Quality of Life of Adults With Congenital Heart Disease in 15 Countries

Evaluating Country-Specific Characteristics

Silke Apers, PhD,[a] Adrienne H. Kovacs, PhD,[b] Koen Luyckx, PhD,[c] Corina Thomet, MSc,[d] Werner Budts, MD, PhD,[e] Junko Enomoto, PhD,[f] Maayke A. Sluman, MD,[g] Jou-Kou Wang, MD, PhD,[h] Jamie L. Jackson, PhD,[i] Paul Khairy, MD, PhD,[j] Stephen C. Cook, MD,[k] Shanthi Chidambarathanu, MD,[l] Luis Alday, MD,[m] Katrine Eriksen, MSc,[n] Mikael Dellborg, MD, PhD,[o,p] Malin Berghammer, PhD,[o] Eva Mattsson, MD, PhD,[q] Andrew S. Mackie, MD,[r] Samuel Menahem, MD,[s] Maryanne Caruana, MD,[t] Gruschen Veldtman, MD,[u] Alexandra Soufi, MD,[v] Anitra W. Romfh, MD,[w] Kamila White, PhD,[x] Edward Callus, PhD,[y] Shelby Kutty, MD,[z] Steffen Fieuws, PhD,[aa] Philip Moons, PhD,[a,o] on behalf of the APPROACH-IS consortium and ISACHD

ABSTRACT

BACKGROUND Measuring quality of life (QOL) is fundamental to understanding the impact of disease and treatment on patients' lives.

OBJECTIVES This study aimed to explore QOL in an international sample of adults with congenital heart disease (CHD), the association between patient characteristics and QOL, and international variation in QOL and its relationship to country-specific characteristics.

METHODS We enrolled 4,028 adults with CHD from 15 countries. QOL was assessed using a linear analog scale (LAS) (0 to 100) and the Satisfaction with Life Scale (SWLS) (5 to 35). Patient characteristics included sex, age, marital status, educational level, employment status, CHD complexity, and patient-reported New York Heart Association (NYHA) functional class. Country-specific characteristics included general happiness and 6 cultural dimensions. Linear mixed models were applied.

RESULTS Median QOL was 80 on the LAS and 27 on the SWLS. Older age, lack of employment, no marriage history, and worse NYHA functional class were associated with lower QOL (p < 0.001). Patients from Australia had the highest QOL (LAS: 82) and patients from Japan the lowest (LAS: 72). Happiness scores and cultural dimensions were not associated with variation in QOL after adjustment for patient characteristics and explained only an additional 0.1% of the variance above and beyond patient characteristics (p = 0.56).

CONCLUSIONS This large-scale, international study found that overall QOL in adults with CHD was generally good. Variation in QOL was related to patient characteristics but not country-specific characteristics. Hence, patients at risk for poorer QOL can be identified using uniform criteria. General principles for designing interventions to improve QOL can be developed. (J Am Coll Cardiol 2016;67:2237–45) © 2016 by the American College of Cardiology Foundation.

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From the [a]KU Leuven, University of Leuven, Department of Public Health and Primary Care, Leuven, Belgium; [b]Peter Munk Cardiac Centre, University Health Network, University of Toronto, Toronto, Canada; [c]KU Leuven, University of Leuven, School of Psychology and Child and Adolescent Development, Leuven, Belgium; [d]University Hospital Bern, Center for Congenital Heart Disease, Bern, Switzerland; [e]KU Leuven, University of Leuven, University Hospitals Leuven, Division of Congenital and Structural Cardiology, Leuven, Belgium; [f]Department of Adult Congenital Heart Disease, Chiba Cardiovascular Center, Chiba, Japan; [g]Academic Medical Center, Department of Cardiology, Amsterdam, the Netherlands; [h]Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan; [i]Center for Biobehavioral Health, Nationwide Children's Hospital, Columbus, Ohio; [j]Adult Congenital Heart Center, Montreal Heart Institute, Université de Montréal, Montreal, Canada; [k]Adult Congenital Heart Disease Center, Heart Institute, Children's Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania; [l]Frontier Lifeline Hospital (Dr. K. M. Cherian Heart Foundation), Chennai, India; [m]Division of Cardiology, Hospital de Niños, Córdoba, Argentina; [n]Oslo University Hospital, Rikshospitalet, Oslo, Norway; [o]The Sahlgrenska Academy at University of Gothenburg, Institute of Medicine, Gothenburg, Sweden, and Centre for Person-Centred Care (GPCC), University of Gothenburg, Gothenburg, Sweden; [p]Adult Congenital Heart Unit, Sahlgrenska University Hospital/Östra and Institute for Medicine, The Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden; [q]Karolinska University Hospital, Stockholm, Sweden; [r]Stollery Children's Hospital, University of Alberta, Edmonton, Canada; [s]Monash Heart, Monash Medical Centre, Monash University, Melbourne, Australia; [t]Department of Cardiology, Mater Dei Hospital, Birkirkara Bypass, Malta; [u]Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; [v]Department

