CORVINUS UNIVERSITY OF BUDAPEST

FINANCIAL TOXICITY AND HEALTH-RELATED QUALITY OF LIFE IN INDONESIAN PATIENTS WITH CANCER

Doctoral Dissertation

Supervisor: Prof. Dr. Fanni Rencz

Stevanus Pangestu Setiawan

Budapest, 2025

Department of Health Policy

Supervisor: Prof. Dr. Fanni Rencz

Corvinus University of Budapest
Doctoral School of Business and Management

FINANCIAL TOXICITY AND HEALTH-RELATED QUALITY OF LIFE IN INDONESIAN PATIENTS WITH CANCER

Doctoral Dissertation

Stevanus Pangestu Setiawan

Budapest, 2025

To Robbyanto Liman, my oldest friend of 25 years and future best man,
*for a lifetime of unwavering friendship and endless **laughter**!*

Contents

List of Figures

List of Tables

List of Abbreviations

ASCOT-Carer	Adult Social Care Outcomes Toolkit for Carers
AXIS	Appraisal Tool for Cross-Sectional Studies
BUI	Breast Utility Instrument
CarerQol-7D	Care-Related Quality of Life
CASP	Critical Appraisal Skills Programme
CFA	Confirmatory Factor Analysis
CFI	Comparative Fit Index
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COREQ	Consolidated Criteria for Reporting Qualitative Studies
COST	Comprehensive Score for Financial Toxicity
DASS-21	Depression, Anxiety, and Stress Scale – 21 Items
DCE	Discrete Choice Experiment
EORTC	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
EORTC QLQ-BR23	EORTC Breast Cancer-Specific Quality of Life Questionnaire
EORTC QLQ-C30	EORTC Core Quality of Life Questionnaire
EORTC QLU-C10D	EORTC Quality Of Life Utility - Core 10 Dimensions
EQ VAS	EQ Visual Analog Scale
EQ-5D-3L	Three-level EQ-5D Version
EQ-5D-5L	Five-level EQ-5D Version
EQ-HWB	EQ Health And Wellbeing
EQ-HWB-S	EQ-HWB Short Version
FACIT-COST	COST: A FACIT Measure of Financial Toxicity
FACT	Functional Assessment of Cancer Therapy
FACT-B	FACT - Breast
FACT-Br	FACT - Brain
FACT-C	FACT - Colorectal
FACT-G	FACT - General
FACT-G7	FACT-G - 7-Item Version
FACT-L	FACT - Lung

FACT-P	FACT - Prostate
FIT	Financial Index of Toxicity
GRC	Global Rating of Change scale
HRQoL	Health-Related Quality of Life
HTA	Health Technology Assessment
HUI	Health Utility Index
IDR	Indonesian Rupiah
IPA	Interpretive Phenomenological Analysis
LMIC	Low- or Middle-Income Country
LSS	Level Summary Score
OFT	Objective Financial Toxicity
OR	Odds Ratio
PBM	Preference-Based Measure
PCA	Principal Component Analysis
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROFFIT	Patient-Reported Outcome for Fighting Financial Toxicity
PROMIS	Patient-Reported Outcomes Measurement Information System
PROMIS CAT	PROMIS Computer Adaptive Tests
PROMIS Global-10	PROMIS 10-Item Global Health Survey
PROMIS-29	PROMIS 29-Item Profile Measure
PROPr	PROMIS-Preference
QALY	Quality-Adjusted Life Year
RMSEA	Root Mean Square Error of Approximation
SES	Standar Effect Size
SF-12	12-Item Short Form Health Survey
SF-36	36-Item Short Form Health Survey
SF-6D	Short Form Health Survey - 6 Dimensions
SFDQ	Subjective Financial Distress Questionnaire
SFT	Subjective Financial Toxicity
SG	Standard Gamble
SRM	Standardized Response Mean

SRMR	Standardized Root Mean Square Residual
SEWBS	Socioeconomic Wellbeing Scale
SWEMWBS	Short Warwick-Edinburgh Mental Wellbeing Scale
TTO	Time Trade-Off
UHC	Universal Healthcare
UWQOL	University of Washington Quality of Life
VAS	Visual Analog Scale
WEMWBS	Warwick-Edinburgh Mental Wellbeing Scale
WHO	World Health Organization
WHOQOL-BREF	WHO Quality of Life Brief Version

ACKNOWLEDGEMENTS

I would like to express my gratitude to the following individuals and institutions for their contributions and support throughout my PhD studies:

To Prof. Fanni Rencz, my supervisor, for her invaluable mentorship, which has been essential for my development as an early-career researcher.

To Prof. Valentin Brodszky, Head of the Department of Health Policy at Corvinus University of Budapest.

To Dr. Dániel Havran, Head of the Finance Track at the Doctoral School of Business and Management.

To Dr. Fredrick Dermawan Purba of Universitas Padjadjaran, lead investigator of the study from which the quantitative data for this dissertation was drawn.

To my research collaborators and co-authors from Sheffield University (Dr. Clara Mukuria), Universitas Padjajaran (Dr. Hari Setyowibowo and Dr. Yohana Azhar), and Universitas Gadjah Mada (Mr. F.A. Nurdiyanto, Ms. Enggar Harjanti, and Ms. Ika Pertiwi).

To my colleagues and fellow PhD candidates at the Department of Health Policy: Dr. Zsuzsanna Beretezky, Dr. Péter Balázs, Dr. Ákos Szabó, and Ms. Anna Nikl.

To the Tempus Public Foundation, for awarding the Stipendium Hungaricum scholarship, which fully funded my studies.

Stevanus Pangestu Setiawan
Budapest, 2025

CHAPTER I

General Introduction

I.1 Cancer

I.1.1 The epidemiology of cancer

Cancer is one of the leading causes of morbidity and mortality in the world. A total of 18.1 million new cancer cases and 9.9 million cancer-related deaths were estimated in 2020.[1-3] Presently, cancer accounts for a very large proportion of global disease burden, measured in disability-adjusted life years (i.e., years of life lost due to premature mortality and years lived with disability).[1-3] Global cancer prevalence is predicted to increase by nearly 50% in 2040 and become the number one cause of mortality within the century.[1,4] The most recent statistics show that the most globally prevalent cancer types by sites are breast, lung, colorectal, prostate and stomach cancers, where lung, colorectal, and liver are the leading cause of cancer mortality.[4]

I.1.2 The economic burden of cancer

Cancer imposes considerable economic toll on patients, households, societies, and health systems.[5] Between 2020 and 2050, the total cost of cancer to the global economy is estimated to reach US$ 25 trillion.[6] The economic burden of cancer comprises healthcare spending as well as non-healthcare areas.[7] Cancer-related healthcare costs include but not limited to inpatient and outpatient care, drugs, and emergency care. However, the greater burden occurs in the non-healthcare areas.[7] From a macroeconomic perspective, cancer exerts negative impact on the economy due to productivity loss from premature mortality and reduced labor engagement, as well as caregiving.[8]

The world is fighting against the cancer disease not only to improve survival and health-related quality of life (HRQoL), but also countering the rising burden.[9] Ultimately, progressing treatment options, equitable access to quality healthcare, and increasing awareness are essential to the improvement of survivorship and reduction of incidence of cancer.[10] Investments in cancer prevention and treatment may be cost-effective and yield favorable returns.[11] This aligns with the global effort to achieve universal healthcare (UHC) and with one of the 17 Sustainable Development Goals established by the United Nations, specifically Goal 3, which focuses on “Good Health and Well-Being”.[12]

The financial impact of cancer can be categorized into direct and indirect costs, placing a burden on patients, their families, and society as a whole. The direct costs can be further classified into medical and non-medical costs. Direct medical costs include those arising from medical management of the disease: drugs, care (inpatient, outpatient, and supportive), and diagnostics. While there is a heterogeneity of costs between patients

with breast cancer, some of the most incurred medical costs include prescribed drugs (e.g., doxorubicin, paclitaxel, and docetaxel for chemotherapy and tamoxifen for hormone therapy), surgery, and diagnostics (e.g., computed tomography scans, magnetic resonance imaging, and CA-153 and CA-199 tumor marker tests).[13,14]

In accessing healthcare, patients are likely to incur additional costs which can be categorized as direct non-medical costs. A few examples include transportation, helper wages or salaries (e.g., drivers and babysitters), and social services. If not covered by the insurance, these direct costs can be considered as out-of-pocket expenditures. A significant component of these costs is caregiving-related expenses, which can take two main forms: formal and informal. Formal caregiving involves professional services, such as paid nursing care and assistance from health aides. Meanwhile, informal caregiving refers to the unpaid care and support given to the patients provided by individuals in the patient's personal network.

In any given disease, productivity loss is generally seen as the main indirect cost which predominantly includes absenteeism, presenteeism, and early retirement. However, some indirect costs in patients with cancer have been more precisely identified: loss of earnings for both patients and informal caregivers, home production losses (e.g., cooking and childcare), patient leisure time costs, and premature death or disability costs.[15,16] These indirect costs, though not incurred as out-of-pocket expenses or direct monetary payments, can be substantial for both patients and societies, as they represent significant opportunity losses.

I.2 Breast cancer

I.2.1 Overview of breast cancer

Breast cancer is a malignancy that originates from the tissues of the breast. It is a cancer which is most often found in women but can also occur in men. While breast cancer is a highly complex and diverse disease, the most dominant histological type which accounts for over 95% cases are adenocarcinomas.[17] Adenocarcinomas are malignant tumors that originate from glandular epithelial cells, commonly found lining the mucosal surfaces within various organs such as the breast, lung, and colon.[18] Carcinomas can occur in the lactiferous ducts (ductal carcinoma) or the lobules, which are the glands responsible for milk production (lobular carcinoma).[19] Ductal carcinoma *in situ* (denoting "in its original place") is a non- or pre-invasive malignancy localized within the mammary ductal epithelium. Another form is the lobular carcinoma *in situ*, which occurs in the

lobules. When the malignancy has grown into the rest of the breast tissue, it is described as invasive or infiltrating. The two most common types of breast cancer that have spread into surrounding breast tissues are invasive ductal carcinoma and invasive lobular carcinoma.[20] Currently, breast cancer treatment strategies include surgery (e.g., breast conservation or breast removal), chemotherapy, radiotherapy, endocrine therapy, and a combination of these.[21]

I.2.2 Epidemiology and economic burden of breast cancer

In 2020, breast cancer became the most prevalent cancer worldwide with new diagnoses surpassing 2.2 million cases.[22] It was also the leading cause of death in female patients with cancer.[4] Globally, women are generally aware of this malignancy although not specifically about the symptoms.[23] Due to progresses in screening and interventions, breast cancer prognoses have significantly improved up to 90% for 5-year survival rates in western countries,[24] particularly those with early stages.[25] However, improvements in treatment modalities and early detection are not equal throughout the world. In developing countries, breast cancer is a greater and more urgent public health challenge due to underfunded healthcare facilities and shortages of medical professionals.[26]

If the current trend continues, newly diagnosed cancer can reach more than 3 million cases annually in 2040.[22] This predicted rise in prevalence of breast cancer is also accompanied by increasing economic costs due to inflation, growing supportive care needs, and the rapid development of new interventions that require rigorous economic evaluations, fueled in part by significant investments from the pharmaceutical industry. In metastatic breast cancer alone, the total costs were estimated to reach US$ 152.4 billion worldwide in 2030, a 140% increase from 2015.[27] Patients with breast cancer are directly impacted, as while state-funded healthcare systems typically cover direct medical costs (e.g., hospital care), they may still face significant non-medical expenditures (e.g., transportation) and indirect costs (e.g., productivity or wage loss).

I.3 Well-being

I.3.1 Definitions of well-being

The well-being construct has been globally promoted for health and social policymaking as a critical measure of outcome.[28] Generally, three theories are used to define well-being. First, the Hedonistic theories, which describe well-being as the balance of pleasure over pain, emphasizing the goal to maximize positive experiences (e.g., joy

and satisfaction) and avoid negative experiences (e.g., pain and distress).[29] Second, the Desire or Preference Satisfaction theory, which focuses on the fulfillment of an individual's wants.[30] Third, the Objective List theory, which defines well-being as the possession of elements that contribute to a good life regardless of preferences or subjective feelings.[31] While each of the three classic theories provide valuable frameworks for understanding well-being, considering the health focus of this dissertation, a definition more closely aligned with health is preferred. Further, the World Health Organization (WHO) characterizes well-being as *"a positive state experienced by individuals and societies."* that includes quality of life and the ability to contribute to the world meaningfully.[32]

I.3.2 Measuring subjective well-being

Well-being relates to overall health, education performance, greater work productivity, prosperity, and relationships in communities.[33,34] Therefore, measuring objective well-being includes indicators such as life expectancy, literacy, and economic output or income.[35] However, since the lives of individuals and societies involve emotions and experiences (e.g., happiness, satisfaction), individual perceptions must be included to fully capture the subjective aspects of well-being. Since 2013, OECD has urged its member countries to measure the subjective well-being of individuals by publishing a measurement guideline.[36] Realizing the limits of economic growth indicator "gross domestic product," they argued the importance of subjective well-being as a measure of societal progress. At the individual level, the most common method to measure subjective well-being employs questionnaires or measures. Some of the most widely used and validated measures include the Satisfaction with Life Scale, Subjective Happiness Scale, WHO 5-item Well-Being Index, Positive and Negative Affect Schedule, WHO Quality of Life Assessment Instrument-100, and Warwick and Edinburgh Mental Wellbeing Scale (WEMWBS).[37-42]

I.4 Health-related quality of life (HRQoL)

Quality of life is a multidimensional framework that refers to how a person values their conditions and way of life. The quality of life framework comprises several life domains, including physical, material, social, productive, emotional, and civic aspects.[43] Due to the extensiveness of the construct, there has been a lack of imprecision in its

definition.[44] In health sciences and policy, the term HRQoL includes only the domains that are part of an individual's health.[45]

I.4.1 Definition of health-related quality of life

Health is defined by the WHO as "*a state of complete physical, mental, and social well-being and not merely the absence of disease and infirmity."*[32] HRQoL is an individual's health status which captures information on the physical, psychological, and social domains of health.[46,47] For example, physical domain includes how an individual can perform daily activities, psychological domain includes the ability to regulate emotions, and social includes maintaining relationships in personal and professional lives. These domains are interconnected within an individual's life experiences, beliefs, expectations and perceptions. Over the past decades, HRQoL measures have become increasingly applied in clinical trials, patient care, and economic evaluations in the health sector.[46,48] In clinical trials and patient care, clinicians can use HRQoL assessments to provide them with important data reported by the patients on how the treatments or interventions impact their lives.

