, but the study included an urban population only, and furthermore, used Thai preferences [37]. Since Vietnam has now had a country-specific value set, this is timely to develop the country-specific EQ-5D-5L population norms.

The second concern is whether EQ-5D-5L can be justified for use in Vietnam. Psychometric properties of the EQ-5D-5L have been proven in several countries and for several disease areas [38–48]. The instrument's reliability, which concerns stability in measuring people’s quality of life, can often be proven by the consistency of HRQOL results obtained through different measurement instruments [38–43], and/or by the repeatability by each time using the instrument [44–46]. Validation of the EQ-5D-5L was also tested via different construction validations, commonly including convergent and known-groups validation. The convergent validation was for strong correlations between postulated dimensions and other dimensions that should, in theory, be considered relevant [49]. Thus, correlations of the five dimensions (mobility, usual activities, self-care, pain/discomfort, and anxiety/depression) with other respective dimensions of other different instrument(s) are often evaluated for convergent validation purposes [46–48]. Meanwhile, the known-groups validation to evaluate the sensitiveness of the instrument is expected to yield distinctive results among different groups of patients [44, 47]. A study on the reliability and convergent validation of the EQ-5D-5L in Vietnam was conducted among HIV/AIDS patients [40], yet the construct validation among people with chronic diseases is still limited. To fill the research gaps, this study aims to provide (1) HRQOL reference data using EQ-5D-5L among the general population and (2) validity tests for the EQ-5D-5L instrument among people living with hypertension in Vietnam.

Methodology
Data was pooled from two separated studies. Data to derive the EQ-5D-5L population norms was taken from the Vietnam EQ-5D-5L valuation study which had been conducted in the general population in 2017 [18]. Due to the shortage in HRQOL data measured from different measurement instruments, the reliability and convergent validity tests were not included. The known-groups validity test was conducted using data from a hypertensive sample of the end-line survey of the "Evaluation of the Ho Chi Minh City Communities for Healthy Hearts" - CH2 project [50].

**Samples**

**The sample for developing EQ-5D-5L reference data**

From the EQ-5D-5L valuation study [18], a general population sample of 1200 adults was used to develop population norms. A multi-stage stratified cluster probabilistic quota-based sampling method was applied. The first stage was to determine an urban and a rural cluster from six provinces of six different geographical regions.

The next stage was to determine quotas for each cluster. The probabilistic quotas were developed based on the fractions of the population’s regions, residency, age groups (18–29 years, 30–44 years, 45–59 years, and 60 + years) and sex (male and female). Details of the sampling have been published elsewhere [18].

**The sample for validity testing of the EQ-5D-5L instrument.**

From the CH2 cohort study [50], a sample from the post-evaluation community survey was used for the known-groups validity of the EQ-5D-5L. The survey was conducted in eight districts of Ho Chi Minh City during 2019. A combination of multistage cluster random sampling techniques was employed to recruit 1296 CH2 participants whose age was 40 years old or above for the survey. The World Health Organization's classification for blood pressure levels to identify people living with hypertension are those with an average systolic blood pressure (SBP) of $\geq 140$ mmHg, and/or an average diastolic blood pressure (DBP) of $\geq 90$ mmHg [51]. Three groups were created based on participants’ hypertension-related status, which included 577 non-hypertensive individuals (SBP|DBP < 140|90 mmHg); 477 who had been clinically diagnosed with hypertension, and 242 individuals with undiagnosed hypertension (SBP|DBP $\geq$ 140|90 mmHg).

**The EQ-5D-5L instrument**

The EQ-5D-5L instrument included five questions and the EQ-VAS. The five questions represented five health dimensions on mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Respondents were asked to describe their current health status for each dimension by five levels of severity: (1) no problems, (2) slight problems, (3) moderate problems, (4) severe problems, and (5) unable to do/extreme problems. The EQ-VAS is a hash-marked scale ranging from 0 to 100, in which “0” indicates the worst imaginable health and “100” means the best imaginable health. The EQ-5D-5L indexes were calculated from the Vietnamese EQ-5D-5L value set [18].

**Data collection**

In both surveys, trained public health staff carried out face-to-face interviews. Participants were recruited using the door-to-door approach. Data used for developing the population norms were participant’s demographic characteristics and self-reported health statuses using the EQ-5D-5L. For the validation study, data of participants’ background; medical history on hypertension (including whether there were clinical diagnoses and comorbidities); health statuses reported via the EQ-5D-5L, and physical measurement outcomes such as height, weight, blood pressure were collected. Physical measurements were carried out by trained public health staff on all participants, with procedures adhering to guidelines of Vietnam’s MOH on general health check-up, the process of height/ weight/ blood pressure measurements, follow-up work after measurements, safety management, etc [52].