ABBREVIATIONS AND ACRONYMS

CHD = congenital heart disease

GLMM = general linear mixed model

IQR = interquartile range

LAS = linear analog scale

NYHA = New York Heart Association

PRO = patient-reported outcome

QOL = quality of life

SWLS = Satisfaction with Life Scale

Living well is as important to most people as living longer. Therefore, the concept of quality of life (QOL) has gained much attention in biomedical science over the past few decades (1,2). In this respect, comprehensive assessments of QOL and other patient-reported outcomes (PROs) have become indispensable (1-4). PROs are descriptions coming directly from patients about how they feel or function in relation to their health and well-being (5), and have been associated with important medical outcomes (6). Although the cardiology community recognizes that it is imperative to assess PROs to better understand the impact of health and disease, these outcomes remain underused in cardiovascular clinical trials (7). Moreover, many studies on PROs in the larger field of chronic diseases use poor-quality instruments (8).

In the cardiac subspecialty of congenital heart disease (CHD), QOL research commenced 40 years ago and has increased exponentially over time (9). To date, more than 230 QOL studies in CHD conducted in 35 countries have been published (9). However, a critical appraisal revealed that most articles on QOL had substantial conceptual and methodological deficits (9), yielding inconsistent results (10,11). Such inconsistencies may be attributable to differences in methodological approaches or to genuine differences in QOL between patients living in different countries (12). Furthermore, these studies investigated only demographic and/or medical predictors of QOL, leaving population measures or cultural dimensions unaddressed. It is reasonable to hypothesize that QOL scores among adults with CHD might be higher in countries known to have higher QOL in the general population (e.g., Denmark, Norway, or Switzerland). This possibility, however, has never been investigated.

To gain a better understanding of QOL in patients with CHD worldwide, it is critical to examine QOL in different countries using a uniform research methodology. This allows us to ascertain whether there are genuine differences in QOL in patients living in different countries, independent of methodological considerations. Furthermore, it enables us to evaluate whether country-specific characteristics explain QOL above and beyond patient characteristics. Therefore, the aims of this study were to: 1) describe QOL in a large international sample of adults with CHD; 2) investigate the association between QOL and patient characteristics (i.e., sociodemographic and medical variables); and 3) explore variation in QOL across countries and investigate the relationship between QOL and country characteristics (i.e., general population happiness and cultural dimensions).

METHODS

We established an international collaborative research group and undertook APPROACH-IS (Assessment of Patterns of Patient-Reported Outcomes in Adults with Congenital Heart disease – International Study). APPROACH-IS is a cross-sectional, multilevel study with a standardized protocol conducted in partnership with the International Society for Adult Congenital Heart Disease (12). Data were collected in 15 countries from 5 continents: Argentina, Australia, Belgium, Canada, France, India, Italy, Japan, Malta, Norway, Sweden, Switzerland, Taiwan, the Netherlands, and the United States. The study was approved by the institutional review board of the University Hospitals Leuven/KU Leuven Belgium (the coordinating center) and the local institutional review board of participating centers when required. All subjects provided written informed consent to participate. Detailed information on the rationale, design, and methods is available in a published methods paper (12).

STUDY POPULATION AND PROCEDURE. A questionnaire package was sent by surface mail or distributed in

of Congenital Heart Disease, Louis Pradel Hospital, Hospices civils de Lyon, Lyon, France; ʷStanford University, Department of Pediatrics and Medicine, Division of Pediatric Cardiology and Cardiovascular Medicine, Palo Alto, California; ˣWashington University and Barnes Jewish Heart & Vascular Center, University of Missouri, Saint Louis, Missouri; ʸDepartment of Pediatric Cardiology and Adult with Congenital Heart Defect, IRCCS Policlinico San Donato, Milan, Italy; ᶻUniversity of Nebraska Medical Center/Children's Hospital and Medical Center, Omaha, Nebraska; and the ᵃᵃKU Leuven, University of Leuven and Universiteit Hasselt, Interuniversity Institute for Biostatistics and Statistical Bioinformatics, Leuven, Belgium.

clinic to patients with CHD. Data collection ran from April 2013 to March 2015. Inclusion criteria were: 1) diagnosis of CHD, defined as a structural abnormality of the heart or intrathoracic great vessels that is present at birth and of actual or potential functional significance (13); 2) 18 years of age or older; 3) diagnosis established before adolescence; 4) continued follow-up at a CHD center or included in a national/regional registry; and 5) physical, cognitive, and language capabilities required to complete self-report questionnaires. Patients with prior heart transplantation or primary pulmonary hypertension were excluded (12).