I.4.2 Health utilities

From a medical standpoint, HRQoL is primarily seen as a health status function, whereas from an economic perspective, it is regarded more as a utility function tied to choices of individuals.[49] This is derived upon the von Neumann-Morgenstern utility theorem regarding decision making under uncertainty.[50] It suggests that rational individuals would maximize utility, that is the appeal of their actions. The utility approach, founded in modern utility theory, enables HRQoL on a scale anchored at zero and one.[45] In a form of economic evaluations of healthcare interventions (cost-utility analysis), HRQoL data can be used to generate health utility values which are used to compute the quality-adjusted life year (QALY) metric.[51] The QALY is a standardized measure of health outcome which combines the impact on both the length and HRQoL. For instance, a QALY gain of one represents the improvement in an individual's overall health equivalent to one year of life lived in perfect health.

The elicitation of health utilities can be conducted through either direct or indirect methods. In direct utility elicitation, individuals from patient populations or the general public are asked to value their own health or hypothetical health states. Generally, they can be classified into cardinal or ordinal methods. The three direct elicitation techniques

using cardinal methods that are most frequently used thus far include the time trade-off (TTO), standard gamble (SG), and visual analogue scale (VAS).[52] Meanwhile, the two most common techniques using ordinal methods include the discrete choice experiment (DCE) and ranking exercises.[53]

TTO involves individuals making a trade-off between two alternatives: time spent in perfect health against time in a health-impaired condition. In SG, individuals would select between a certain but less desirable health state and taking a gamble with an uncertain outcome which may lead to either being in perfect health or worsening the condition (or death).[52] In VAS, individuals are asked to rate their health status directly on a scale, typically ranging from 0 ("dead") to 100 ("full health"); however, it is important to note that VAS is not a preference elicitation method, as it does not involve making choices or trade-offs. In DCE, individuals are asked to select their preferred option from a set of two or more alternatives, each characterized by different levels of features of attributes. Meanwhile ranking exercises involve individuals ranking alternatives or attributes (e.g., from best to worst) according to their preferences.[53] Alternatively, in indirect utility elicitation, individuals would complete an HRQoL measure whose results would then be transformed into utility values using a value set developed using direct utility assessment.[54]

Overall, the literature indicates a clear preference for indirect elicitation techniques in generating utilities for cancer, primarily due to their practicality.[55-59] Choice-based direct techniques, such as TTO and SG, are often challenging for individuals to comprehend and apply effectively. In contrast, indirect techniques are less cognitively demanding, more cost-effective, and easier to implement. Additionally, the use of generic instruments in indirect approaches enables the comparison of QALYs across diverse patient groups and diseases. As a result, many health technology assessment (HTA) agencies recommend indirect elicitation technique as the preferred method.[60-62]

I.4.3 HRQoL measures in cancer

There are two fundamental approaches to measuring HRQoL: preference-based and non-preference-based methods.[63] Preference-based measures (PBMs) consist of a multi-domain descriptive system for describing different health states and value set (or algorithm) which represents the preferences of general public for the different health states. The use of PBMs enables the computation of health utility values, whereas non-

PBMs focus on measuring HRQoL without incorporating preferences in the assessment.[51,64,65] A few examples of PBMs include the EQ-5D, Health Utility Index (HUI), and Short Form 6 Dimension (SF-6D).[66-68]

HRQoL measures can also be classified as generic or disease-specific categories. Generic measures are developed to assess HRQoL across a broad range of populations and health conditions. Alternatively, disease-specific measures are designed to focus on the unique aspects of health related to diseases or conditions. Where generic measures serve a necessary role for comparability across different diseases, disease-specific measures are more sensitive in detecting changes that are important to patients and clinicans.[69]

Therefore, in the context of cancer, there can be four types of HRQoL measures based on the 'preference or non-preference-based measures' and 'generic or disease-specific measures' classifications: generic non-PBMs, generic PBMs, cancer-specific non-PBMs, and cancer-specific PBMs (Table I.1).

Table I.1. Classification of HRQoL measures in cancer

	Preference-based	**Non-preference-based**
Generic	EQ-5D, SF-6D	PROMIS Global Health, SF-36
Cancer-specific	EORTC QLU-C10D, FACT-8D	EORTC QLQ-C30, FACT-G

Some examples are as follows: i) Generic non-PBMs: Patient-Reported Outcomes Measurement Information System (PROMIS) Global Health and 36-Item Short Form Health Survey (SF-36),[70,71] ii) Generic PBMs: EQ-5D, PROMIS-Preference (PROPr), and SF-6D,[66,68,72] iii) cancer-specific non-PBMs: the Functional Assessment of Cancer Therapy – General (FACT-G) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Version 3.0 (EORTC QLQ-C30),[73,74] and iv) cancer-specific PBMs: EORTC Quality of Life Utility Measure-Core 10 dimensions (EORTC QLU-C10D) FACT – Eight Dimension (FACT-8D).[75,76] To date, the most commonly used method for deriving health utility values in breast cancer is indirect elicitation through the generic PBM EQ-5D.[59]

I.4.4 Breast-cancer specific HRQoL measures

More specified than the cancer-specific measures of HRQoL, some instruments have been developed for the breast cancer population. Commonly, a breast cancer-

specific measure would include questions that are generally experienced by patients with cancer complemented with specific items related to the symptoms and overall experience of breast cancer. The two most used and validated breast cancer-specific HRQoL non-PBMs are the EORTC Breast Cancer-Specific Quality of Life Questionnaire-23 item (EORTC QLQ-BR23) and FACT-Breast (FACT-B).[77] The 37-item FACT-B consists of the 27 items from the FACT-G and 10 "additional concerns" items (breast cancer subscale), such as shortness of breath, self-consciousness about the way one dresses, bothered by hair loss, worry about other family members getting the same illness, and ability to feel like a woman.[78] Examples of breast cancer-related questions from EORTC QLQ-BR23 include swollen breast, skin problems, or oversensitivity in the area of affected breast.[79]

At the time of writing this dissertation, two breast cancer-specific PBMs are being developed to better address the concerns of women with breast cancer and reflect their preferences: BREAST-Q Utility and Breast Utility Instrument (BUI).[80,81] Some breast cancer-specific (candidate) dimensions shared by these two measures include breast appearance, body image, and interest in sex.

I.5 Financial toxicity

Financial well-being is an important construct that may affect the overall health of individuals.[82] However, the diagnosis and treatment of cancer potentially leads to catastrophic financial burden.[83] The term "financial toxicity" has been coined in the literature to describe the negative impact of cancer care on financial well-being.[83] This phenomenon has been documented worldwide regardless of the country's income status and health or social security systems.[84,85] Generally, there are two forms of financial toxicity: objective and subjective.[86,87] Objective financial toxicity can be measured using quantifiable economic metrics (e.g., the monetary amount of out-of-pocket healthcare expenses or its ratio to household income), or activities performed to cope with the financial burden (e.g., incurring debt and selling assets). Subjective financial toxicity refers to the perception of the patients regarding their financial distress. The measurement of subjective financial toxicity requires the use of patient-reported measures to capture their lived experiences, e.g., Breast Cancer Finances Survey Inventory, Socioeconomic Wellbeing Scale, and COST: A FACIT Measure of Financial Toxicity.[88-90]

The financial toxicity construct can be understood through a conceptual model based on Bartley's theory of health inequality, which encompasses three key approaches:

material, psychosocial, and behavioral.[91,92] The material perspective can be used to describe the financial resources that an individual possesses or their access to such resources. The psychosocial perspective then describes the emotional and psychological aspects of an individual's financial conditions, may manifest in forms such as financial satisfaction, financial worry, or financial efficacy. The third perspective, behavioral, describes the real actions performed by individuals in response to their financial situation, such as economizing, incurring debt, or even ceasing treatments. Together, these three perspectives are interrelated in explaining how financial toxicity manifests in patients: material deprivation, negative psychosocial response, and the adverse consequences of the preceding two factors.

Patients with cancer who experience financial toxicity are more likely to compromise their treatment which is necessary for their survival chances.[93-95] Treatment non-adherence is just one of the potential consequences of financial toxicity as patients may not be able to afford prescribed medications. In cases where treatments are covered by health insurance, patients experiencing financial toxicity may not be able to pay for other out-of-pocket expenditures. This includes non-medical (e.g., transportation to medical facilities) and medical (e.g., supplements or medical examinations not covered by insurance) costs. When financial well-being is improved, it may bring a positive influence on the HRQoL and general well-being.[96] Moreover, in oncology, HRQoL is an important health outcome construct; the improvement of HRQoL potentially improves the prognosis and survival of patients.[97-100] By improving the financial well-being of patients, through alleviating their objective financial burden and subjective financial distress, it may promote treatment adherence which contributes to the improved health outcomes and increased chances of survival of. At the same time, patients with better HRQoL may experience less financial toxicity due to their ability to remain produtive and maintain an income. Therefore, a connection between financial toxicity and HRQoL may be suggested, highlighting the importance of comprehensive support in cancer care.

I.6 The Indonesian context

In 2014, Indonesia introduced a National Health Insurance scheme called the *Jaminan Kesehatan Nasional* (JKN) which was aimed at achieving UHC for Indonesians.[101] The JKN united the previously fragmented protection schemes into the world's largest single-payer health insurance system managed by the Social Security Agency on Health (BPJS-Kesehatan).[102] According to the WHO, UHC means that every

person can access comprehensive quality health services they need, precisely when and where they need them, and without experiencing financial hardship.[103]

The BPJS-Kesehatan has enrolled at least 91% of the Indonesian population, approximately 248 million, as JKN members in 2023. However despite this high level of penetration, substantial health inequity persists, as seen in the distribution of healthcare professionals and medical equipment.[102,104] Further challenges also include stigma, education, and other cultural barriers.[105] Due to healthcare disparities, some specific subpopulations may face more challenges in accessing care. For instance, those living in rural areas having to incur more nonhealthcare expenses to reach a medical facility (e.g., transportation or additional accommodation for outpatients). Moreover, approximately 61% of registered JKN members are recipients of government subsidies, therefore coming from the lower income group, i.e., a well-studied socioeconomic determinant of financial toxicity.[106-108] This suggests that even the insured population may be prone to financial toxicity. In Indonesia, along with cardiovascular diseases, cancer is a major cause of mortality.[109] Cancer is also the second costliest chronic disease financed by JKN system,[110] where the most prevalent cases by organs are breast, cervical, lung, and colorectal.[111-113]

I.7 Aims of the dissertation

This dissertation encompasses five chapters with the primary purpose of studying HRQoL, well-being, and financial toxicity, and their associations in patients with cancer in Indonesia. The specific research objectives are outlined as follows:

1. Perform a systematic literature review and meta-analysis on studies investigating the association of financial toxicity and HRQoL in cancer patients.
2. Explore how patients with cancer experience financial toxicity in Indonesia using interpretive phenomenological analysis.
3. Validate the Indonesian version of the FACIT-COST in a breast cancer population in Indonesia.
4. Validate the EQ Health and Wellbeing (EQ-HWB), EQ-HWB Short (EQ-HWB-S), EQ-5D-5L, FACT-G, FACT-8D, WEMWBS, and Short WEMWBS (SWEMWBS) in a breast cancer population in Indonesia.
5. Investigate the associations between financial toxicity, well-being, and HRQoL in patients with breast cancer in Indonesia.

I.8 Outline of the dissertation

Chapter II provides a systematic literature review on the association between financial toxicity and HRQoL, highlighting the research gaps that motivate the subsequent studies. **Chapter III** employs interpretive phenomenological analysis to provide insight into the lived experience of financial toxicity in Indonesian patients with cancer. Serving as the sole qualitative study, this chapter acts as a preliminary empirical exploration of the financial toxicity phenomenon in Indonesia. The following three chapters present results from the quantitative survey with a breast cancer sample. **Chapter IV** validates the FACIT-COST subjective financial toxicity measure, while **Chapter V** validates several measures of health-related quality of life and wellbeing (EQ-HWB, EQ-HWB-S, EQ-5D-5L, FACT-G, FACT-8D, WEMWBS, and SWEMWBS). **Chapter VI** serves as an additional empirical quantitative chapter, exploring the associations between financial toxicity, well-being, and HRQoL. Lastly, **Chapter VII** concludes the dissertation with a summary of findings, methodological considerations, future research directions, and theoretical and policy implications.