**Analysis**

Generally, differences on distributions of the five dimensions five levels among sub-groups were tested using Pearson chi-square tests. Even though the EQ-VAS and EQ-5D-5L indexes were not normally distributed for both samples, these sample sizes were,
however, large enough to assume normal distributions according to the central limit theorem [53]. Therefore, the differences of the EQ-VAS and EQ-5D-5L indexes among sub-groups were tested using either T-tests (applying to two-group categorical variables), or ANOVA tests (applying to homogenous variance and more-than-two-group categorical variables), or Kruscal Wallis H-Tests (applying to non-homogenous variance and more-than-two-group categorical variables). The Poc-hoc analysis to examine differences among multiple pairwise comparisons was performed using Bonferroni tests. A significance level of 0.05 was used for all statistical tests. Data was analysed using STATA version 14 software [54].

The EQ-5D-5L population norms

The EQ-5D-5L population norms were derived from the data given by the general population sample. Of which, the EQ-VAS and the five dimension questions were self-reported, and the EQ-5D-5L indexes were calculated using the Vietnam value set [18]. The analysis on EQ-5D-5L population norms followed the standardised method recommended by the EuroQol Group [20]. Descriptive statistics of the five dimensions five levels, EQ-VAS and EQ-5D-5L indexes were categorised into gender and age groups. Among these, percentages of answers for the five dimensions five levels were presented; EQ-VAS and EQ-5D-5L indexes were reported in means, standard deviations, ranges of min – max and interquartile, respectively. Differences of the EQ-5D-5L' outcomes were statistically tested.

Known-groups validation

As data was given from the CH2 project using only the EQ-5D-5L to measure people’s HRQOL, the known-groups validation was tested. The EQ-5D-5L indexes were computed based on the Vietnam value set [18]. Literature suggested that the presence of hypertension and comorbidities was associated with lower HRQOL [55–57]. Also, patients who were aware of their hypertension status reported a poorer quality of life [58, 59]. Hence, a hypothesis was formulated that, as the EQ-VAS and EQ-5D-5L indexes would be higher among non-hypertensive people, indicating better HRQOL, such indexes would be lower among those with hypertension. Correspondingly, people with undiagnosed hypertension would have better HRQOL than those of the hypertension-diagnosed group. In addition, HRQOL of hypertensive people was often suggested to be lower among females, people with more comorbidities, less education, older ages, and higher body mass indexes (BMI) [60, 61]. Statistical tests were performed to test the hypothesis and differences of EQ-VAS and EQ-5D-5L indexes regarding gender; age; education; marital status; BMI classifications, and number of comorbidities. The associations of these characteristics with the EQ-VAS and the EQ-5D-5L indexes were tested using a multivariate linear regression model among people living with clinical diagnoses for hypertension.

Results

The EQ-5D-5L population norms

Figure 1 shows characteristics of the general population sample. Overall, the sample distribution was similar among sub-groups of genders; age groups; geographic regions, and education levels. The present sample was most attributed to Kinh (major ethnicity) people, groups of individuals living in rural areas, married individuals, and those having a paid job. Socio-demographic characteristics of the present sample were inline with those of the national adult population. Nevertheless, the education level of participants and proportion of younger people in this sample were higher than the national average.