QUALITY OF LIFE. Relying on thorough conceptual grounds (2), QOL was defined as "the degree of overall life satisfaction that is positively or negatively influenced by individuals' perception of certain aspects of life important to them, including matters both related and unrelated to health" (14). Using this conceptualization, QOL refers to a global perspective and is not limited to health-related factors. Consistent with this definition, 2 instruments to assess QOL were administered: a linear analog scale (LAS) and the Satisfaction with Life Scale (SWLS). A critical appraisal demonstrated that the use of these 2 instruments produced a more robust score than the use of other instruments (9).

The LAS is a vertically oriented line that ranges from 0 (worst imaginable QOL) to 100 (best imaginable QOL) (15). The LAS has well-established reliability and validity for adults with CHD (15) and it is used frequently in medical research (16,17).

The SWLS assesses a person's global judgment of life satisfaction and comprises 5 statements with a response scale ranging from 1 (strongly disagree) to 7 (strongly agree). A score of 20 represents the neutral point on the scale (18). The SWLS has good psychometric properties (15,19).

PATIENT- AND COUNTRY-SPECIFIC CHARACTERISTICS. Demographic data including sex, age, marital status, educational level, employment status, and patient-reported New York Heart Association (NYHA) functional class assessment were collected using a self-report questionnaire. The complexity of patients' heart defects (simple, moderate, or complex) was extracted from medical records (12).

Country-specific data on happiness (i.e., a population measure) were drawn from the World Happiness Report 2013 (20). This report presents national happiness levels based on surveys administered from 2010 through 2012 in 156 countries. More specifically, individual respondents in the World Happiness Report study were asked to evaluate their lives by imagining life as a ladder, with the best possible life

for them as a 10 and the worst possible life as a 0 (the Cantril ladder) (20).

Scores on the dimensions of national culture (scale from 0 to 100) were based on extensive research conducted by Hofstede in 76 countries and regions (21). This validated model includes 6 dimensions: a power distance index (higher scores reflect higher levels of acceptance that power is distributed unequally in society), individualism versus collectivism (high scores reflect individualistic societies), masculinity versus femininity (higher scores reflect more masculine societies directed toward achievement and success), uncertainty avoidance index (higher scores reflect societies that are more rigid in beliefs and behaviors), long-term orientation versus short-term normative orientation (thriftiness and perseverance are associated with higher scores), and indulgence versus restraint (higher scores are observed in societies that foster gratification of human drives related to enjoying life and having fun) (21). Scores on happiness and cultural dimensions per country are described in the Online Table 1.

STATISTICAL ANALYSES. Continuous data are presented as medians and interquartile ranges (IQR). Categorical variables are presented as absolute numbers and percentages. The association of patient- and country-specific characteristics with QOL was estimated through general linear mixed models (GLMM). A 2-level structure, in which patients were nested within countries, was assumed because differences between countries was the focus of this study. A 3-level model that considers within-country variations was not feasible computationally given the large number of countries with only 1 participating center. Empirical Bayes estimates with 95% confidence intervals for the country-specific QOL levels were obtained from the GLMM. A (pseudo) R^2 statistic referred to as R^2_{SAS} in Shtatland et al. (22) was derived from the model chi-square. This measure is an estimate of the percentage explained variance. When reported for the random country effect or for a set of fixed predictors, these are similar in spirit as the semipartial R^2 (but still approximations).

Linearity was verified for continuous predictors and no deviations were observed. Chi-square and Mann-Whitney U tests were used to compare variables between subjects with and without missing information (data on file). Given the relatively small proportion of patients with missing values, multiple imputation was not used to address missing values as this would unnecessarily complicate data analysis. Therefore, only patients for whom full data were available for all variables of interest (n = 3,777 or

93.8%) were included in the GLMM. Data analysis was performed using SAS software, version 9.2 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Overall, 4,028 adults with CHD were enrolled in the study. Characteristics of the total sample are detailed in Table 1. Patients had a median age of 32 years and 53% were women. The majority of patients had a white or Caucasian background, had a high school degree, worked part or full time, were married or living with a partner, and had no children. With regard to medical characteristics, 49% had CHD of moderate complexity and 54% reported they were in NYHA functional class I (asymptomatic). A detailed description of patient characteristics per country is provided in the Online Table 2 showing that, for example, 19% of patients came from the United States.