References

1 Bray F, Laversanne M, Weiderpass E, Soerjomataram I. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer*. 2021;127(16):3029-3030. doi:10.1002/cncr.33587

2. Kocarnik JM, Compton K, Dean FE, et al. Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life Years for 29 Cancer Groups From 2010 to 2019: A Systematic Analysis for the Global Burden of Disease Study 2019. *JAMA Oncol*. 2022;8(3):420-444. doi:10.1001/jamaoncol.2021.6987

3. Vos T, Lim SS, Abbafati C, et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396(10258):1204-1222.

4. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-249. doi:10.3322/caac.21660

5. Landrigan PJ, Fuller R, Acosta NJR, et al. The Lancet Commission on pollution and health. *Lancet*. Feb 3 2018;391(10119):462-512. doi:10.1016/s0140-6736(17)32345-0

6. Kreier F. Cancer will cost the world $25 trillion over next 30 years. *Nature*. 2023;doi:10.1038/d41586-023-00634-9

7. Luengo-Fernandez R, Leal J, Gray A, Sullivan R. Economic burden of cancer across the European Union: a population-based cost analysis. *Lancet Oncol*. 2013;14(12):1165-74. doi:10.1016/s1470-2045(13)70442-x

8. Chen S, Cao Z, Prettner K, et al. Estimates and Projections of the Global Economic Cost of 29 Cancers in 204 Countries and Territories From 2020 to 2050. *JAMA Oncol*. 2023;9(4):465-472. doi:10.1001/jamaoncol.2022.7826

9. Prager GW, Braga S, Bystricky B, et al. Global cancer control: responding to the growing burden, rising costs and inequalities in access. *ESMO Open*. 2018;3(2):e000285. doi:10.1136/esmoopen-2017-000285

10. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. *CA Cancer J Clin*. 2023;73(1):17-48. doi:10.3322/caac.21763

11. World Health Organization. Saving lives, spending less: the case for investing in noncommunicable diseases. 2021.

12. Nations. U. *The Sustainable Development Goals Report 2023: Special Edition*. UN; 2023.

13. Schneider PP, Ramaekers BL, Pouwels X, et al. Direct Medical Costs of Advanced Breast Cancer Treatment: A Real-World Study in the Southeast of The Netherlands. *Value Health*. 2021;24(5):668-675. doi:10.1016/j.jval.2020.12.007

14. McCowan C, Wang S, Thompson AM, Makubate B, Petrie DJ. The value of high adherence to tamoxifen in women with breast cancer: a community-based cohort study. *Br J Cancer*. 2013;109(5):1172-1180. doi:10.1038/bjc.2013.464

15. Iragorri N, de Oliveira C, Fitzgerald N, Essue B. The Indirect Cost Burden of Cancer Care in Canada: A Systematic Literature Review. *Appl Health Econ Health Policy*. 2021;19(3):325-341. doi:10.1007/s40258-020-00619-z

16. Jo C. Cost-of-illness studies: concepts, scopes, and methods. *Clin Mol Hepatol*. 2014;20(4):327-37. doi:10.3350/cmh.2014.20.4.327

17. Makki J. Diversity of Breast Carcinoma: Histological Subtypes and Clinical Relevance. *Clin Med Insights Pathol*. 2015;8:23-31. doi:10.4137/CPath.S31563

18. Mullangi S, Lekkala MR. Adenocarcinoma. *StatPearls*. StatPearls Publishing

19. American Cancer Society. Types of Breast Cancer. Accessed 19 January 2023, https://www.cancer.org/cancer/types/breast-cancer/about/types-of-breast-cancer.html

20. Mouabbi JA, Hassan A, Lim B, Hortobagyi GN, Tripathy D, Layman RM. Invasive lobular carcinoma: an understudied emergent subtype of breast cancer. *Breast Cancer Res Treat*. 2022;193(2):253-264. doi:10.1007/s10549-022-06572-w

21. Harbeck N, Penault-Llorca F, Cortes J, et al. Breast cancer. *Nat Rev Dis Primers*. 2019;5(1):66. doi:10.1038/s41572-019-0111-2

22. Arnold M, Morgan E, Rumgay H, et al. Current and future burden of breast cancer: Global statistics for 2020 and 2040. *Breast*. 2022;66:15-23. doi:10.1016/j.breast.2022.08.010

23. Wang Y-J, Wang F, Yu L-X, et al. Worldwide review with meta-analysis of women's awareness about breast cancer. *Patient Education and Counseling*. 2022;105(7):1818-1827. doi:10.1016/j.pec.2021.12.012

24. Nardin S, Mora E, Varughese FM, et al. Breast Cancer Survivorship, Quality of Life, and Late Toxicities. *Front Oncol*. 2020;10:864. doi:10.3389/fonc.2020.00864
25. Taylor C, McGale P, Probert J, et al. Breast cancer mortality in 500 000 women with early invasive breast cancer diagnosed in England, 1993-2015: population based observational cohort study. *Bmj*. 2023;381:e074684. doi:10.1136/bmj-2022-074684
26. Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. *Br J Radiol*. 2022;95(1130):20211033. doi:10.1259/bjr.20211033
27. Gogate A, Wheeler SB, Reeder-Hayes KE, et al. Projecting the Prevalence and Costs of Metastatic Breast Cancer From 2015 through 2030. *JNCI Cancer Spectr*. 2021;5(4)doi:10.1093/jncics/pkab063
28. Layard R. Wellbeing as the Goal of Policy. *LSE Public Policy Review*. 2021;2(2)
29. Veenhoven R. Hedonism and happiness. *J Happiness Stud*. 2003;4:437-457.
30. Hausman DM, McPherson MS. Preference satisfaction and welfare economics. *Economics & Philosophy*. 2009;25(1):1-25.
31. Rice CM. Defending the objective list theory of well-being. *Ratio*. 2013;26(2):196-211.
32. Nutbeam D, Muscat DM. Health Promotion Glossary 2021. *Health Promot Int*. 2021;36(6):1578-1598. doi:10.1093/heapro/daaa157
33. Hey N, Brunetti S. Wellbeing evidence at the heart of policy. *What Works Wellbeing*. 2020;
34. Ruggeri K, Garcia-Garzon E, Maguire Á, Matz S, Huppert FA. Well-being is more than happiness and life satisfaction: a multidimensional analysis of 21 countries. *Health Qual Life Outcomes*. 2020;18(1):192. doi:10.1186/s12955-020-01423-y
35. Durand M. The OECD better life initiative: How's life? and the measurement of well-being. *Rev Income Wealth*. 2015;61(1):4-17.
36. OECD. *OECD Guidelines on Measuring Subjective Well-being*. 2013.
37. Diener E, Emmons RA, Larsen RJ, Griffin S. The Satisfaction With Life Scale. *J Pers Assess*. 1985;49(1):71-5. doi:10.1207/s15327752jpa4901_13
38. Lyubomirsky S, Lepper HS. A measure of subjective happiness: Preliminary reliability and construct validation. *Soc Indic Res*. 1999;46:137-155.
39. Organization WH. *Wellbeing measures in primary health care/the DepCare Project: report on a WHO meeting: Stockholm, Sweden, 12–13 February 1998*. 1998.
40. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*. 1988;54(6):1063-70. doi:10.1037//0022-3514.54.6.1063
41. Power M, Harper A, Bullinger M. The World Health Organization WHOQOL-100: tests of the universality of Quality of Life in 15 different cultural groups worldwide. *Health Psychol*. 1999;18(5):495-505. doi:10.1037//0278-6133.18.5.495
42. Tennant R, Hiller L, Fishwick R, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes*. 2007;5:63. doi:10.1186/1477-7525-5-63
43. Felce D. Defining and applying the concept of quality of life. *J Intellect Disabil Res*. 1997;41 (Pt 2):126-35. doi:10.1111/j.1365-2788.1997.tb00689.x
44. Karimi M, Brazier J. Health, Health-Related Quality of Life, and Quality of Life: What is the Difference? *Pharmacoeconomics*. 2016;34(7):645-649. doi:10.1007/s40273-016-0389-9
45. Torrance GW. Utility approach to measuring health-related quality of life. *J Chronic Dis*. 1987;40(6):593-603. doi:10.1016/0021-9681(87)90019-1
46. Romero M, Vivas-Consuelo D, Alvis-Guzman N. Is Health Related Quality of Life (HRQoL) a valid indicator for health systems evaluation? *Springerplus*. 2013;2(1):664. doi:10.1186/2193-1801-2-664
47. Yin S, Njai R, Barker L, Siegel PZ, Liao Y. Summarizing health-related quality of life (HRQOL): development and testing of a one-factor model. *Popul Health Metr*. 2016;14:22. doi:10.1186/s12963-016-0091-3
48. Lin X-J, Lin IM, Fan S-Y. Methodological issues in measuring health-related quality of life. *Tzu Chi Medical Journal*. 2013;25(1):8-12. doi:10.1016/j.tcmj.2012.09.002
49. Salvador-Carulla L, Lucas R, Ayuso-Mateos JL, Miret M. Use of the terms" Wellbeing" and" Quality of Life" in health sciences: a conceptual framework. *Eur Psychiatry*. 2014;28(1):50-65.
50. Von Neumann J, Morgenstern O. Theory of games and economic behavior, 2nd rev. 1947;
51. Brazier J, Ratcliffe J, Saloman J, Tsuchiya A. *Measuring and valuing health benefits for economic evaluation*. Oxford University Press; 2017.
52. Whitehead SJ, Ali S. Health outcomes in economic evaluation: the QALY and utilities. *Br Med Bull*. 2010;96(1):5-21. doi:10.1093/bmb/ldq033

53. Ali S, Ronaldson S. Ordinal preference elicitation methods in health economics and health services research: using discrete choice experiments and ranking methods. *Br Med Bull*. 2012;103(1):21-44. doi:10.1093/bmb/lds020
54. Prosser LA, Grosse SD, Wittenberg E. Health Utility Elicitation. *Pharmacoeconomics*. 2012;30(2):83-86. doi:10.2165/11597720-000000000-00000
55. Houten R, Fleeman N, Kotas E, Boland A, Lambe T, Duarte R. A systematic review of health state utility values for thyroid cancer. *Qual Life Res*. 2021;30(3):675-702. doi:10.1007/s11136-020-02676-2
56. Hao Y, Wolfram V, Cook J. A structured review of health utility measures and elicitation in advanced/metastatic breast cancer. *Clinicoecon Outcomes Res*. 2016;8:293-303. doi:10.2147/ceor.S100448
57. Pourrahmat M-M, Kim A, Kansal AR, et al. Health state utility values by cancer stage: a systematic literature review. *Eur J Health Econ*. 2021;22(8):1275-1288. doi:10.1007/s10198-021-01335-8
58. Magnus A, Isaranuwatchai W, Mihalopoulos C, Brown V, Carter R. A Systematic Review and Meta-Analysis of Prostate Cancer Utility Values of Patients and Partners Between 2007 and 2016. *MDM Policy & Practice*. 2019;4(1):2381468319852332. doi:10.1177/2381468319852332
59. Kaur MN, Yan J, Klassen AF, et al. A Systematic Literature Review of Health Utility Values in Breast Cancer. *Med Decis Making*. 2022;42(5):704-719. doi:10.1177/0272989x211065471
60. Kennedy-Martin M, Slaap B, Herdman M, et al. Which multi-attribute utility instruments are recommended for use in cost-utility analysis? A review of national health technology assessment (HTA) guidelines. *Eur J Health Econ*. 2020;21(8):1245-1257. doi:10.1007/s10198-020-01195-8
61. Rowen D, Azzabi Zouraq I, Chevrou-Severac H, van Hout B. International Regulations and Recommendations for Utility Data for Health Technology Assessment. *Pharmacoeconomics*. 2017;35(Suppl 1):11-19. doi:10.1007/s40273-017-0544-y
62. Rencz F, Gulácsi L, Drummond M, et al. EQ-5D in Central and Eastern Europe: 2000-2015. *Qual Life Res*. 2016;25(11):2693-2710. doi:10.1007/s11136-016-1375-6
63. Drummond MF, Sculpher MJ, Claxton K, Stoddart GL, Torrance GW. *Methods for the economic evaluation of health care programmes*. Oxford university press; 2015.
64. Rowen D, Rivero-Arias O, Devlin N, Ratcliffe J. Review of Valuation Methods of Preference-Based Measures of Health for Economic Evaluation in Child and Adolescent Populations: Where are We Now and Where are We Going? *Pharmacoeconomics*. 2020;38(4):325-340. doi:10.1007/s40273-019-00873-7
65. Peasgood T, Mukuria C, Carlton J, Connell J, Brazier J. Criteria for item selection for a preference-based measure for use in economic evaluation. *Qual Life Res*. 2021;30(5):1425-1432. doi:10.1007/s11136-020-02718-9
66. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727-36. doi:10.1007/s11136-011-9903-x
67. Horsman J, Furlong W, Feeny D, Torrance G. The Health Utilities Index (HUI): concepts, measurement properties and applications. *Health Qual Life Outcomes*. 16 2003;1:54. doi:10.1186/1477-7525-1-54
68. Brazier JE, Mulhern BJ, Bjorner JB, et al. Developing a New Version of the SF-6D Health State Classification System From the SF-36v2: SF-6Dv2. *Med Care*. 2020;58(6):557-565. doi:10.1097/mlr.0000000000001325
69. Patrick DL, Deyo RA. Generic and disease-specific measures in assessing health status and quality of life. *Med Care*. 1989;27(3 Suppl):S217-32. doi:10.1097/00005650-198903001-00018
70. Hays RD, Bjorner JB, Revicki DA, Spritzer KL, Cella D. Development of physical and mental health summary scores from the patient-reported outcomes measurement information system (PROMIS) global items. *Qual Life Res*. 2009;18(7):873-80. doi:10.1007/s11136-009-9496-9
71. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992;30(6):473-83.
72. Dewitt B, Feeny D, Fischhoff B, et al. Estimation of a Preference-Based Summary Score for the Patient-Reported Outcomes Measurement Information System: The PROMIS(®)-Preference (PROPr) Scoring System. *Med Decis Making*. 2018;38(6):683-698. doi:10.1177/0272989x18776637
73. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 3 1993;85(5):365-76. doi:10.1093/jnci/85.5.365
74. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol*. 1993;11(3):570-9. doi:10.1200/jco.1993.11.3.570