Table 1 shows the percentages self-reporting the five dimensions five levels by age groups of the general population sample. The percentage of participants that reported having full health was 54.4% and such indexes decreased by age. Respondents reported fewer problems in self-care and usual activities than the other dimensions. The number of individuals that reported having problems at higher levels increased for the subsequent age groups. People of the youngest age group (18–24 years) were shown to have slight problems in all five dimensions; and moderate problems with anxiety/depression (3.2%) and pain/discomfort (2.3%). People aged 25–64 years reported having from "slight" to “extreme problems” in all dimensions, while the worst problems were mainly in mobility, pain/discomfort, and anxiety/depression. Females seemed to have more problems than males in all age groups. The proportion of females reporting “no problems” in self-care (about 98%) and usual activities (about 95%) were similar for males, yet their reporting of “no problems” was slightly lower in mobility (88.9%; a 2.9% difference), and lower in
pain/discomfort (61.3%; a 8.8% difference), as well as anxiety/depression (77.7%; a 5.6% difference), respectively. Patterns of the five dimensions five levels for females and males in all age groups are in online resource 1.
| Dimension         | 18–24 | 25–34 | 35–44 | 45–54 | 55–64 | 65+  | Total |
|-------------------|-------|-------|-------|-------|-------|------|-------|
| **Mobility**      |       |       |       |       |       |      |       |
| No problems       | 98.2% | 95.9% | 93.2% | 83.4% | 81.0% | 68.8%| 90.4% |
| Slight problems   | 1.8%  | 4.1%  | 5.5%  | 15.0% | 16.8% | 26.0%| 8.5%  |
| Moderate problems | 0.4%  | 0.5%  | 1.5%  | 2.6%  | 0.5%  |      |       |
| Severe problems   | 0.8%  | 1.1%  | 0.7%  | 2.6%  | 0.6%  |      |       |
| Unable to walk    |       |       |       |       |       |      |       |
| Pearson chi2 (Pr) | 100.9 (0.00) |       |       |       |       |      |       |
| **Self-care**     |       |       |       |       |       |      |       |
| No problems       | 100%  | 99.4% | 98.7% | 97.9% | 94.9% | 94.8%| 98.3% |
| Slight problems   | 0.6%  | 0.4%  | 2.1%  | 5.1%  | 3.9%  | 1.4% |       |
| Moderate problems | 0.8%  | 1.3%  | 0.3%  |       |       |      |       |
| Severe problems   |       |       |       |       |       | 1.3% | 0.3%  |
| Unable to wash or dress | | | | | | | |
| Pearson chi2 (Pr) | 32.9 (0.00) |       |       |       |       |      |       |
| **Usual activities** | | | | | | | |
| No problems       | 98.6% | 96.2% | 95.3% | 95.2% | 92.0% | 88.3%| 95.3% |
| Slight problems   | 1.4%  | 3.8%  | 3.0%  | 4.8%  | 8.0%  | 10.4%| 4.3%  |
| Moderate problems | 1.7%  |       |       | 0.3%  |       |      |       |
| Severe problems   |       |       |       | 1.3%  | 0.1%  |      |       |
| Unable to do usual activities | | | | | | | |
| Pearson chi2 (Pr) | 48.7 (0.00) |       |       |       |       |      |       |
| **Pain/ Discomfort** | | | | | | | |
| No pain           | 76.4% | 78.0% | 65.4% | 49.2% | 52.6% | 45.4%| 65.7% |
| Slight pain       | 21.3% | 19.9% | 31.2% | 41.7% | 39.4% | 39.0%| 29.3% |
| Moderate pain     | 2.3%  | 2.1%  | 2.1%  | 6.4%  | 5.1%  | 15.6%| 4.0%  |
| Severe pain       | 1.3%  | 2.7%  | 2.9%  | 1.0%  |       |      |       |
| Extreme pain      |       |       |       |       |       |      |       |
| Pearson chi2 (Pr) | 113.2 (0.00) |       |       |       |       |      |       |
| **Anxiety/ Depression** | | | | | | | |
| Not anxious       | 76.4% | 83.5% | 80.2% | 82.9% | 75.9% | 80.5%| 80.3% |
| Slightly anxious  | 20.4% | 15.0% | 15.6% | 13.4% | 19.0% | 14.3%| 16.3% |
| Moderately anxious| 3.2%  | 0.6%  | 2.5%  | 2.1%  | 2.9%  | 5.2% | 2.3%  |
| Severely anxious  | 0.6%  | 1.3%  | 1.6%  | 2.2%  | 0.0%  | 0.9% |       |
| Extremely anxious | 0.3%  | 0.4%  | 0.0%  | 0.0%  | 0.0%  | 0.2% |       |
| Pearson chi2 (Pr) | 23.3 (0.27) |       |       |       |       |      |       |
Table 2 shows results of EQ-VAS and EQ-5D-5L indexes by sub-groups of the general population sample. Overall, the mean EQ-VAS and EQ-5D-5L indexes were 81.10 and 0.94, respectively. The mean EQ-VAS and EQ-5D-5L indexes were found to be 1.46 and 0.02 higher among males than among females (p-value 0.06 and 0.00), respectively. A significant reduction trend was observed in EQ-VAS and EQ-5D-5L indexes across people aged from 25 to 65+ years (p-value < 0.01). The EQ-VAS and EQ-5D-5L indexes, among people having an education level at high school or higher, or not being unemployed, or being single, were significantly higher than the other counterparts (p-value < 0.05). By geographical region, the EQ-VAS was shown to be statistically lower among people living in the Central Coast areas, in comparison with individuals in the Red River, South East, and Mekong River areas. Results of statistic tests on differences of EQ-VAS and EQ-5D-5L indexes of the general sample from the Poc-hoc analysis are presented in online resource 2.
|                          | EQ VAS                           | EQ-5D-5L                        |
|--------------------------|----------------------------------|--------------------------------|
|                          | Mean (SD)                        | Mean (SD)|
|                          | Min-Max; IQR                     | Min-Max; IQR|
|                          | p-value                          | p-value|
| **Total**                | 81.10 (13.35)                    | 0.94 (0.09) |
|                          | 10–100; 20                       | 0.29-1; 0.08 |
| **Gender***              |                                  | **0.00** |
| Female                   | 80.38 (13.70)                    | 0.93 (0.09) |
|                          | 10–100; 20                       | 0.29-1; 0.08 |
| Male                     | 81.84 (12.94)                    | 0.95 (0.08) |
|                          | 30–100; 11                       | 0.36-1; 0.08 |
| **Age group**            |                                  | **0.00** |
| 18–24                    | 83.96 (10.26)                    | 0.96 (0.06) |
|                          | 50–100; 10                       | 0.76-1; 0.08 |
| 25–34                    | 84.36 (11.04)                    | 0.96 (0.06) |
|                          | 40–100; 10                       | 0.68-1; 0.07 |
| 35–44                    | 81.75 (13.80)                    | 0.94 (0.09) |
|                          | 20–100; 15                       | 0.29-1; 0.08 |
| 45–54                    | 78.73 (13.69)                    | 0.92 (0.1) |
|                          | 50–100; 20                       | 0.56-1; 0.15 |
| 55–64                    | 74.82 (15.93)                    | 0.91 (0.11) |
|                          | 10–100; 15                       | 0.49-1; 0.15 |
| 65+                      | 73.36 (15.44)                    | 0.89 (0.12) |
|                          | 40–100; 10                       | 0.42-1; 0.15 |
| **Highest education**   |                                  | **0.00** |
| Primary and lower        | 77.67 (16.10)                    | 0.92 (0.12) |
|                          | 20–100; 20                       | 0.29-1; 0.08 |
| Secondary                | 79.84 (14.06)                    | 0.93 (0.09) |
|                          | 10–100; 20                       | 0.49-1; 0.08 |
| High school              | 82.56 (11.59)                    | 0.95 (0.07) |
|                          | 50–100; 10                       | 0.62-1; 0.08 |
| Undergraduate and higher | 83.43 (11.34)                    | 0.95 (0.06) |
|                          | 40–100; 10                       | 0.57-1; 0.08 |
| **Geographic regions**   |                                  | **0.26** |
| Northern mountains       | 80.10 (13.01)                    | 0.93 (0.10) |
|                          | 35–100; 20                       | 0.36-1; 0.13 |
| Red River delta          | 82.05 (11.79)                    | 0.95 (0.07) |
|                          | 40–100; 11                       | 0.67-1; 0.08 |
| Highlands                | 80.06 (13.08)                    | 0.94 (0.09) |
|                          | 50–100; 20                       | 0.49-1; 0.08 |
| Central Coast            | 77.80 (15.35)                    | 0.93 (0.11) |
|                          | 20–100; 20                       | 0.29-1; 0.08 |
| South-East               | 82.43 (11.89)                    | 0.95 (0.07) |
|                          | 50–100; 10                       | 0.57-1; 0.08 |
| Mekong river delta       | 83.43 (13.56)                    | 0.95 (0.08) |
|                          | 10–100; 10                       | 0.56-1; 0.08 |
| **Residence***           |                                  | **0.58** |
| Rural                    | 80.70 (13.63)                    | 0.94 (0.09) |
|                          | 20–100; 20                       | 0.29-1; 0.08 |
| Urban                    | 81.80 (12.82)                    | 0.94 (0.08) |
|                          | 10–100; 15                       | 0.49-1; 0.08 |
| **Ethnicity***           |                                  | **0.00** |
| Kinh (as majority)       | 81.24 (13.39)                    | 0.94 (0.08) |
|                          | 10–100; 20                       | 0.29-1; 0.08 |
| Others                   | 79.34 (12.86)                    | 0.92 (0.11) |
|                          | 40–100; 20                       | 0.36-1; 0.15 |
| **Religion***            |                                  | **0.80** |
| Having no religion       | 81.34 (13.23)                    | 0.94 (0.09) |
|                          | 10–100; 20                       | 0.29-1; 0.08 |