AIM 1: OVERALL QOL. For the total sample of participants who completed surveys (n = 3,952), the median QOL on the LAS was 80.0 (IQR: 70 to 90) on a scale ranging from 0 to 100. Figure 1 displays the distribution of QOL scores for this sample. There was large variability in QOL scores, with the majority of patients (91.2%) reporting a score of >50. More specifically, 25.8% of patients had a score between 71 and 80, 27.3% had a score between 81 and 90, and 17.4% had a score between 91 and 100 (Figure 1). The median QOL score on the SWLS was 27.0 (IQR: 22 to 30) on a scale from 5 to 35 (n = 3,892). Scores on the LAS and SWLS by country are provided in the Online Table 2.

AIM 2: ASSOCIATION WITH PATIENT CHARACTERISTICS. In multivariable GLMM analyses, older age; job seeking, being unemployed, or disabled; never having been married; and higher NYHA functional classes were associated with worse QOL (p < 0.001) (Table 2). Sex, educational level, and defect complexity were not associated with QOL. In all, 21.5% of variation in QOL was explained in the GLMM. Approximate estimates for the semipartial R^2 were 20.0% and 2.8% for patient characteristics and the country differences, respectively. A similar pattern of results emerged with regard to the association with QOL as measured by the SWLS. For reasons of clarity and to optimize readability, we report QOL for the LAS only for aims 2 and 3.

AIM 3: INTERNATIONAL VARIATION IN QOL AND ASSOCIATION WITH COUNTRY-SPECIFIC CHARACTERISTICS. Figure 1 represents between- and within-country variations in QOL as measured with the LAS. Countries are ranked in descending order of QOL

TABLE 1 Demographic and Medical Variables*		
	No. of Respondents	n (%)
Female	4,012	2,115 (52.7)
Median age, yrs	4,021	32.0 (IQR: 25-42)
Background	3,944	
Middle-Eastern or Arabic		52 (1.3)
Asian		781 (19.8)
Black or African-American		41 (1.0)
Hispanic or Latino		131 (3.3)
White or Caucasian		2,908 (73.7)
Other		31 (0.8)
Educational level	3,989	
Less than high school		223 (5.6)
High school		1,715 (43.0)
College degree		846 (21.2)
University degree		1,205 (30.2)
Employment status	4,005	
Part-time or full-time work		2,554 (63.7)
Homemaker or retired		331 (8.3)
Job seeking, unemployed, or disability		515 (12.9)
Full-time student		327 (8.2)
Other		278 (6.9)
Marital status	4,008	
Never married		1,753 (43.7)
Married or living with partner		2,045 (51.0)
Divorced or widowed		204 (5.1)
Other		6 (0.2)
Children (yes)	4,004	1,584 (39.6)
Patient-reported NYHA assessment	3,927	
Class I†		2,109 (53.7)
Class II		1,375 (35.0)
Class III		287 (7.3)
Class IV‡		156 (4.0)
Complexity of heart defect	4,028	
Simple		1,040 (25.8)
Moderate		1,957 (48.6)
Complex		1,031 (25.6)

Values are n (%) unless otherwise indicated. *Total population = 4,028. †Not limited during physical activities. ‡Unable to be physically active without experiencing discomfort.

IQR = interquartile range; NYHA = New York Heart Association functional class.

estimates. Australia had the highest QOL estimate (82.1) and Japan the lowest (71.6), representing a quite large gap of 10.5 points. In total, 4 countries had an estimate of ≥80, including Australia, Switzerland, the United States, and Malta. All other countries, with the exception of Japan, had an estimate of ≥75. Important intracountry variations were observed (Figure 1). Scores between 61 and 100 occurred frequently in all countries (darker shades of blue), whereas scores between 0 and 60 occurred in ≤10% of patients for the majority of countries (lighter shades of blue). These results depict how intercountry variation in QOL was relatively minor compared with intracountry variation in QOL.