75. King MT, Costa DS, Aaronson NK, et al. QLU-C10D: a health state classification system for a multi-attribute utility measure based on the EORTC QLQ-C30. *Qual Life Res*. 2016;25(3):625-36. doi:10.1007/s11136-015-1217-y
76. King MT, Norman R, Mercieca-Bebber R, et al. The Functional Assessment of Cancer Therapy Eight Dimension (FACT-8D), a Multi-Attribute Utility Instrument Derived From the Cancer-Specific FACT-General (FACT-G) Quality of Life Questionnaire: Development and Australian Value Set. *Value Health*. 2021;24(6):862-873. doi:10.1016/j.jval.2021.01.007
77. Salas M, Mordin M, Castro C, Islam Z, Tu N, Hackshaw MD. Health-related quality of life in women with breast cancer: a review of measures. *BMC Cancer*. 15 2022;22(1):66. doi:10.1186/s12885-021-09157-w
78. Brady MJ, Cella DF, Mo F, et al. Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument. *J Clin Oncol*. 1997;15(3):974-86. doi:10.1200/jco.1997.15.3.974
79. Sprangers MA, Groenvold M, Arraras JI, et al. The European Organization for Research and Treatment of Cancer breast cancer-specific quality-of-life questionnaire module: first results from a three-country field study. *J Clin Oncol*. 1996;14(10):2756-2768. doi:10.1200/jco.1996.14.10.2756
80. Kaur MN, Klassen AF, Xie F, et al. An international mixed methods study to develop a new preference-based measure for women with breast cancer: the BREAST-Q Utility module. *BMC Women's Health*. 2021;21(1):8. doi:10.1186/s12905-020-01125-z
81. Tsui TCO, Trudeau ME, Mitsakakis N, Krahn MD, Davis AM. Developing the Breast Utility Instrument to Measure Health-Related Quality-of-Life Preferences in Patients with Breast Cancer: Selecting the Item for Each Dimension. *MDM Policy Pract*. 2022;7(2):23814683221142267. doi:10.1177/23814683221142267
82. Netemeyer RG, Warmath D, Fernandes D, Lynch Jr JG. How am I doing? Perceived financial well-being, its potential antecedents, and its relation to overall well-being. *Journal of Consumer Research*. 2018;45(1):68-89.
83. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. *CA Cancer J Clin*. 2018;68(2):153-165. doi:10.3322/caac.21443
84. Bhoo-Pathy N, Ng CW, Lim GC, et al. Financial Toxicity After Cancer in a Setting With Universal Health Coverage: A Call for Urgent Action. *J Oncol Pract*. 2019;15(6):e537-e546. doi:10.1200/jop.18.00619
85. Donkor A, Atuwo-Ampoh VD, Yakanu F, et al. Financial toxicity of cancer care in low- and middle-income countries: a systematic review and meta-analysis. *Support Care Cancer*. 2022;30(9):7159-7190. doi:10.1007/s00520-022-07044-z
86. Witte J, Mehlis K, Surmann B, et al. Methods for measuring financial toxicity after cancer diagnosis and treatment: a systematic review and its implications. *Ann Oncol*. 2019;30(7):1061-1070. doi:10.1093/annonc/mdz140
87. Chan RJ, Gordon LG, Tan CJ, et al. Relationships Between Financial Toxicity and Symptom Burden in Cancer Survivors: A Systematic Review. *J Pain Symptom Manage*. 2019;57(3):646-660.e1. doi:10.1016/j.jpainsymman.2018.12.003
88. Given BA, Given CW, Stommel M. Family and out-of-pocket costs for women with breast cancer. *Cancer Pract*. 1994;2(3):187-93.
89. Head BA, Faul AC. Development and validation of a scale to measure socioeconomic well-being in persons with cancer. *J Support Oncol*. 2008;6(4):183-92.
90. de Souza JA, Yap BJ, Hlubocky FJ, et al. The development of a financial toxicity patient-reported outcome in cancer: The COST measure. *Cancer*. 2014;120(20):3245-53. doi:10.1002/cncr.28814
91. Bartley M, Kelly-Irving M. *Health inequality: an introduction to concepts, theories and methods*. John Wiley & Sons; 2024.
92. Tucker-Seeley RD, Thorpe RJ. Material-Psychosocial-Behavioral Aspects of Financial Hardship: A Conceptual Model for Cancer Prevention. *Gerontologist*. 2019;59(Suppl 1):S88-s93. doi:10.1093/geront/gnz033
93. Bhanvadia SK, Psutka SP, Burg ML, et al. Financial Toxicity Among Patients with Prostate, Bladder, and Kidney Cancer: A Systematic Review and Call to Action. *Eur Urol Oncol*. 2021;4(3):396-404. doi:10.1016/j.euo.2021.02.007
94. Tran G, Zafar SY. Financial toxicity and implications for cancer care in the era of molecular and immune therapies. *Ann Transl Med*. 2018;6(9):166. doi:10.21037/atm.2018.03.28
95. Ürek D, Uğurluoğlu Ö. Predictors of financial toxicity and its associations with health-related quality of life and treatment non-adherence in Turkish cancer patients. *Support Care Cancer*. 2022;30(1):865-874. doi:10.1007/s00520-021-06491-4

96. Brüggen EC, Hogreve J, Holmlund M, Kabadayi S, Löfgren M. Financial well-being: A conceptualization and research agenda. *J Bus Res*. 2017;79:228-237.
97. Quinten C, Coens C, Mauer M, et al. Baseline quality of life as a prognostic indicator of survival: a meta-analysis of individual patient data from EORTC clinical trials. *Lancet Oncol*. 2009;10(9):865-71. doi:10.1016/s1470-2045(09)70200-1
98. van Nieuwenhuizen AJ, Buffart LM, Brug J, Leemans CR, Verdonck-de Leeuw IM. The association between health related quality of life and survival in patients with head and neck cancer: a systematic review. *Oral Oncol*. 2015;51(1):1-11. doi:10.1016/j.oraloncology.2014.09.002
99. van Nieuwenhuizen AJ, Buffart LM, Langendijk JA, et al. Health-related quality of life and overall survival: a prospective study in patients with head and neck cancer treated with radiotherapy. *Qual Life Res*. 2021;30(4):1145-1153. doi:10.1007/s11136-020-02716-x
100. Sitlinger A, Zafar SY. Health-Related Quality of Life: The Impact on Morbidity and Mortality. *Surg Oncol Clin N Am*. 2018;27(4):675-684. doi:10.1016/j.soc.2018.05.008
101. Pisani E, Olivier Kok M, Nugroho K. Indonesia's road to universal health coverage: a political journey. *Health Policy Plan*. 2017;32(2):267-276. doi:10.1093/heapol/czw120
102. Agustina R, Dartanto T, Sitompul R, et al. Universal health coverage in Indonesia: concept, progress, and challenges. *Lancet*. 2019;393(10166):75-102. doi:10.1016/s0140-6736(18)31647-7
103. Cotlear D, Nagpal S, Smith O, Tandon A, Cortez R. *Going universal: how 24 developing countries are implementing universal health coverage from the bottom up*. World Bank Publications; 2015.
104. Asante A, Cheng Q, Susilo D, et al. The benefits and burden of health financing in Indonesia: analyses of nationally representative cross-sectional data. *Lancet Glob Health*. 2023;11(5):e770-e780. doi:10.1016/s2214-109x(23)00064-5
105. Septiono W. Equity challenges in Indonesian health care. *Lancet Glob Health.* 2023;11(5):e646-e647. doi:10.1016/S2214-109X(23)00110-9
106. Boby JM, Rajappa S, Mathew A. Financial toxicity in cancer care in India: a systematic review. *Lancet Oncol*. 2021;22(12):e541-e549. doi:10.1016/s1470-2045(21)00468-x
107. Xu B, Hu L, Cheng Q, W KWS. A systematic review of financial toxicity among cancer patients in China. *Asia Pac J Oncol Nurs*. 2022;9(8):100071. doi:10.1016/j.apjon.2022.04.010
108. Çeli KY, Çeli KS, Sarıköse S, Arslan HN. Evaluation of financial toxicity and associated factors in female patients with breast cancer: a systematic review and meta-analysis. *Support Care Cancer*. 2023;31(12):691. doi:10.1007/s00520-023-08172-w
109. US Centers for Disease Control and Prevention. Indonesia Fact Sheet. 2021. Accessed 3 January 2025, https://www.cdc.gov/global-health/countries/indonesia.html
110. Kosen S. Coverage and implementation of healthcare delivery for cancer under national health insurance, experience of Indonesia. *Lancet Reg Health Southeast Asia*. 2022;6:100065. doi:10.1016/j.lansea.2022.100065
111. Puspitaningtyas H, Espressivo A, Hutajulu SH, Fuad A, Allsop MJ. Mapping and Visualization of Cancer Research in Indonesia: A Scientometric Analysis. *Cancer Control*. 2021;28:10732748211053464. doi:10.1177/10732748211053464
112. Gondhowiardjo S, Christina N, Ganapati NPD, et al. Five-Year Cancer Epidemiology at the National Referral Hospital: Hospital-Based Cancer Registry Data in Indonesia. *JCO Glob Oncol*. 2021;7:190-203. doi:10.1200/go.20.00155
113. World Health Organization. Cancer Indonesia 2020 country profile. Accessed January 3 2025, https://cdn.who.int/media/docs/default-source/country-profiles/cancer/idn-2020.pdf?sfvrsn=46ea6569_2&download=true

CHAPTER II

Comprehensive Score for Financial Toxicity and Health-Related Quality of Life in Patients With Cancer and Survivors: A Systematic Review and Meta-Analysis

Published as:
Pangestu, S., & Rencz, F. (2023). Comprehensive Score for Financial Toxicity and Health-Related Quality of Life in Patients With Cancer and Survivors: A Systematic Review and Meta-Analysis. *Value in Health*, *26*(2), 300–316. https://doi.org/10.1016/j.jval.2022.07.017

ABSTRACT

Objectives: Financial toxicity is recognised as an important adverse effect of cancer treatment that may decrease patients' health-related quality of life (HRQoL). We aim to perform a systematic review and meta-analysis on studies investigating the association of HRQoL and financial toxicity measured with the Comprehensive Score for Financial Toxicity (COST) in cancer patients and survivors.

Methods: A systematic literature search was completed in PubMed, Web of Science, CINAHL, and PsycInfo (last update April 2022). Methodological quality of included studies was assessed using Appraisal Tool for Cross-Sectional Studies and Critical Appraisal Skills Programme Cohort Study Checklist. Where possible, study outcomes were pooled by random-effects meta-analysis.

Results: Thirty-one studies were included with a combined sample of 13,481 patients and survivors with more than 25 cancer types from nine countries. Nineteen different validated HRQoL instruments were used in these studies, with FACT-G (n=9), EORTC QLQ-C30 (n=5) and EQ-5D (n=5) being the most common. All but one included studies reported that higher financial toxicity was significantly associated with worse HRQoL. Ten HRQoL domains were correlated with financial toxicity, including physical health (r=0.34-0.66), social health (r=0.16-0.55), mental health (r=0.21-0.54), and daily functioning (r=0.23-0.52). The meta-analysis indicated a moderate correlation between financial toxicity and overall HRQoL as measured by FACT instruments (r=0.49, 95%CI: 0.44-0.54).

Conclusions: This is the first systematic review and meta-analysis to summarise the literature on the association of financial toxicity and HRQoL in cancer patients and survivors. Our findings substantiate financial toxicity as a relevant outcome of cancer care that is associated with a decline of HRQoL.

II.1 INTRODUCTION

Cancer is among the leading causes of premature death in the world and it is responsible for a large proportion of global disease burden in terms of disability-adjusted life years.[1-3] Worldwide cancer prevalence is estimated to increase by nearly 50% in the coming decade.[4] Global economic cost of cancer is estimated to exceed US$ 1 trillion annually from productivity loss and premature mortality,[5] imposing a severe economic burden on patients, healthcare systems, and society. At an individual level, treatment of cancer may lead to catastrophic health expenditures and medical bankruptcy.[6] The financial burden of cancer treatment on patients remains a prevalent issue,[7] even in countries with universal public healthcare systems.[8]

In oncology, the term 'financial toxicity' was introduced to describe financial adverse effects of treatment.[9] There are two forms of financial toxicity: objective and subjective. Objective financial toxicity relates to the quantifiable treatment costs, such as out-of-pocket healthcare expenditures,[10] while subjective financial toxicity refers to patients' perceived distress arising from the costs of their treatment.[11] A recent study showed an exponential association between objective and subjective financial toxicity.[12] Unlike the objective form, which can be measured with economic metrics (e.g., the ratio of out-of-pocket health care expenditures to income), subjective financial toxicity is more challenging to assess because it involves quantifying perceptions using patient-reported outcome measures. There are generic instruments, i.e., non-exclusive for cancer, that can be used to measure subjective financial toxicity in any health condition, such as the InCharge Personal Financial Well-Being Scale.[13] Specifically in cancer care, a few cancer-specific measures have been developed, which include Cancer Finances Survey,[14] Socioeconomic Well-Being Scale,[15] Comprehensive Score for Financial Toxicity (COST),[16] and Financial Index of Toxicity.[17]

Health-related quality of life (HRQoL) is a key outcome in oncology and improving it may influence the prognosis and survival of patients.[18] Cancer may seriously disrupt patients' HRQoL, causing physical, mental, and social health problems.[19-21] Recently, a large number of studies described the association between higher financial toxicity and worse HRQoL in cancer patients and survivors, using both qualitative and quantitative methods.[8,22-27] Financial toxicity is a form of deprivation of financial well-being, which is the perception of being able to sustain current and anticipated desired living standards

and financial freedom.[28,29] It is often intensified by the negative employment and subsequent income effects of cancer.[30] Some documented health-related implications of financial toxicity include medication cessation and adverse mental health consequences, such as developing depression and anxiety.[25,31] This signifies financial toxicity as a potentially important predictor of HRQoL. So far, a systematic review has summarised the factors associated with financial toxicity in cancer patients,[24] but this was limited to urological malignancies and did not specifically focus on subjective financial toxicity and HRQoL outcomes.