Notes: *Results from T-Tests. **Results from ANOVA tests (p-value < 0.00 for Bartlett's tests). IQR: interquartile range.
|                          | EQ VAS          |                          | EQ-5D-5L values                  |
|--------------------------|-----------------|--------------------------|----------------------------------|
|                          | Mean (SD)       | Min-Max; IQR             | p-value                          | Mean (SD) | Min-Max; IQR | p-value |
| **Having religion**      |                 |                          |                                  |           |              |        |
|                          | 80.11 (13.81)   | 30–100; 20               | 0.94 (0.09)                      | 0.56-1; 0.08 |            |        |
| **Marital status**       |                 |                          |                                  |           |              |        |
| Single                   | 83.47 (11.28)   | 50–100; 10               | **0.00**                         | 0.96 (0.06) | 0.68-1; 0.08 | **0.00** |
| Married                  | 80.70 (13.69)   | 10–100; 20               | 0.94 (0.09)                      | 0.29-1; 0.08 |            |        |
| Separated/Widowed/Divorced | 77.68 (14.70)   | 40–100; 20               | 0.91 (0.11)                      | 0.42-1; 0.15 |            |        |
| **Occupation**           |                 |                          |                                  |           |              |        |
| Having paid work         | 81.85 (12.88)   | 20–100; 15               | **0.00**                         | 0.95 (0.08) | 0.29-1; 0.08 | 0.06    |
| Student/Retired/Housewives | 79.93 (14.06)   | 10–100; 20               | 0.93 (0.09)                      | 0.56-1; 0.08 |            |        |
| Unemployed               | 69.26 (14.46)   | 40–90; 20                | 0.89 (0.16)                      | 0.42-1; 0.15 |            |        |
| **Having health insurance** |               |                          |                                  |           |              |        |
| No                       | 80.41 (13.72)   | 30–100; 20               | 0.32                             | 0.95 (0.08) | 0.57-1; 0.08 | **0.02** |
| Yes                      | 81.31 (13.23)   | 10–100; 20               | 0.94 (0.09)                      | 0.29-1; 0.08 |            |        |