FIGURE 1 QOL in Adults with Congenital Heart Disease

Country	Linear Analog Scale Quality of Life										EB estimate quality of life (95%CI)
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	91-100	
Australia	0.0%	0.0%	0.0%	3.0%	3.0%	1.5%	12.9%	20.5%	33.3%	25.8%	82.1 (79.6;84.6)
Switzerland	0.0%	0.4%	0.4%	2.2%	4.4%	6.6%	11.0%	16.9%	31.6%	26.5%	81.4 (79.5;83.2)
USA	0.1%	1.1%	1.5%	1.9%	4.8%	3.7%	10.5%	22.5%	28.2%	25.7%	80.4 (79.3;81.6)
Malta	0.0%	0.9%	0.0%	0.0%	4.3%	5.1%	11.1%	32.5%	34.2%	12.0%	80.1 (77.5;82.8)
the Netherlands	0.4%	0.0%	0.8%	0.4%	0.4%	2.4%	17.3%	37.3%	28.5%	12.4%	79.9 (78.0;81.8)
Sweden	0.9%	0.9%	1.5%	2.6%	3.1%	4.6%	12.6%	20.9%	29.2%	23.7%	79.4 (78.0;80.9)
Argentina	1.2%	0.0%	0.6%	0.0%	3.5%	6.4%	15.0%	30.1%	35.3%	8.1%	79.3 (77.1;81.6)
Italy	0.0%	0.0%	0.0%	3.2%	6.3%	3.2%	12.7%	30.2%	30.2%	14.3%	79.2 (75.9;82.5)
France	0.0%	0.0%	0.0%	2.1%	6.3%	5.3%	17.9%	25.3%	25.3%	17.9%	78.6 (75.8;81.5)
Belgium	0.0%	0.7%	1.1%	1.5%	4.4%	5.5%	16.5%	33.5%	28.3%	8.5%	77.0 (75.2;78.9)
India	1.5%	0.0%	1.0%	2.5%	6.1%	10.6%	19.2%	21.2%	17.7%	20.2%	76.9 (74.8;79.0)
Norway	0.0%	1.2%	1.2%	4.0%	5.2%	6.4%	16.8%	24.3%	23.7%	17.3%	76.9 (74.6;79.1)
Canada	0.8%	0.2%	1.4%	1.6%	4.3%	8.4%	19.9%	28.3%	23.8%	11.5%	76.1 (74.7;77.5)
Taiwan	0.0%	0.4%	1.6%	0.8%	6.8%	9.6%	18.1%	31.3%	24.9%	6.4%	75.6 (73.7;77.5)
Japan	1.6%	2.4%	4.0%	4.0%	8.3%	7.1%	15.4%	24.1%	21.3%	11.9%	71.6 (69.7;73.5)
											Median quality of life (IQR)
Total Sample	0.5%	0.7%	1.3%	1.9%	4.6%	5.8%	14.9%	25.8%	27.3%	17.4%	80.0 (70-90)

In this heat map showing distribution of quality of life (QOL), countries are ranked in descending order of QOL estimates. These Empirical Bayes (EB) estimates are derived from the general linear mixed model without adjustment for patient and country-specific characteristics; based on the linear analog scale for QOL. **Darker shades of blue** represent more frequent scores as compared with **lighter shades of blue**. CI = confidence interval; IQR = interquartile range.

A weak positive relationship between national happiness levels and QOL was suggested (**Central Illustration**). Univariable analyses showed that this relationship was not significant (p = 0.0624) (**Table 3**). For example, India had the lowest score in terms of happiness from all participating countries, but this did not correspond with its ranking in terms of QOL estimates (**Central Illustration**). Similar figures demonstrate weak relationships between QOL and cultural dimensions (Online Figures 1 to 6). Univariable analyses demonstrated that these relationships were nonsignificant (**Table 3**). Adjusted for patient characteristics, the multivariable GLMM analyses showed that happiness (p = 0.5563) and cultural dimensions (p = 0.5552) were not associated with variation in QOL (**Table 3**). Indeed, adding happiness and cultural dimensions only increased the explained variance by 0.1% (21.6% vs. 21.5%).

DISCUSSION

APPROACH-IS investigated QOL in adults with CHD in 15 countries on 5 continents using a uniform approach that included patient- and country-specific characteristics. We found that QOL was generally good with a median score of 80 on the LAS (range: 0 to 100) and a median score of 27 on the SWLS (range: 5 to 35). Nonetheless, nearly 1 in 10 patients had a QOL of ≤50 on the LAS. These findings indicate that, as a group, adults with CHD are generally satisfied with their lives; however, a subset of patients experience impaired QOL. Given the association between PROs, such as QOL, and important medical outcomes (6,23), it is of paramount importance that health care professionals identify patients with poor QOL and target interventions accordingly.