Therefore, we aim to perform a systematic review and meta-analysis on studies investigating the association of subjective financial toxicity and HRQoL in cancer patients and survivors. Previous systematic reviews have highlighted the lack of uniformity and the frequent use of non-validated instruments in the measurement of subjective financial toxicity.[7,24,32,33] To ensure robustness of data and allow for quantitative synthesis, this systematic review is centralised on COST, the most widely used and validated cancer-specific measure of financial toxicity. Other financial toxicity instruments available are often lacking evidence of validity, not cancer-specific, or not precisely designed to capture subjective financial toxicity such as the use of items or subscales of a HRQoL measure (e.g., the financial difficulty item of EORTC QLQ-C30).[24] Whereas COST is not only the most used measure of financial toxicity in cancer patients, but also one with wide availability in multiple languages and sufficient evidence of good measurement properties across different cancer types, cultures, and countries.[34]

II.2 METHODS

II.2.1 Search strategy

This systematic review and meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines.[35] Four electronic databases (PubMed, Web of Science, Cumulative Index to Nursing and Allied Health Literature, and PsycInfo) were searched and updated in April 2022. The protocol of this systematic review and meta-analysis was registered in PROSPERO under number CRD42022302272.

The search strategy was compiled based on keywords related to cancer, financial toxicity, and HRQoL (Appendix II.1). For cancer, we used a PubMed cancer filter developed by the National Library of Medicine and the National Cancer Institute.[36] This filter combines

a set of Medical Subject Headings (MeSH) terms for neoplasms and cancer-related journal titles and text words. For HRQoL, the search terms were compiled based on a filter to identify HRQoL studies and a list of instrument names from a systematic literature review about HRQoL instruments used in cancer.[37,38] Financial toxicity search terms were adopted from a previous systematic review on financial toxicity in patients with urologic cancer,[24] combined with several other terms that we had identified during preliminary literature search. Google Scholar was also used for citation tracking and manual hand-searching of literature.

II.2.2 Study inclusion and exclusion criteria

Studies were included if they: (i) were published in English, (ii) were published as original research articles, (iii) had any study design that involved primary data collection, (iv) involved patients and/or survivors with any type of cancer aged at least 18 years who had undergone treatment for cancer, (v) measured financial toxicity using COST (any version), and (vi) measured HRQoL using any standardised and validated instrument (i.e., instruments consisting of a standard set of questions with a scoring system and adhering to quality criteria for measurement properties of health status measures).

Studies were excluded if they: (i) were not published in English, (ii) were published as reviews, editorials, or conference publications, (iii) did not include primary data collection, (iv) involved pediatric cancer patients or diseases other than cancer, (v) did not measure financial toxicity using COST, (vi) did not involve HRQoL outcomes that were measured using a standardised and validated instrument, and (vii) did not analyse the association between financial toxicity and HRQoL. Pediatric oncology patients were excluded because COST was developed to be responded by cancer patients 18 years and older and our review aimed to focus on patients' perception and experience of financial toxicity and HRQoL, i.e., not proxy or observer reported.

The inclusion of studies was performed independently by the two authors. The inclusion and exclusion criteria were applied to titles and abstracts to identify relevant studies. Full-text articles were also screened to assure the inclusion of eligible studies. Discrepancies between reviewers were solved through discussion until reaching a consensus.

II.2.3 The Comprehensive Score for Financial Toxicity (COST)

COST is a patient-reported outcome measure for subjective financial toxicity in patients with any kind of cancer.[16] The instrument has a recall period of 7 days. The

original version (V1) consists of 11 items, and the most recent second version (V2) has 12 items. The items relate to financial adequacy, psychosocial reaction, financial efficacy and satisfaction, and the impact of financial hardship on family, among others. Each item has the following 5 response options: “not at all” (=0), “a little bit” (=1), “somewhat” (=2), “quite a bit” (=3), and “very much” (=4). Seven items are scored in reverse (items 2, 3, 4, 5, 8, and 9). A total score is computed from the sum of items 1 through 11 for either version of the scale (excluding item 12 for V2 of the scale). The total score ranges from 0 to 44, where lower scores indicate worse financial toxicity.

II.2.4 Data extraction

The following data were extracted from the included studies: title, author names, year of publication, country, sample size, sex ratio, study design, cancer type, treatment status, cancer stage, time since diagnosis, COST instrument version, COST language version, HRQoL instrument(s) used, statistical analysis method(s) performed, and main findings. The main findings included the results of the statistical analysis (e.g., correlation coefficients, beta coefficients, and p-values) and the conclusion about the association between financial toxicity and HRQoL (e.g., higher financial toxicity was associated with worse HRQoL). Data extraction was completed by S.P. and verified by F.R.

II.2.5 Critical appraisal of included studies

Two critical appraisal tools were employed to assess the methodological quality of the included studies. The Appraisal Tool for Cross-Sectional Studies (AXIS) and the Critical Appraisal Skills Programme (CASP) Cohort Study Checklist were used for cross-sectional and cohort study designs, respectively.[39,40] All subparts of the studies (including introduction, methods, results, and discussion) were evaluated. The AXIS includes twenty items with “yes”, “no”, and “unclear” responses. The CASP Cohort Study checklist consists of twelve items with “yes”, “no”, and “can’t tell” responses. For the sake of consistency, critical appraisal responses on both appraisal tools that were initially “yes” and “no” were relabelled as “favourable” and “unfavourable” as two AXIS components were originally scored reversely. The responses “unclear” and “can’t tell” were reported under “unclear”. Percentage scores were computed by dividing the number of favourable responses with the total number of items of the respective appraisal.

For both appraisal tools, a study was assessed to be: (i) good quality if its score was equal to or exceeded 70% of the total, (ii) fair quality if the score was between 60% and

69.9%, and (iii) low quality if the score was below 60%.[41] S.P. performed the critical appraisal of the included studies and F.R. verified them. Discrepancies were resolved through discussion.

II.2.6 Qualitative and quantitative syntheses

Extracted HRQoL outcomes were categorised as total or overall HRQoL scores and domain scores (e.g., mental or emotional, social, and physical health). Every HRQoL domain was extracted except financial difficulties because it was considered as a possible direct measure of financial toxicity.

Meta-analysis was performed to pool good-quality studies using the same HRQoL instrument family, where at least three studies were available. Among the statistical methods employed in the included studies, only bivariate correlations were reported in sufficient number of studies for meta-analysis. The meta-analysis was conducted on the correlation coefficients (Spearman's or Pearson's) between COST and HRQoL scores. The absolute value was taken for the correlation coefficients to correct for the directionality of the scales. Then, the coefficients were transformed into z values using Fisher's transformation.[42,43] Next, we performed a random-effects meta-analysis using the transformed values. Finally, we converted back the Fisher's z transformed correlations to *r* for the sake of presentation. Correlation coefficients were interpreted as follows: very weak (<0.2), weak (0.20-0.39), moderate (0.40-0.59), strong (0.60-0.79), and very strong (≥0.8).[44]

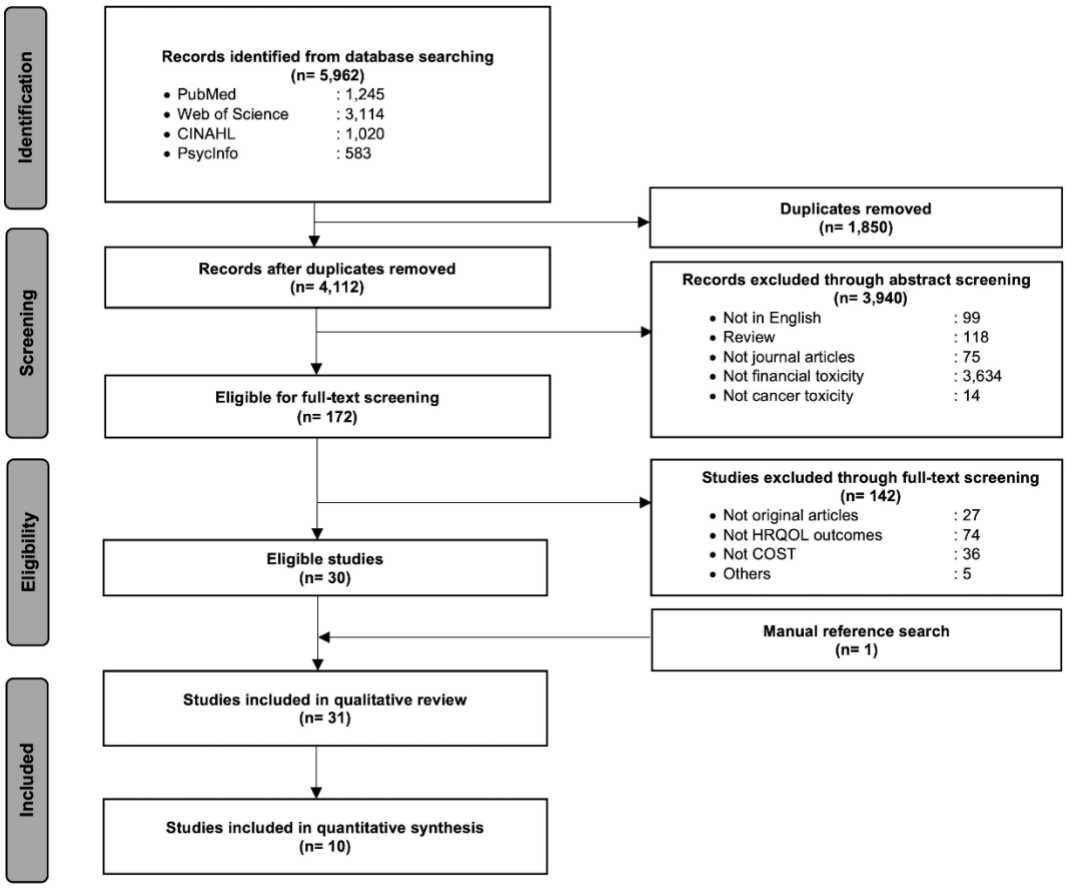
Prior to performing meta-analysis, heterogeneity was tested using I-squared statistic. The outcomes were deemed to be heterogeneous if the I-squared statistic was greater than 30%.[45,46] When moderate heterogeneity was detected (I-square statistic between 30 and 60%),[46] we used a random-effects model with restricted maximum likelihood estimator.[47,48] Forest plots were generated to present the summary of individual and pooled correlation coefficients. Narrative synthesis was presented for results that were ineligible for meta-analysis due to substantial heterogeneity (I-squared statistic greater than 60%) or insufficient number of studies reporting the correlation between COST and HRQoL scores using the same instrument family. Publication bias was assessed using Egger's regression, where a p-value lower than 0.05 indicated possible publication bias.[49] The meta-analysis was performed in Jamovi statistical software.[50]

II.3 RESULTS

II.3.1 Study selection

A sum of 5,962 records were identified from the systematic search of electronic databases (Figure II.1). After removal of duplicates and screening of titles and abstracts for eligible

Figure II.1. PRISMA flow diagram



Abbreviations
PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analyses; CINAHL: Cumulative Index to Nursing and Allied Health Literature; HRQOL: health-related quality of life, COST: Comprehensive Score for Financial Toxicity

studies, 172 full-text articles were screened for inclusion. A total of 30 studies fulfilled all the inclusion criteria. Afterwards, one additional study was added through manual hand-searching on Google Scholar. Thus, 31 studies were included in this systematic review.[51-81]

Table II.1. Overall study characteristics

Author (year)	**Country**	**Study design**	**Sample size**	**Mean age (±SD)** (* indicates median)	**Female sex ratio**	**Cancer type**	**Cancer stage**	**Time since diagnosis**	**Treatment status**	**COST version**	**COST language**	**HRQOL instrument**
Akin-Odanye, et al. (2021)[51]	Nigeria	CS	173	71.57 ±11.18	0	Prostate	NR	NR	Active	V2	NR	FACT-P
Belcher, et al. (2021)[52]	US	CS	78	56.6 ± 12.2	56.4%	Breast, gastrointestinal, lung, liver, prostate, melanoma, pancreatic, head and neck, gynaecologic, kidney, and others	Advanced	35.5 months, median	Active, palliative care	V1	English	SF-36
Benedict, et al. (2022)[53]	US	CS	273	54.65 ± 12.08	100%	Breast, gynaecologic (incl. ovarian, cervical, uterine/endometrial, vaginal, vulvar, peritoneal, and fallopian tube carcinoma)	0-4	3.42 years, average	Active and completed	V2	English	FACT-G
Bouberhan, et al. (2019)[54]	US	CS	240	56*	100%	Gynaecologic (ovarian, uterine, cervical, and vaginal)	1-4, benign	2 years, median	Active and in surveillance	V1	English, Spanish, Mandarin Chinese, Portuguese, Haitian Creole	EQ VAS (EQ-5D descriptive system was not used)
Chan, et al. (2021)[55]	China	CS	640	59.9 ± 11.1	64.2%	Breast, gynaecologic, head and neck, gastrointestinal, genitourinary, lung, haematologic, brain, endocrine glands, bone and soft tissue, and others	1-4	14 months, median	Active and completed	V2	Mandarin Chinese	FACT-G