**Notes:** *Results from T-Tests. **Results from ANOVA tests (p-value < 0.00 for Bartlett’s tests). IQR: interquartile range*

**Known-groups validation**

Table 3 shows CH2’ sample characteristics and its results on the EQ VAS, EQ-5D-5L indexes. Overall, demographic characteristics were similar among the non-hypertensive; diagnosed hypertension and undiagnosed hypertension groups. Nevertheless, characteristics of older age, higher rates of unemployment, and higher numbers of comorbidities, were more frequent among individuals living with hypertension both with and without a diagnosis, than those who were non-hypertensive. The percentage of “full health” self-reported by people living with hypertension (62.70%), was smaller than among those who were in the non-hypertensive and undiagnosed hypertension group (both at 71.90%). The mean EQ-VAS was found to be the highest in the undiagnosed hypertension group (76.95), followed by the non-hypertensive (76.65), and the diagnosed hypertension group (71.48). The mean EQ-5D-5L value showed a slight downward trend with the non-hypertensive (0.97), undiagnosed hypertension (0.96), and diagnosed hypertension groups (0.94), respectively. The mean EQ-VAS and EQ-5D-5L indexes of people in the diagnosed hypertension group were statistically significantly smaller than they were in the other two groups (p-value < 0.05). Results of EQ-VAS and EQ-5D-5L indexes were reported comparably between people from the non-hypertensive and undiagnosed hypertension group. Results of statistic tests on differences of EQ-VAS and EQ-5D-5L indexes of the CH2 sample from the Poc-hoc analysis are presented in online resource 3.
Table 3
EQ-VAS and EQ-5D-5L indexes by hypertensive groups.

|                              | Non-hypertensive group | Diagnosed with hypertension group | Un-diagnosed with hypertension group |
|------------------------------|------------------------|----------------------------------|--------------------------------------|
|                              | n (%)                  | VAS (mean; SD)                   | Value (mean; SD)                     | n (%)                  | VAS (mean; SD)                   | Value (mean; SD)                     | n (%)                  | VAS (mean; SD)                   | Value (mean; SD)                     |
| N                            | 577                    | 477                              | 242                                  |
| Reporting full health        | 415 (71.92)            | 299                              | 174 (71.90)                          |
| Age group                    |                        |                                  |                                      |                        |                                  |                                      |                        |                                  |                                      |
| 40–49                        | 268 (46.45)            | 77.39 (14.43)                    | 0.97 (0.06)                          | 88 (18.45)             | 75.52 (14.63)                    | 0.95 (0.11)                          | 92 (38.02)             | 75.48 (13.65)                    | 0.97 (0.07)                          |
| 50–59                        | 200 (34.66)            | 76.86 (14.47)                    | 0.96 (0.07)                          | 164 (34.38)            | 72.07 (17.55)                    | 0.94 (0.11)                          | 90 (37.19)             | 77.91 (12.93)                    | 0.96 (0.1)                          |
| 60+                          | 109 (18.89)            | 74.45 (14.39)                    | 0.97 (0.05)                          | 225 (47.17)            | 69.51 (16.11)                    | 0.93 (0.14)                          | 60 (24.79)             | 77.76 (17.03)                    | 0.97 (0.05)                          |
| p value**                    | 0.11                   | 0.08                             | 0.00                                 | 0.43                   | 0.29                             | 0.98                                 |
| Gender                       |                        |                                  |                                      |                        |                                  |                                      |                        |                                  |                                      |
| Male                         | 236 (40.90)            | 75.97 (13.69)                    | 0.98 (0.05)                          | 236 (40.90)            | 72.25 (16.21)                    | 0.95 (0.11)                          | 172 (71.07)            | 76.55 (14.7)                     | 0.97 (0.07)                          |
| Female                       | 341 (59.10)            | 77.12 (14.96)                    | 0.96 (0.07)                          | 341 (59.10)            | 70.73 (16.75)                    | 0.92 (0.14)                          | 70 (28.93)             | 77.9 (13.32)                     | 0.95 (0.1)                          |
| p value*                     | 0.35                   | 0.00                             | 0.32                                 | 0.03                   | 0.51                             | 0.14                                 |
| Marital status               |                        |                                  |                                      |                        |                                  |                                      |                        |                                  |                                      |
| Single                       | 30 (5.20)              | 75.97 (14.1)                     | 0.96 (0.06)                          | 22 (4.61)              | 69 (26.66)                       | 0.93 (0.12)                          | 10 (4.13)              | 80.8 (15.87)                     | 0.96 (0.06)                          |
| Married                      | 467 (80.94)            | 76.72 (14.16)                    | 0.97 (0.06)                          | 373 (78.20)            | 72.19 (15.71)                    | 0.94 (0.13)                          | 207 (85.54)            | 77.05 (14.42)                    | 0.97 (0.06)                          |
| Separate/divorce/widow      | 80 (13.86)             | 76.5 (16.33)                     | 0.96 (0.08)                          | 82 (17.19)             | 68.96 (16.34)                    | 0.93 (0.09)                          | 25 (10.33)             | 74.6 (12.74)                     | 0.91 (0.16)                          |
| p value**                    | 0.79                   | 0.90                             | 0.22                                 | 0.34                   | 0.48                             | 0.06                                 |
| Highest education            |                        |                                  |                                      |                        |                                  |                                      |                        |                                  |                                      |
| Primary and lower            | 246 (42.63)            | 76.09 (16.25)                    | 0.96 (0.07)                          | 210 (44.03)            | 69.72 (16.76)                    | 0.92 (0.14)                          | 106 (43.80)            | 78.06 (15.08)                    | 0.97 (0.09)                          |
| Secondary                    | 167 (28.94)            | 76.08 (12.77)                    | 0.97 (0.05)                          | 139 (29.14)            | 72.07 (17.18)                    | 0.95 (0.09)                          | 70 (28.93)             | 75.58 (12.73)                    | 0.97 (0.06)                          |
| High school and higher       | 164 (28.42)            | 78.07 (13.13)                    | 0.98 (0.05)                          | 128 (26.83)            | 73.72 (15.01)                    | 0.95 (0.12)                          | 66 (27.27)             | 76.63 (14.63)                    | 0.96 (0.07)                          |
| p value**                    | 0.45                   | 0.12                             | **0.05**                             | 0.24                   | 0.25                             | 0.44                                 |
| BMI                          |                        |                                  |                                      |                        |                                  |                                      |                        |                                  |                                      |
| <18.5 (underweight)         | 51 (8.84)              | 71.08 (14.88)                    | 0.96 (0.06)                          | 26 (5.45)              | 68.27 (14.14)                    | 0.95 (0.1)                          | 13 (5.37)              | 74.62 (13.46)                    | 0.98 (0.04)                          |