Patient characteristics linked with poorer QOL are older age; job seeking, being unemployed, or disabled; never having been married; and poorer NYHA functional class. Knowledge of these patient characteristics may assist providers in identifying patients at risk for decreased QOL. However, these patient characteristics explained a relatively small proportion of the variability in QOL (<20%). Future challenges include identifying other influential factors. Sex, educational level, and defect complexity were not related to QOL, indicating that symptoms experienced by patients (i.e., patient-reported NYHA

TABLE 2   Patient Characteristics as QOL Predictors*

	Univariable Models		Multivariable Model†	
	Estimate (SE)	p Value	Estimate (SE)	p Value
Sex		0.0156		0.1938
Men	1.3 (0.5)		0.6 (0.5)	
Women	#		#	
Age	-0.1 (0.02)	<0.001	-0.1 (0.03)	<0.001
Educational level		<0.001		0.7482
Less than high school	-7.1 (1.2)	<0.001	-1.1 (1.2)	0.3443
High school	-2.9 (0.6)	<0.001	0.1 (0.6)	0.8471
College degree	-0.8 (0.8)	0.3195	-0.1 (0.7)	0.8440
University degree	#		#	
Employment status		<0.001		<0.001
Part-time or full-time work	-1.2 (1.03)	0.2346	#	
Homemaker or retired	-5.6 (1.3)	<0.001	-0.4 (1.0)	0.7284
Job seeking, unemployed, or disability	-14.8 (1.2)	<0.001	-7.5 (0.8)	<0.001
Full-time student	-1.6 (1.3)	0.2186	0.1 (1.0)	0.9374
Other	#		2.0 (1.0)	0.0411
Marital status		0.0002		<0.001
Never married	-7.1 (6.7)	0.2921	-2.6 (0.6)	<0.001
Married or living with partner	-5.5 (6.7)	0.4141	#	
Divorced or widowed	-10.0 (6.8)	0.1430	1.6 (1.1)	0.1698
Other	#		0.01 (7.4)	0.9986
Patient-reported NYHA assessment		<0.001		<0.001
Class I‡	27.9 (1.3)	<0.001	24.1 (1.3)	<0.001
Class II	20.9 (1.3)	<0.001	17.9 (1.3)	<0.001
Class III	10.3 (1.5)	<0.001	9.6 (1.5)	<0.001
Class IV§	#		#	
Disease complexity		0.0001		0.9685
Simple	3.0 (0.8)	<0.001	-0.2 (0.7)	0.8241
Moderate	2.3 (0.6)	0.0005	-0.02 (0.6)	0.9682
Complex	#		#	

*Results from general linear mixed models (GLMMs) with patient characteristics as predictors for quality of life (QOL) using the linear analog scale (LAS) in adults with congenital heart disease (n = 3,777). †Total explained variability derived from the chi-square statistic: 21.5%. Random country effect: chi-square = 106.2 (p < 0.001); explained variability by country derived from the chi-square statistic: 2.8%. Results based on the LAS for QOL. ‡Not limited during physical activities. §Unable to be physically active without experiencing discomfort. #Reference category.

Abbreviations as in **Table 1**.

>10-point difference in adjusted QOL for countries at either end of the spectrum (i.e., Australia and Japan) suggests that further investigation of explanatory factors is warranted (e.g., workload, income, perceptions of people with chronic illnesses, response patterns, and willingness to endorse poorer QOL on surveys).

Investigating the potential impact of country-specific characteristics represents a new approach in clinical QOL research, reflecting an important addition to the assessment of patient-related factors. Indeed, most studies on QOL are oriented toward demographic and/or medical variables (11) and neglect population measures, although QOL is also shaped by cultural characteristics (27). Prior studies in nonmedical populations have shown that culture can influence how individuals report their life satisfaction (27,28). Japanese and Taiwanese students, for example, were less likely to use extremes of a life satisfaction response scale as compared with American students (29). This phenomenon was not observed in the present study, as shown in the heat map (**Figure 1**). Against our expectations, national happiness level and cultural dimensions were not associated with QOL variation in the present study, after adjustment for patient characteristics. This implied that adults with CHD at risk for poor QOL can be identified using the same criteria, irrespective of their country of residence. Furthermore, general principles can be developed to design interventions to improve QOL. Nonetheless, future work should examine other country-specific characteristics that may account for variation in QOL between nations, such as health care system factors like access to care (30,31).