Author (year)	Country	Study design	Sample size	Mean age (±SD) (* indicates median)	Female sex ratio	Cancer type	Cancer stage	Time since diagnosis	Treatment status	COST version	COST language	HRQOL instrument
Coroneos, et al. (2020)[56]	US	CS	532	58 ± 12	100%	Breast	0-3, undetermined	NR	Completed (Post-surgery)	V1	English	BREAST-Q and SF-12 (Only 1 out of 3 BREAST-Q domains used)
De Souza, et al. (2017)[57]	US	CS	233	58.42 ± 11.47	58.4%	American Joint Committee on Cancer Stage 4 solid tumour (incl. breast, gastrointestinal, head and neck, pancreatic, prostate, lung, and bladder)	4	<1 year (39%); >1 year (61%)	Active	V1	English	FACT-G and EORTC QLQ-C30
Durber, et al. (2021)[58]	Australia	CS	257	63*	54%	Breast, lung, skin, gastrointestinal, gynaecologic, central nervous system, urologic, head and neck, multiple cancers, sarcoma, and others	1-4, not staged	<1 year (48%), >1 year (52%)	Active and without	V1	English	FACT-G
Ehlers, et al. (2021)[59]	US	CS	226	68*	36%	Bladder	Noninvasive, invasive, metastatic	2 years (12%), 2-5 years (47%),>5 years (40%)	Active and in surveillance	V1	English	EQ-5D-5L
Esselen, et al. (2021)[60]	US	CS	334	55*	100%	Gynaecologic (ovarian, uterine, and cervical)	1-4	5 years, median	Active and in remission	V1	English	EQ-5D-3L
Gordon, et al. (2020)[61]	Australia	CS	204	58.7 ± 11.7	50%	Neuroendocrine tumour (incl. gastrointestinal, pancreatic, liver, and lung)	NR	<3 years (45%), >3 years (55%)	NR	V1	English	EQ-5D-5L

Author (year)	Country	Study design	Sample size	Mean age (±SD) (* indicates median)	Female sex ratio	Cancer type	Cancer stage	Time since diagnosis	Treatment status	COST version	COST language	HRQOL instrument
Hazell, et al. (2020)[62]	US	CS	131	65*	47.3%	Lung	2-4	NR	Active and newly diagnosed	V2	English	FACT-L
Kalra, et al. (2020)[63]	India	CS	147	38*	32.5%	Brain	1-4	NR	Active	V2	English	FACT-Br
Liang, et al. (2021)[64]	US	PC (6 months)	121	60	100%	Gynaecologic (ovarian, uterine, cervical, vulvar, and vaginal)	NR	NR	Active and completed	V1	English	FACT-G
Mady, et al. (2019)[65]	US	CS	104	64*	23.1%	Head and neck (larynx, oral cavity, and oropharynx)	1-4	NR	Completed	V1	English	UWQOL
McLean, et al. (2021)[66]	Australia	CS	53	63.5*	55%	Solid organ malignancy	Early and advanced	NR	Active	V1	English	EORTC QLQ-C30
Mejri, et al. (2021)[67]	Tunisia	CS	179	52 ± 12.3	70.9%	Breast, gastrointestinal, and lung	0-4	NR	Active	V1	Arabic	FACT-G

Author (year)	Country	Study design	Sample size	Mean age (±SD) (* indicates median)	Female sex ratio	Cancer type	Cancer stage	Time since diagnosis	Treatment status	COST version	COST language	HRQOL instrument
Miller, et al. (2021)[68]	US	CS	196	32.2± 4.5	40.1%	Gastrointestinal (colon and rectal)	1-4	NR	Active, completed, and in surveillance	V1	English	FACT-C
Pavela, et al. (2021)[69]	US	CS	2,755	NR	77.1%	American Joint Committee on Cancer Stage 4 solid tumour	4	NR	Active	V1	English	PROMIS Global-10
Petruzzi, et al. (2022)[70]	US	CS	115	54.6 ± 11.6	66%	Gastrointestinal, haematologic, breast, lung, and others	1-4	NR	Active	NR	English	FACT-G, PROMIS CAT (Anxiety, Depression, Fatigue, Pain Interference, and Physical Function)
Phillips, et al. (2021)[71]	US	CS	115	NR	57%	Gastrointestinal, haematologic, lung, and breast	1-4	0-6 months (28%), 7-18 months (23%), 19-35 months (26%), >36 months (23%)	Active	V1	English, Spanish	FACT-G
Ripamonti, et al. (2020)[72]	Italy	CS	118	61.46 ± 12.7	NR	Breast, lung, gastrointestinal, liver, endometrial, prostate, sarcoma, bladder, head and neck, lymphoma, leukemia, myeloma, and others	NR	NR	Active and completed	V1	Italian	EORTC QLQ-C30

Author (year)	**Country**	**Study design**	**Sample size**	**Mean age (±SD)** (* indicates median)	**Female sex ratio**	**Cancer type**	**Cancer stage**	**Time since diagnosis**	**Treatment status**	**COST version**	**COST language**	**HRQOL instrument**
Rosenzweig, et al. (2019)[73]	US	CS	145	58.1 ± 12.5	100%	Breast	4	NR	Active	V1	English	FACT-B
Shim, et al. (2021)[74]	South Korea	CS	4297	50.4 ± 8.6	100%	Breast	0-4	NR	Completed	V1	Korean	EORTC QLQ-C30
Thom, et al. (2021)[75]	US	CS	106	63.0 ± 12.54	43%	Melanoma	3-4	NR	Active and completed	V1	English	EORTC QLQ-C30
Urek and Ugurluoglu (2022)[76]	Turkey	CS	316	56*	42.1%	Gastrointestinal, haematologic, breast, lung, musculoskeletal system, and others	1-4, not staged	<15 months (49%), >15 months (51%)	Active	V1	Turkish	FACT-G
Ver Hoeve, et al. (2021)[77]	US	CS	103	67.28 ± 10.12	48%	Breast, gastrointestinal, head and neck, lung, and prostate	1-3	NR	Completed	V1	English	PROMIS-29
R.H. Xu, et al. (2022)[78]	China	CS	590	NR	44.7%	Liver, breast, kidney, gastrointestinal, thyroid, lung, oesophageal, cervical, bladder, lymphoma	NR	NR	Active, completed	V2	Mandarin Chinese	EQ-5D-5L

Author (year)	Country	Study design	Sample size	Mean age (±SD) (* indicates median)	Female sex ratio	Cancer type	Cancer stage	Time since diagnosis	Treatment status	COST version	COST language	HRQOL instrument
T. Xu, et al. (2022)[79]	China	CS	152	62.1*	46.7%	Lung	3-4	NR	NR	V1	Mandarin Chinese	FACT-L
Yu, et al. (2020)[80]	China	PC (6 months)	440	57.0 ± 9.2	54.30%	Lung, gastrointestinal, and breast	1-4	0-2 months	Active and completed	V1	Mandarin Chinese	WHOQOL-BREF
Yusuf, et al. (2022)[81]	US	CS	108	55*	100%	Breast	0-4	7.89 months, mean	Completed	V1	English	FACT-G7

Abbreviations
COST= Comprehensive Score for Financial Toxicity, HRQOL= health-related quality of life, V1= 11-item first version, V2= 12-item second version, CS= cross-sectional study design, PC: prospective cohort study design, NR: not reported, FACT= Functional Assessment of Cancer Therapy, FACT-P= FACT – Prostate cancer, SF-36= 36-Item Short Form Health Survey, FACT-G= FACT - General, EQ VAS= EuroQol Visual Analogue Scale, SF-12= 12-Item Short Form Health Survey, EORTC QLQ-C30= European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire, EQ-5D-5L= 5-level EQ-5D version, EQ-5D-3L= 3-level EQ-5D version, FACT-L= FACT - Lung cancer, FACT-Br= FACT - Brain cancer, UWQOL= University of Washington Quality of Life, FACT-C= FACT - Colorectal cancer, PROMIS= Patient-Reported Outcomes Measurement Information System, PROMIS Global-10, PROMIS 10-Item Global Health Survey, PROMIS CAT= PROMIS Computer Adaptive Tests, FACT-B= FACT - Breast cancer, PROMIS-29= PROMIS 29-Item Profile Measure, WHOQOL-BREF= World Health Organization Quality of Life Brief Version, FACT-G7: FACT-G - 7-Item Version

II.3.2 Characteristics of included studies

Table II.1 presents the complete overall study characteristics. The included studies were published between 2017 and 2022, with more than two-thirds of them published in 2021 or 2022 (n=21, 68%). Twenty-nine of the study designs were cross-sectional (94%) and the remaining two were prospective cohort studies with a follow-up period of six months (6%). The studies were conducted in the US (n=18, 58%), China (n=4, 13%), Australia (n=3, 10%), India (n=1, 3%), Italy (n=1, 3%), Nigeria (n=1, 3%), South Korea (n=1, 3%), Tunisia (n=1, 3%), and Turkey (n=1, 3%). The most used languages for the survey instruments were English (n=22, 71%) and Mandarin Chinese (n=5, 16%). The total patient sample size of all included studies was 13,481. The sample size of individual studies ranged from 53 to 4,297 with a median of 179. Among 17 studies (55%) that reported the mean age of respondents, the overall mean age was 57 years. There were eight studies (26%) that included only female respondents and one study (3%) that included only male respondents. The remaining 22 studies (71%) included both sexes.

The investigated cancer types varied widely. The most studied types of cancer included breast (n=17, 55%), lung (n=15, 48%), gastrointestinal (n=13, 42%), and gynaecologic (n=8, 26%). There were studies that recruited patients with different types of cancer (n=21, 68%), while others considered solely one type of cancer (n=10, 32%). Twenty-six of the studies (84%) recruited patients up to stage IV of cancer. Thirteen studies (42%) reported the time since cancer diagnosis that ranged from ‘between 0 and 2 months’ to ‘more than 5 years.’ Active or completed interventions that were reported in all the studies included chemotherapy (n=22, 71%), surgery (n=17, 55%), radiotherapy (n=15, 48%), hormone therapy (n=9, 29%), and immunotherapy (n=8, 26%).

Twenty-four studies measured financial toxicity using the 11-item first version of COST (77%), six studies used the 12-item second version (19%), and one study did not report the version. A total of 19 HRQoL instruments were identified from the included studies (Table II.2). These instruments can be categorised into three types: generic (n=9), cancer-specific (n=3), and condition-specific (n=7). EQ-5D was the most used generic HRQoL instrument (n=5, 16%), with the three-level (EQ-5D-3L) version used in one study, the five-level (EQ-5D-5L) version used in three studies, and one study used EQ VAS without the descriptive system. The most used cancer-specific HRQoL instruments were FACT-G (n=9, 29%) and EORTC QLQ-C30 (n=5, 16%). The most used condition-specific HRQoL instrument was FACT-L (n=2, 6%), which was developed for patients

Table II.2. HRQoL instruments and usage in the included studies

Type of instrument	Instrument name	Study (n)	Cancer type*													
			Brain	Breast	Endocrine	GI	Gynaecologic	HNC	Haematologic	Liver	Lung	MS	Prostate	Skin	Urologic	Others
Generic	EQ-5D-5L[59,61,78]	3		✓	✓	✓	✓	✓		✓	✓				✓	✓
	EQ-5D-3L[60]	1					✓									
	EQ VAS[54] (EQ-5D descriptive system not used)	1					✓									
	PROMIS-29[77]	1		✓		✓		✓			✓		✓			
	PROMIS CAT[70]	1		✓		✓			✓		✓					✓
	PROMIS Global-10[**69]	1														
	SF-12[56]	1		✓												
	SF-36[52]	1		✓		✓	✓	✓		✓	✓		✓	✓	✓	✓
	WHOQOL-BREF[80]	1		✓		✓					✓					
Cancer-specific	FACT-G[53,55,57,58,64,67,70,71,76]	9	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓
	EORTC QLQ-C30[57,66,72,74,75]	5		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
	FACT-G7[81]	1		✓												
Condition-specific	FACT-L[62,79]	2									✓					
	FACT-B[73]	1		✓												
	FACT-Br[63]	1	✓													
	FACT-C[68]	1				✓										
	FACT-P[51]	1											✓			
	BREAST-Q[56]	1		✓												
	UWQOL[65]	1						✓								

*Cancer types were grouped into larger categories, **Cancer type not reported

Abbreviations

EQ-5D-5L= 5-level EQ-5D version, EQ-5D-3L= 3-level EQ-5D version, EQ VAS= EuroQol Visual Analogue Scale, PROMIS= Patient-Reported Outcomes Measurement Information System, PROMIS-29= PROMIS 29-Item Profile Measure, PROMIS CAT= PROMIS Computer Adaptive Tests, PROMIS Global-10, PROMIS 10-Item Global Health Survey, SF-12= 12-Item Short Form Health Survey, SF-36= 36-Item Short Form Health Survey, WHOQOL-BREF= World Health Organization Quality of Life Brief Version, FACT= Functional Assessment of Cancer Therapy, FACT-G= FACT - General, EORTC QLQ-C30= European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire, FACT-G7: FACT-G - 7-Item Version, FACT-L= FACT - Lung cancer, FACT-B= FACT - Breast cancer, FACT-Br= FACT - Brain cancer, FACT-C= FACT - Colorectal cancer, FACT-P= FACT – Prostate cancer, UWQOL= University of Washington Quality of Life, GI= Gastrointestinal, HNC= Head and neck, MS= Musculoskeletal

with lung cancer.

II.3.3 Methodological quality of included studies

Figure II.2 presents the appraisal scores of each included study. The appraisal scores of the cross-sectional studies using AXIS ranged from 14 (70%) to 19 (95%) out of 20 (n=29, *M=16.2* [81%], *SD*=0.97 [4.9%]).