Notes: *Results from T-Tests. ** Results from ANOVA.
### Table 4

| 18.5–24.9 (normal) | Non-hypertensive group | Diagnosed with hypertension group | Un-diagnosed with hypertension group |
|---------------------|------------------------|-----------------------------------|--------------------------------------|
|                     | EQ VAS (mean; SD)      | EQ-5D-5L value (mean; SD)         |                                      |
| 421 (72.96)         | 76.79 (14.36)          | 71.63 (16.79)                     | 166 (68.60)                          |
| 76.79 (14.36)       | 71.63 (16.79)          | 0.94 (0.11)                       | 77.02 (15.08)                        |
| >25 (overweight/obesity) | 105 (18.20)           | 78.81 (14.08)                     | 63 (26.03)                           |
|                     | 78.81 (14.08)          | 71.74 (16.31)                     | 77.26 (12.37)                        |
| p value**           | 0.00                   | 0.58                              | 0.97                                 |
|                     | 0.41                   | 0.94                              | 0.91                                 |

**Occupation**

|                      | Unemployed             | Having a paid job                 |                                      |
|----------------------|------------------------|-----------------------------------|                                      |
|                      | EQ VAS (mean; SD)      | EQ-5D-5L value (mean; SD)         |                                      |
| 29 (5.03)            | 73.62 (15.11)          | 68.86 (18.96)                     | 72.76 (16.23)                        |
| 70 (14.68)           | 407 (85.32)            | 0.89 (0.18)                       | 0.95 (0.1)                           |
| p value*             | 0.25                   | 0.15                              | 0.09                                 |
|                      | 0.94                   | 0.00                              | 0.44                                 |

**Having comorbidity**

|                     | No                     | Yes                               |                                      |
|---------------------|------------------------|-----------------------------------|                                      |
|                      | EQ VAS (mean; SD)      | EQ-5D-5L value (mean; SD)         |                                      |
| 510 (88.39)          | 77.05 (14.28)          | 72.58 (15.36)                     | 77.72 (13.58)                        |
| 311 (65.20)          | 166 (34.80)            | 0.95 (0.11)                       | 0.97 (0.08)                          |
| p value*             | 0.07                   | 0.05                              | 0.01                                 |
|                      | 0.01                   | 0.00                              | 0.67                                 |

**Hypertension status**

|                      | EQ VAS (mean; SD)      | EQ-5D-5L value (mean; SD)         |                                      |
|----------------------|------------------------|-----------------------------------|                                      |
| Non-hypertensive     | 76.65 (14.45)          | 0.97 (0.06)                       |                                      |
| Un-diagnosed for hypertension | 76.95 (14.29) | 0.96 (0.08)                       |                                      |
| Diagnosed for hypertension | 71.48 (16.48) | 0.94 (0.12)                       |                                      |
| p value**            | 0.00                   | 0.00                              |                                      |