STUDY LIMITATIONS. This study had extensive power because of the large sample size. Indeed, no previous survey on QOL in CHD had incorporated more than 4,000 patients and encompassed 5 continents. The number of missing values on all variables of interest was low (data on file), which minimized the potential impact of missing data on obtained results. Third, measurement of QOL was based on a solid conceptualization, which was lacking in several previous studies (8,9). The LAS and the SWLS were utilized to assess QOL. These instruments have been used previously in different countries and their use was associated with higher quality scores (9). Although we only reported results on inferential statistics with regard to the LAS, an analogous pattern of results emerged for the SWLS. Hence, our conclusions are based on a single-item QOL measure, but can be extended to the multiple-item SWLS. Indeed, prior

assessment) were more important contributory factors to QOL than defect complexity. On an international scale, these results confirmed earlier findings that QOL is related marginally to the severity of the heart defect (objective criterion) and more strongly correlated with illness perceptions and appraisal of functional status (subjective criteria) (14,24,25). Therefore, patients with complex CHD might report a good QOL, particularly if they do not experience functional impediments or symptoms on a day-to-day basis (26).
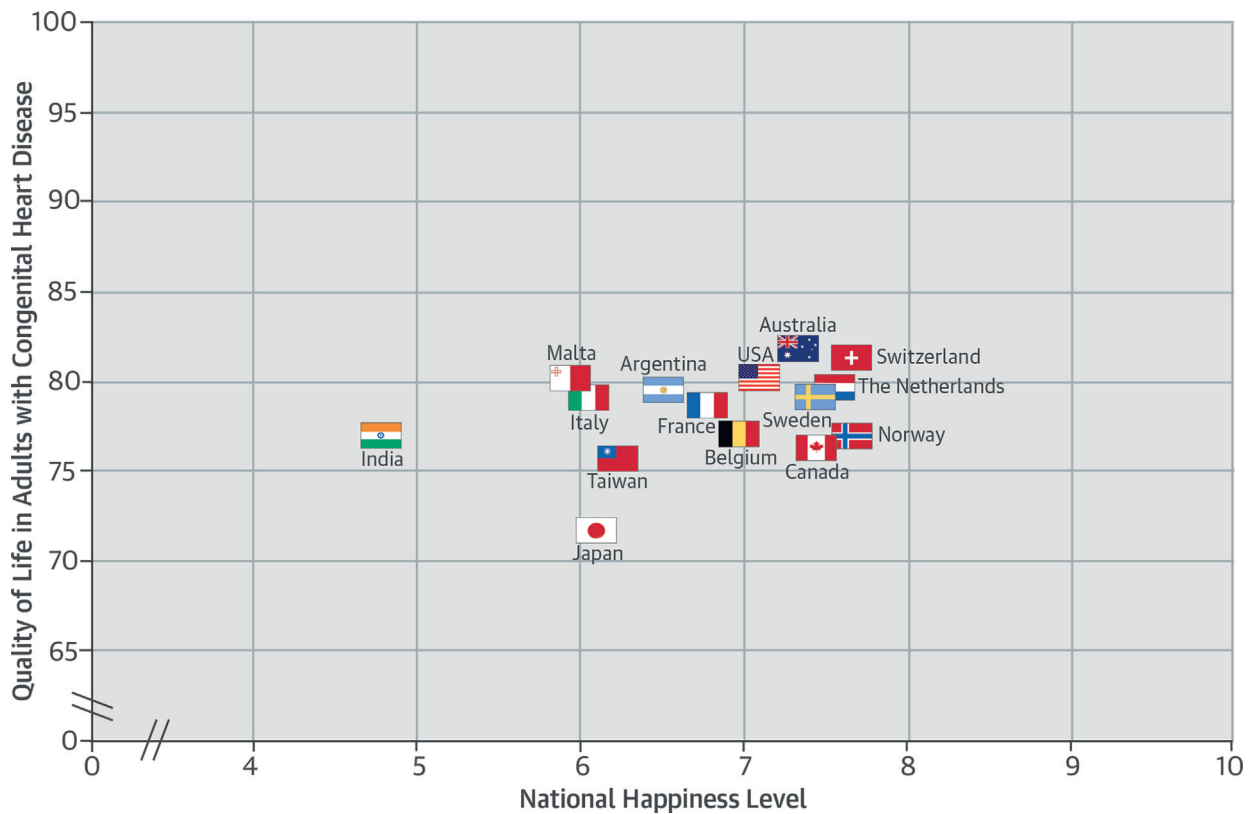
Findings from our study demonstrated that QOL in adults with CHD varied across countries. This international variation in QOL remained after adjustment for patient- and country-specific characteristics. Although a few points separated most countries, a

CENTRAL ILLUSTRATION QOL and National Happiness Levels per Country

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In this study, quality of life (QOL) in adults with congenital heart disease was estimated using empirical Bayes estimates derived from the general linear mixed model without adjusting for patient and country-specific characteristics and are based on the linear analog scale for QOL. When compared with the national happiness levels based on the World Happiness Report 2013, a weak positive relationship was suggested between the 2, although the relationship was not statistically significant.

research showed that single-item life satisfaction measures perform similarly compared with a multiple item instrument (32).