The two prospective cohort studies that were rated using CASP received scores of 10 (83%) and 11 (92%) out of 12, respectively. The three AXIS components in which most studies had unfavourable responses were (i) description of non-responders (n=26, 84%), (ii) measures to address and categorise non-responders (n=25, 81%), and (iii) justification of sample size (n=22, 71%). However, as every study had an AXIS or CASP score of greater than or equal to 70%, it can be concluded that all included studies had generally good methodological quality.

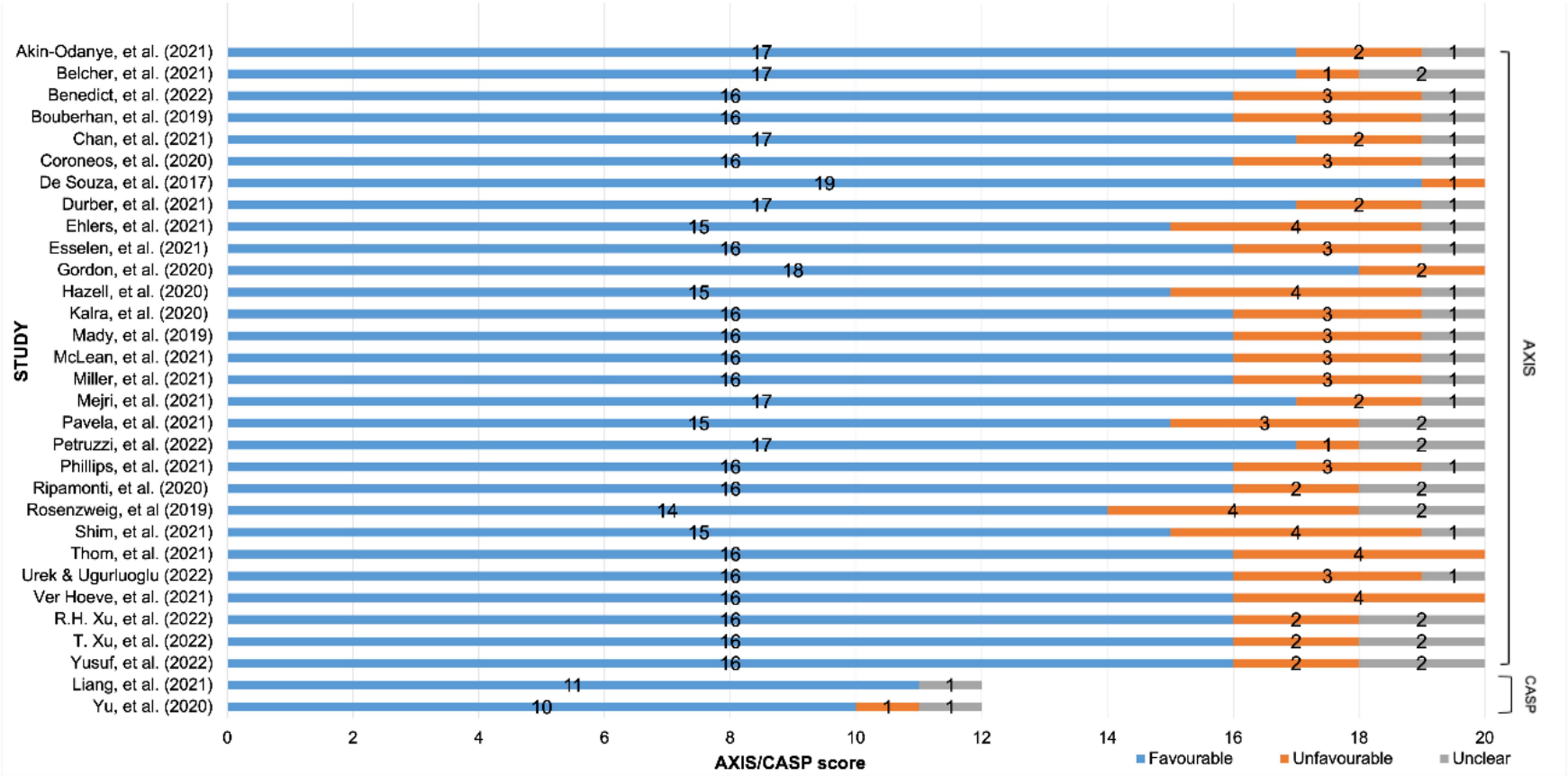
II.3.4 Qualitative synthesis

Table II.3 summarises the main findings and statistical analysis techniques used in the included studies. In assessing the association between financial toxicity and HRQoL, 16 studies (52%) performed univariate analysis, four studies (13%) performed multivariate analysis, and 11 (35%) performed both.

1. Univariate analyses

The univariate approaches used in the included studies consisted of correlation analysis (n=23, 74%), bivariate linear regression (n=5, 16%), Wilcoxon rank-sum test (n=2, 6%), and student's t-test (n=1, 3%). For correlation analysis, 17 studies used Pearson's correlation, three studies used Spearman's correlation, and three did not specify the type. All but one studies using univariate analyses,[68] reported a significant association between financial toxicity and HRQoL. Across the four studies that employed bivariate linear regressions to predict HRQoL from COST scores, none used the same HRQoL instruments: BREAST-Q and SF-12,[56] FACT-Br,[63] EORTC QLQ-C30,[66] FACT-C.[68] One study estimated a different model by regressing COST scores on FACT-G7.[81]

Figure II.2. Methodological quality assessment of the included studies



Abbreviations
AXIS, Appraisal tool for Cross-Sectional Sudies; CASP, Critical Appraisal Skills Program Cohort Study Checklist

Table II.3. Summary of findings of the included studies

Author (Year)	Main finding	Statistical analysis
Akin-Odanye, et al. (2021)[51]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-P correlation: r= 0.416 (p<0.01) - COST and FACT-P regression: B= 0.392, b =0.181 (p<0.05)	(i) Correlation (Unspecified) (ii) Multivariate linear regression (Hierarchical)
Belcher, et al. (2021)[52]	**Higher financial toxicity is associated with worse HRQOL** - COST and SF-36 Physical Functioning correlation: r= 0.062 (p= 0.599) - COST and SF-36 Role Limitations (Physical) correlation: r= 0.282 (p= 0.015) - COST and SF-36 Pain correlation: r= 0.320 (p= 0.005) - COST and SF-36 General Health correlation: r= 0.025 (p= 0.832) - COST and SF-36 Social Functioning correlation: r= 0.183 (p= 0.119) - COST and SF-36 Role Limitations (Emotional) correlation: r= 0.276 (p= 0.017) - COST and SF-36 Energy/Fatigue correlation: r= 0.014 (p= 0.236) - COST and SF-36 Emotional Well-Being correlation: r= 0.393 (p<0.001) - COST and SF-36 Role Limitations (Physical) regression: B= 1.31, b= 0.38 (p<0.01) - COST and SF-36 Pain regression: B= 1.03, b= 0.41 (p<0.01) - COST and SF-36 Role Limitations (Emotional) regression: B= 0.94, b= 0.23 (p= 0.104) - COST and SF-36 Emotional Well-Being regression: B= 0.65, b= 0.27 (p<0.05)	(i) Pearson's correlation (ii) Multivariate linear regression (Hierarchical)
Benedict, et al. (2022)[53]	**Higher financial toxicity is associated with worse HRQOL** COST and FACT-G regression: B= 0.88, b= 0.58 (p < 0.001)	Multivariate linear regression (Stepwise)
Bouberhan, et al. (2019)[54]	**Higher financial toxicity is associated with worse self-reported health** COST and EQ VAS correlation: r= 0.47 (p<0.001)	Spearman's correlation
Chan, et al. (2021)[55]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-G correlation: (r= -0.46 (p<0.001) - COST and FACT-G Physical Well-Being correlation: r= -0.34 (p<0.001) - COST and FACT-G Social/Family Well-Being correlation: r= -0.23 (p<0.001) - COST and FACT-G Emotional Well-Being correlation: r= -0.42 (p<0.001) - COST and FACT-G Functional Well-Being correlation: r= -0.39 (p<0.001)	Pearson's correlation
Coroneos, et al. (2020)[56]	**Higher financial toxicity is associated with worse HRQOL** *(i) Pearson* Entire Cohort - COST and BREAST-Q Psychosocial Well-Being correlation: r= 0.54 (p<0.0001) - COST and SF-12 Physical correlation: r= 0.41 (p<0.0001) - COST and SF-12 Mental: r= 0.52 (p<0.0001) Reconstruction sub-cohort - COST and BREAST-Q Psychosocial Well-Being correlation: r= 0.49 (p<0.0001) - COST and SF-12 Physical correlation: r= 0.43 (p<0.0001) - COST and SF-12 Mental correlation: r= 0.48 (p<0.0001) *(ii) Change in HRQOL (95%CI) per unit of COST score*	(i) Pearson's correlation (ii) Bivariate linear regression (iii) Multivariate linear regression

Author (Year)	Main finding	Statistical analysis
	Entire cohort - BREAST-Q Psychosocial Well-Being 0.99 (0.86-1.12) - SF-12 Physical 0.38 (0.31-0.46) - SF-12 Mental 0.49 (0.42-0.56) Reconstruction sub-cohort - BREAST-Q Psychosocial Well-Being 0.90 (0.73-1.07) - SF-12 Physical 0.39 (0.30-0.48) - SF-12 Mental 0.45 (0.36-0.55) *(iii) Change in HRQOL (95%CI) per unit of COST score* Entire cohort - BREAST-Q Psychosocial Well-Being 0.89 (0.76-1.03) - SF-12 Physical 0.32 (0.24-0.40) - SF-12 Mental 0.45 (0.38-0.52) Reconstruction sub-cohort - BREAST-Q Psychosocial Well-Being 0.80 (0.63-0.97) - SF-12 Physical 0.32 (0.23-0.41) - SF-12 Mental 0.37 (0.27-0.46)	
De Souza, et al. (2017)[57]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-G correlation: r= 0.42 (p<0.001) - COST and EORTC QLQ-C30 correlation: r= 0.33 (p<0.001)	Pearson's correlation
Durber, et al. (2021)[58]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-G correlation: r=0.53 (p<0.0001) - COST and FACT-G Physical Well-Being correlation: r=0.40 (p<0.0001) - COST and FACT-G Emotional Well-Being correlation: r=0.43 (p<0.0001) - COST and FACT-G Social Well-Being correlation: r= 0.18 (p<0.0001) - COST and FACT-G Functional Well-Being correlation: r= 0.35 (p<0.0001) - FACT-G Physical Well-Being and COST regression: b= 0.504, 95%CI 0.344-0.665 (p<0.0001) - FACT-G Emotional Well-Being and COST regression: b= 0.499, 95%CI 0.384-0.796 (p<0.0001) - FACT-G Functional Well-Being and COST regression: b= 0.442, 95%CI 0.264-0.62 (p<0.0001)	(i) Spearman's correlation (ii) Multivariate linear regression
Ehlers, et al. (2021)[59]	**Higher financial toxicity is associated with worse HRQOL** COST (M= 28.4) and EQ-5D-5L Wilcoxon rank-sum test (p<0.001)	Wilcoxon rank-sum test
Esselen, et al. (2021)[60]	**Higher financial toxicity is associated with worse HRQOL** COST and EQ-5D-3L correlation: r = 0.49 (p<0.001).	Spearman's correlation
Gordon, et al. (2020)[61]	**Higher financial toxicity is associated with worse HRQOL** COST and EQ-5D-5L: *Unadjusted scores (p<0.001)* - With financial toxicity: M= 0.47, 95%CI, 0.67-0.75 - No financial toxicity: M= 0.71, 95%CI 0.41-0.54 *Adjusted scores (p=0.01)*	(i) Student's t Test (ii) Generalized Linear Model

Author (Year)	Main finding	Statistical analysis
	- With financial toxicity: M= 0.53, 95%CI, 0.45-0.61 - No financial toxicity: M= 0.69, 95%CI, 0.65-0.73	
Hazell, et al. (2020)[62]	**Higher financial toxicity is associated with worse HRQOL** COST and FACT-L correlation: r=0.41 (p<0.0001)	Pearson's correlation
Kalra, et al. (2020)[63]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-Br TOI correlation (p<0.001) - COST and FACT-G correlation (p<0.001) - COST and FACT-Br Total correlation (p<0.001) - COST and FACT-Br TOI regression: beta= 2.4 - COST and FACT-G regression: beta= 2.0 - COST and FACT-Br Total regression: beta= 3.0	(i) Pearson's correlation (ii) Bivariate linear regression
Liang, et al. (2021)[64]	**Higher financial toxicity is associated with worse HRQOL** At baseline, 3 months, and 6 months: - COST and FACT-G correlations: r=0.63, r=0.61, r=0.60 - COST and FACT-G Physical Well-Being correlation: r=0.66, r=0.62, r=0.52 - COST and FACT-G Social Well-Being correlation: r= 0.30, r=0.33, r=0.37 - COST and FACT-G Emotional Well-Being correlation: r= 0.37, r=0.54, r=0.43 - COST and FACT-G Functional Well-Being correlation: r=0.42, r=0.47, and r=0.46	Correlation (Unspecified)
Mady, et al. (2019)[65]	**Higher financial toxicity is associated with worse HRQOL** COST and UWQOL regression: Roy's Greatest Root Value 0.08, F-value 3.61, beta= 0.47 (p= 0.03)	Multivariate linear regression
McLean, et al. (2021)[66]	**Higher financial toxicity is associated with worse HRQOL** - COST and EORTC QLQ-C30 correlation: r=0.73 - COST and EORTC QLQ-C30 regression: b= -0.90, p=0.004, 95%CI -1.51 -0.30	(i) Pearson's correlation (ii) Bivariate linear regression
Mejri, et al. (2021)[67]	**Higher financial toxicity is associated with worse HRQOL** COST and FACT-G correlation: r= 0.39 (p=0.047)	Pearson's correlation
Miller, et al. (2021)[68]	**Financial toxicity is not associated with HRQOL** - COST and FACT-C regression: b= 1.01 (p>0.10) - COST and FACT-C Emotional Well-Being regression: b= 0.33 (p>0.10) - COST and FACT-C Physical Well-Being regression: b= 0.32 (p>0.10) - COST and FACT-C Social Well-Being regression: b= -0.03 (p>0.10) - COST and FACT-C Functional Well-Being regression: b= 0.20 (p>0.10)	Bivariate linear regression
Pavela, et al. (2021)[69]	**Higher financial toxicity is associated with worse HRQOL** - COST and PROMIS-10 Physical Global Health correlation: r= 0.46 (p<0.0001) - COST and PROMIS-10 Mental Global Health correlation: r= 0.45 (p<0.0001) - COST and PROMIS-10 Physical Global Health regression: beta= 0.28 (p<0.0001) - COST and PROMIS-10 Mental Global Health regression: beta= 0.13 (p<0.0001)	(i) Pearson's correlation (ii) Multivariate linear regression
Petruzzi, et al. (2022)[70]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-G regression: b= 0.17 (p=0.008)	Multivariate linear regression