**Poc-hoc analysis for hypertensive groups**

|                      | Non-hypertensive (mean difference; p value) | Diagnosed for hypertension (mean difference; p value) | Non-hypertensive (mean difference; p value) | Diagnosed for hypertension (mean difference; p value) |
|----------------------|--------------------------------------------|------------------------------------------------------|--------------------------------------------|------------------------------------------------------|
| Diagnosed for hypertension | -5.00 (0.00)                              | -0.03 (0.00)                                        |                                            |                                                        |
| Undiagnosed for hypertension | 0.00 (1.00)                               | 5.00 (0.00)                                         | -0.00 (1.00)                              | 0.03 (0.00)                                          |

**Notes:** *Results from T-Tests. ** Results from ANOVA.

Table 4 shows associations between demographic factors and, respectively, the EQ-VAS and EQ-5D-5L indexes among the diagnosed hypertension group. A total of 472 people with a diagnosis for hypertension self-reported their health status via the EQ VAS. Statistics shows decrements in the EQ-VAS by higher age and number of comorbidities, whereas the factor of having completed high school and above was associated with a higher EQ-VAS. The EQ-5D-5L indexes were derived from answers from all 477 respondents in the diagnosed hypertension group. Associations for lower EQ-5D-5L indexes were found in people of older ages (β= -0.001; p-value = 0.019), females (β= -0.024; p-value = 0.048), people suffering from an incremental comorbidity (β= -0.013; p-value = 0.028), and measured obese people (β= -0.081; p-value = 0.007). An education level of having completed high school and above was associated with higher EQ-5D-5L indexes (β = 0.027; p-value = 0.049).
### Table 4
Factors associated with EQ VAS and EQ-5D-5L indexes, individuals diagnosed with hypertension

|                      | EQ VAS |                     |                     | EQ-5D-5L value |                     |                     |
|----------------------|--------|---------------------|---------------------|----------------|---------------------|---------------------|
|                      | Coeff. | P-value             | 95%CI               | Coeff.         | P-value             | 95%CI               |
| N                    | 472    |                     |                     | 477            |                     |                     |
| R-squared            | 0.050  |                     |                     | 0.060          |                     |                     |
| Age                  | -0.156 | **0.049**           | [-0.311; -0.001]    | -0.001         | **0.019**           | [-0.003; 0]         |
| Gender (Ref: Male)   |        |                     |                     |                |                     |                     |
| Female               | -1.199 | 0.462               | [-4.401; 2.004]     | -0.024         | **0.048**           | [-0.048; 0]         |
| Education (Ref: primary school) |       |                     |                     |                |                     |                     |
| Secondary school     | 1.522  | 0.405               | [-2.067; 5.112]     | 0.022          | 0.101               | [-0.004; 0.049]     |
| High school and higher | 3.868  | **0.036**           | [0.25; 7.487]       | 0.027          | **0.049**           | [0; 0.054]          |
| Relationship (Ref: Don't have partner) |       |                     |                     |                |                     |                     |
| Have partner         | 1.191  | 0.610               | [-2.667; 5.049]     | -0.018         | 0.219               | [-0.047; 0.011]     |
| Number of comorbidities | -2.462 | **0.002**           | [-3.991; -0.932]    | -0.013         | **0.028**           | [-0.024; -0.001]    |
| BMI (Ref: Normal from 18.5–24.9) |       |                     |                     |                |                     |                     |
| Underweight (BMI < 18.5) | -3.309 | 0.330               | [-9.979; 3.362]     | 0.005          | 0.832               | [-0.045; 0.055]     |
| Overweight (BMI from 25–29.9) | 0.235  | 0.891               | [-3.14; 3.61]       | -0.006         | 0.656               | [-0.031; 0.019]     |
| Obese (BMI > 30)     | -0.777 | 0.845               | [-8.6; 7.047]       | -0.081         | **0.007**           | [-0.14; -0.023]     |
| Constant             | 81.741 | 0.000               | [69.69; 93.793]     | 1.067          | 0.000               | [0.977; 1.157]      |

### Discussion

This study has provided the EQ-5D-5L reference data in Vietnam, which was presented with regards to age and gender for the descriptive part of the five dimensions five levels, EQ-VAS and EQ-5D-5L indexes. Additionally, this study demonstrated the validity of the EQ-5D-5L instrument among people living with hypertension. The EQ-5D-5L was shown to be responsive to changes in HRQOL among participants with less desirable health statuses.