For most participating countries, data from only 1 center were available. Although some participating centers are national reference centers accommodating patients from all over the country, this might hamper the representativeness. As a result, it was not possible to distinguish between variations between centers and countries. Second, we did not collect data on QOL from a control group. Future studies should explore differences between QOL in patients and controls from an international perspective. Indeed, it might be possible that differences between patients and controls in the respective countries are mainly due to the variation in QOL in the general population, rather than in the patient group. It is possible that selection bias could affect the results. Because of the

TABLE 3 Country-Specific Characteristics as Additional QOL Predictors*

	Univariable Models		Multivariable Model†	
	Estimate (SE)	p Value	Estimate (SE)	p Value
National happiness levels‡ (0–10)	0.5 (1.0)	0.0624	1.2 (2.1)	0.5563
Cultural dimensions§ (0–100)				0.5552‖
Power distance index	-0.03 (0.1)	0.5513	0.1 (0.1)	0.5636
Individualism vs. collectivism	0.01 (0.04)	0.7928	-0.1 (0.1)	0.3385
Masculinity vs. femininity	-0.02 (0.03)	0.5611	-0.004 (0.03)	0.9052
Uncertainty avoidance index	-0.01 (0.04)	0.7032	-0.01 (0.04)	0.7367
Long-term orientation vs. short-term normative orientation	-0.05 (0.03)	0.0914	-0.1 (0.04)	0.0306
Indulgence vs. restraint	0.04 (0.05)	0.4232	-0.02 (0.1)	0.8218

*Results from GLMMs with country-specific characteristics as additional QOL predictors (LAS) in adults with congenital heart disease (n = 3,777). †The multivariable model also contains all patient characteristics included in **Table 2** as predictors, but results are reported only for country-specific characteristics. Total explained variability derived from the chi-square statistic: 21.6%; random country effect: chi-square = 63.9 (p < 0.001); explained variability by country derived from the chi-square statistic: 1.7%. ‡Based on the World Happiness Report 2013. §Based on dimensions of national culture by Hofstede. ‖p value based on chi-square statistic (likelihood-ratio test with 6 degrees of freedom) to test any effect of the 6 cultural dimensions. Results based on the LAS for QOL. Abbreviations as in **Tables 1 and 2**.

in-clinic recruitment in most participating centers, it was not possible to determine precise response rates or to compare background data from responders and nonresponders. One exception in this matter was data coming from Sweden. Eligible patients were selected from a national registry, and comparison of demographic and clinical data revealed only small differences between responders and nonresponders (data submitted). All continents were represented in the study, except for Africa. Logistics and limited funding made it too difficult for African centers to participate. Furthermore, the care of adult CHD patients is an issue only in some African countries. Fifth, we were not able to verify differential item functioning in this study. Differential item functioning means that people from different groups (e.g., North American vs. Asian patients) have a different probability of giving a certain response on a questionnaire. Differential item functioning should be an area of scrutiny in future analyses of international PRO data.

In conclusion, this is the first large-scale international study comprehensively assessing QOL in patients with CHD. Overall QOL in adults with CHD was found to be generally good and QOL varied across countries. This between-country variation was related to some patient characteristics, including age, marital status, employment status, and patient-reported NYHA functional class assessment. Country-specific characteristics, including national happiness level and cultural dimensions, were not responsible for variation in QOL.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Philip Moons, Academic Center for Nursing and Midwifery, KU Leuven, Kapucijnenvoer 35, Box 7001, B-3000 Leuven, Belgium. E-mail: philip.moons@kuleuven.be.

PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: QOL among adults with congenital heart disease is generally good but varies across countries. Most variation is related to patient characteristics rather than country-specific factors. Hence, uniform criteria can be used across geographical borders to identify patients facing better or worse QOL outcomes.

TRANSLATIONAL OUTLOOK: More research should be aimed at defining features of health care delivery systems in various nations that influence QOL among patients with adult CHD.

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APPENDIX For supplemental tables as well as a list of the collaborators, please see the online version of this article.