A strength of this study’s EQ-5D-5L population norms was the neutral context sample. Responses were pooled across the country by geographical regions, gender, age, and residence settings. In a previous EQ-5D-5L population norms study, results were derived from the data of an urban population and EQ-5D-5L indexes were calculated using Thai value set [37]. However, EQ-5D-5L indexes in the present study were estimated using the Vietnamese preference-based value set. Additionally, the percentage reporting full health in the previous study was about 67.4%, which was 13% higher than the present study. Findings here of EQ-5D-5L population norms, therefore, could be perceived as more neutral context HRQOL reference data. The mean EQ-5D-5L value for Vietnamese adults was about 0.94, which was in line with the range of indexes across countries, from 0.89 in Poland [21] to 0.96 in China [31]. The present study shows the same pattern of the EQ-5D-5L reference data compared to the previous studies. For example, the EQ-5D-5L indexes were reported to be lower for females than males; or higher for people having an education from high school and higher. Such results have been similarly found in the previous Vietnamese EQ-5D-5L population norms study [37]; China [31]; Hong Kong [33]; Indonesia [34] and Spain [24]. The EQ-5D-5L indexes in this study showed a linear relationship with age for both genders. Nevertheless, the linear relationship was inconsistent for females, i.e., the mean EQ-5D-5L value was slightly lower among younger females aged 18–24 years than those in the age group of 25–34 years. The EQ-5D-5L population norms in Australia [23] and Hong Kong [33] also reported similar linear relationships between the EQ-5D-5L value and age. Moreover, results showed statistically significant differences of EQ-VAS across the six geographical regions, seemingly that
people from mountainous or poorer regions (e.g., the Central coast, the Highlands, the northern mountainous areas) were more likely to have smaller EQ-VAS and EQ-5D-5L indexes than the others. This may have implied a hint of inequity in people’s HRQOL overall, in examples regarding education status, residential areas, occupation, marital status, ethnicity, and more.

With respect to the known-groups validation, the EQ-5D-5L instrument was responsive in a way so that better HRQOL was more frequently reported by both people living with better health and people not being aware of their disease. The rates of people at full health, the EQ-VAS and EQ-5D-5L indexes, were similar between the two groups of non-hypertensive and undiagnosed hypertensive individuals, while such indicators were lower among those with diagnosed hypertension. Similar findings were also found in a study in Rio [62]. The presence of a clinical diagnosis for hypertension was statistically associated with 0.03 lower EQ-5D-5L indexes and 5 points lower for the EQ-VAS, which was in line with a similar study in China [61]. Moreover, the EQ-VAS and the EQ-5D-5L were proven to be higher among people who did not have any comorbidity, as in previous literature [56, 63].

Generally, the known-groups validity of the EQ-5D-5L instrument has been verified among Vietnamese living with hypertension. Whilst higher EQ-5D-5L indexes were associated with people who have completed college or higher; the lower EQ-5D-5L indexes were associated with older age; being female, having BMI classified as obese, and having more comorbidities among people diagnosed for hypertension. Such findings aligned with both international [55–62] and national [63–65] literature.

With respect to the use of EQ-5D-5L population norms as a reference to compare HRQOL, results found in this study appear to suggest that people with hypertension may have lower EQ-VAS points, but higher EQ-5D-5L indexes than the general population. In particular, the EQ-VAS among diagnosed and undiagnosed groups for hypertension were at 71.48 and 76.96, whereas the EQ-VAS among the general population at the same age (40 years and above) ranged from 73.36 to 78.73. For the EQ-5D-5L indexes, the range of the general population was from 0.89 to 0.92, whilst it was 0.96 among the hypertension-undiagnosed group, and 0.94 among the diagnosed group. The average HRQOL of non-hypertensive people from the CH2 project was also reported to be higher than that of the general population. However, the higher HRQOL of people from the CH2 cohort in comparison with the general population can be explained by the better living conditions of the CH2 population, as 95% of participants from the CH2 project had a paid job, and their residence had received more investment from the Head of the Ho Chi Minh City’s People Committee with several urban infrastructure and community-based healthcare interventions.

Conclusion

This study has provided EQ-5D-5L population norms for the general population and evidence for known-groups validity of the EQ-5D-5L instrument among hypertensive people in Vietnam. Findings from this study have addressed two main literature gaps in Vietnam, which were: (1) the population norms in context neutral HRQOL reference data; and (2) that EQ-5D-5L can distinguish the HRQOL differences between hypertensive people, undiagnosed-hypertensive people, and people with normal blood pressure status.

Declarations

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Conflicts of interest

The authors declare no conflicts of interest regarding the publication of this article.

Availability of data and material

Un-identified data is attached in online resource 4.

Code availability
Not applicable

Authors' contributions

Vu Quynh Mai: Conceptualisation; data collection and management, data analysis, manuscript writing and reviewing.

Hoang Van Minh: Conceptualisation, supervision, manuscript reviewing.

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Lars Lindholm: Supervision, manuscript reviewing.

Sun Sun: Conceptualization, manuscript reviewing.

Klas Goran Sahlen: Conceptualisation; supervision, manuscript reviewing.

Ethical approval

The study designs were considered and approved by the Ethical Review Board for Biomedical Research at the Hanoi University of Public Health (Identification number: 374/2017/YTCC-HD3 and 300/2019/YTCC-HD3).

Consent to participation

All individuals were introduced about the project (including rationale, objectives) and were explained about why they were invited, their rights in participation (voluntary participation, pause/stop at any time), confidentiality process (un-identified personal data, data storage); potential harms and benefits (to participants and the country) and data usage (for scientific purposes only, e.g. published reports, articles). Written consent forms were obtained from participants before the interviews and the consent forms are stored at the Hanoi University of Public Health.

Consent for publication

The authors declare no objection regarding the publication of this article.

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