Author (Year)	Main finding	Statistical analysis
	- COST and PROMIS Anxiety regression: b= -0.08 (p=0.59) - COST and PROMIS Depression regression: b= 0.06 (p=0.69) - COST and PROMIS Fatigue regression: b= -0.2 (p=0.15) - COST and PROMIS Pain Interference regression: b= -0.06 (p=0.66) - COST and PROMIS Physical Function regression: b= -0.02 (p=0.9)	
Phillips, et al. (2021)[71]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-G regression for raw score: b=0.59 (p<0.01) - COST and FACT-G regression for US population standardised T-scores: b= 0.32 (p<0.01) - COST and FACT-G regression for adult cancer patients standardised T-scores: b= 0.34 (p<0.01)	Multivariate linear regression
Ripamonti, et al. (2020)[72]	**Higher financial toxicity is associated with worse HRQOL** COST and EORTC QLQ-C30 correlation: r= -0.52 (p<0.001)	Pearson's correlation
Rosenzweig, et al. (2019)[73]	**Higher financial toxicity is associated with worse HRQOL** COST and FACT-B correlation: r=0.56 (p<0.0001)	Pearson's correlation
Shim, et al. (2021)[74]	**Higher financial toxicity is associated with worse HRQOL:** - COST and EORTC QLQ-C30 Global Health Status correlation: r= 0.36 - COST and EORTC QLQ-C30 Physical Functioning correlation: r= 0.30 - COST and EORTC QLQ-C30 Role Functioning correlation: r= 0.32 - COST and EORTC QLQ-C30 Emotional Functioning correlation: r= 0.37 - COST and EORTC QLQ-C30 Cognitive Functioning correlation: r= 0.30 - COST and EORTC QLQ-C30 Social Functioning correlation: r= 0.44 - COST and EORTC QLQ-C30 Fatigue correlation: r= -0.30 - COST and EORTC QLQ-C30 Nausea and Vomiting correlation: r= -0.18 - COST and EORTC QLQ-C30 Pain correlation: r= -0.26 - COST and EORTC QLQ-C30 Dyspnea correlation: r= -0.21 - COST and EORTC QLQ-C30 Sleep Disorder correlation: r= -0.21 - COST and EORTC QLQ-C30 Appetite Loss correlation: r= -0.16 - COST and EORTC QLQ-C30 Constipation correlation: r= -0.14 - COST and EORTC QLQ-C30 Diarrhea correlation: r= -0.14 *p-values not reported	Pearson's correlation
Thom, et al. (2021)[75]	**Higher financial toxicity is associated with worse HRQOL** - COST and EORTC QLQ-C30 Global Health Status correlation: r= 0.44 (p<0.001) - COST and EORTC QLQ-C30 Social correlation: r= 0.55 (p<0.001) - COST and EORTC QLQ-C30 Emotional correlation: r= 0.45 (p<0.001) - COST and EORTC QLQ-C30 Physical correlation: r= 0.33 (p<0.001) - COST and EORTC QLQ-C30 Role correlation: r= 0.52 (p<0.001) - COST and EORTC QLQ-C30 Cognitive correlation: r= 0.22 (p<0.001) *Partial correlation, when controlling for age:* - COST and EORTC QLQ-C30 Global Health Status correlation: r= 0.11 (p=0.03) - COST and EORTC QLQ-C30 Financial Difficulties correlation: r=0.62 (p<0.001)	(i) Pearson's correlation (ii) Partial Correlation

Author (Year)	Main finding	Statistical analysis
	- COST and EORTC QLQ-C30 Social correlation: r=0.34 (p<0.001) - COST and EORTC QLQ-C30 Emotional correlation: r=0.22 (p=0.03) - COST and EORTC QLQ-C30 Role correlation: r=0.26 (p<0.01)	
Urek and Ugurluoglu (2022)[76]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-G Physical Well-Being correlation r= 0.405 (p<0.001) - COST and FACT-G Social/Family Well-Being correlation r= 0.160 (p<0.001) - COST and FACT-G Emotional Well-Being correlation r= 0.344 (p<0.001) - COST and FACT-G Functional Well-Being correlation r= 0.226 (p<0.001) - COST and FACT-G regression: b= 0.389 (p<0.001)	(i) Pearson's correlation (ii) Multivariate linear regression
Ver Hoeve, et al. (2021)[77]	**Higher financial toxicity is associated with worse HRQOL** - COST and PROMIS-29 Anxiety correlation: r= -0.34 (p=0.001) - COST and PROMIS-29 Depression correlation: r= -0.21 (p=0.031) - COST and PROMIS-29 Fatigue correlation: = -0.41, (p=0.000) - COST and PROMIS-29 Sleep correlation: r= -0.25 (p=0.010) - COST and PROMIS-29 Pain correlation: r= -0.27 (p=0.006) - COST and PROMIS-29 Physical Functioning correlation: r= 0.31 (p=0.001) - COST and PROMIS-29 Social Functioning correlation: r= -0.31 (p=0.002) - COST and PROMIS-29 Anxiety regression: B= -0.09, b= -0.28 (p=0.012) - COST and PROMIS-29 Fatigue regression: B= -0.16, b= -0.16 (p=0.001) - COST and PROMIS-29 Pain interference regression: B= -0.07, b= -0.07 (p=0.206) - COST and PROMIS-29 Physical Functioning regression: B= 0.11, b= 0.11 (p=0.020) - COST and PROMIS-29 Social Functioning regression: B= -0.17, b=-0.17 (=0.013)	(i) Pearson's correlation (ii) Multivariate linear regression
R.H. Xu, et al. (2022)[78]	**Higher financial toxicity is associated with worse HRQOL** (i) Wilcoxon rank-sum test *COST and physical dimensions of EQ-5D-5L (p<0.001):* - Mobility: no problem (M=14.8), some problems (M= 11) - Self-Care: no problem (M=14.9), some problems (M= 10.2) - Usual Activities: no problem (M=15.6), some problems (M= 10.4) - Pain/Discomfort: no problem (M= 17.1), some problems (M= 17.4) (ii) Latent class analysis *Divided into four classes based on their health statuses measured using four physical dimensions of EQ-5D-5L (mobility, self-care, usual activities, and pain/discomfort) and three subscales of DASS-21 (depression, anxiety, and stress); Class 1: low physical and psychological (M= 11.9), Class 2: high physical and low psychological (M= 10.9), Class 3: low physical and high psychological (M= 8.1), Class 4: high physical and psychological (M= 16.9)* -COST and the four latent classes (p<0.001)	(i) Wilcoxon rank-sum test (ii) Latent class analysis
T. Xu, et al. (2022)[79]	**Higher financial toxicity is associated with worse HRQOL** COST and FACT-L correlation: r= 0.44 (p<0.0001)	Pearson's correlation

Author (Year)	Main finding	Statistical analysis
Yu, et al. (2020)[80]	**Higher financial toxicity is associated with worse HRQOL** COST and WHOQOL-BREF correlation: r= 0.34 (p<0.01)	Correlation (Unspecified)
Yusuf, et al. (2022)[81]	**Higher financial toxicity is associated with worse HRQOL** - COST and FACT-G7 correlation: r= 0.617 (p<0.0001) - COST and FACT-G7 bivariate regression: beta= 0.973 (p<0.0001) - COST and FACT-G7 multivariate regression: beta= 0.874 (p<0.0001)	(i) Pearson's correlation (ii) Bivariate linear regression (iii) Multivariate linear regression

Abbreviations

B= unstandardised coefficient, b= standardised coefficient, beta= not indicated whether standardised or not, COST= Comprehensive Score for Financial Toxicity, HRQOL= health-related quality of life, M= mean score of COST, FACT= Functional Assessment of Cancer Therapy, FACT-P= FACT – Prostate cancer, SF-36= 36-Item Short Form Health Survey, FACT-G= FACT - General, EQ VAS= EuroQol Visual Analogue Scale, SF-12= Short Form Health Survey, EORTC QLQ-C30= European Organisation for Research and Treatment of Cancer Core Quality of Life Questionnaire, EQ-5D-5L= 5-level EQ-5D version, EQ-5D-3L= 3-level EQ-5D version, FACT-L= FACT - Lung cancer, FACT-Br= FACT - Brain cancer, UWQOL= University of Washington Quality of Life, FACT-C= FACT - Colorectal cancer, PROMIS= Patient-Reported Outcomes Measurement Information System, PROMIS Global-10, PROMIS 10-Item Global Health Survey, PROMIS CAT= PROMIS Computer Adaptive Tests, FACT-B= FACT - Breast cancer, PROMIS-29= PROMIS 29-Item Profile Measure, DASS-21, Depression= Anxiety= and Stress Scale – 21 Items, WHOQOL-BREF= World Health Organization Quality of Life Brief Version, FACT-G7: FACT-G - 7-Item Version

2. Multivariate analyses

Among multivariate approaches, multivariate linear regression (n=12, 39%), generalised linear model (n=1, 3%), partial correlation (n=1, 3%), and latent class analysis (n=1, 3%) were performed in the included studies. All these studies reported significantly better HRQoL in cancer patients with lower financial toxicity. Nine studies reported financial toxicity as a significant predictor of HRQoL using multivariate regression models.[51-53,56,61,65,71,76,77] For instance, every one-point increase in COST score, which indicated less financial toxicity, improved HRQoL scores measured with different instruments by 0.59 points (FACT-G),[71] 0.47 points (UWQOL),[65] and 0.39 points (FACT-P).[51] All these regression models were adjusted for socio-demographic factors. These included age,[51-53,56,61,65,71,76,77] employment status,[53,56,76,77] education,[51,53,76,77] race,[52,53,71] sex,[71,77] (loss of) income,[65,71] and marital status.[51,76] Further, in several studies the regression models were controlled for clinical variables, such as comorbidities,[51,61] cancer type,[71,76] cancer stage,[53,71] and cancer recurrence.[53,71] Four other studies estimated multivariate regression models differently by using HRQoL to predict financial toxicity.[58,69,70,81] One study determined the association between COST and EORTC QLQ-C30 using partial correlation while controlling for patients' age.[75] Another study used latent class analysis to compare COST scores of patients grouped into four latent classes based on EQ-5D-5L responses.[78]

3. Qualitative synthesis of correlations

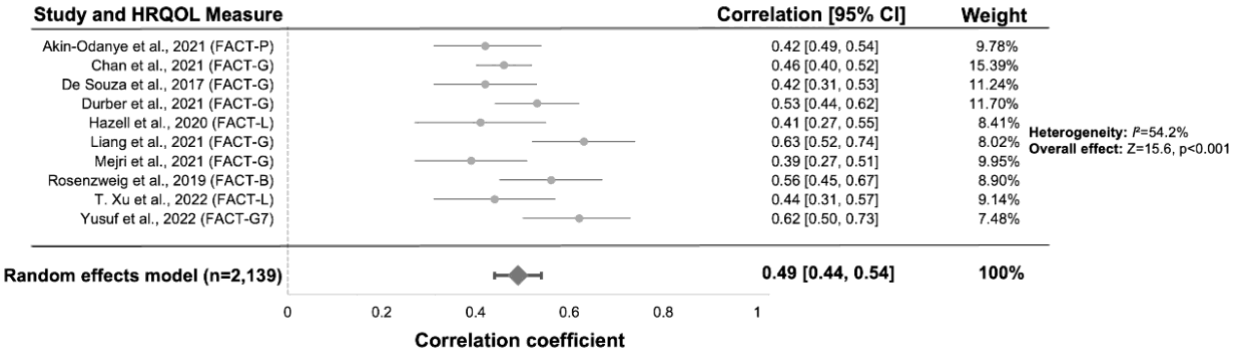
Ten studies (32%) reported correlations between COST and any HRQoL domain scores (Appendix II.2). Ten HRQoL domains were included in these correlation analyses: physical health (r=0.34-0.66), social health (r=0.16-0.55), mental health (r=0.21-0.54), daily functioning (r=0.23-0.52), global health (r=0.03-0.44), fatigue (r=0.01-0.41), physical functioning (r=0.06-0.33), pain (r=0.26-0.32), cognitive functioning (r=0.22-0.30), and sleep (r=0.21-0.25).

II.3.5 Quantitative synthesis

Meta-analysis was only possible for overall HRQoL scores. Ten studies involving 2,139 patients measured the association between financial toxicity and overall HRQoL using the following cancer-specific and condition-specific instruments: FACT-G, FACT-

G7, FACT-B, FACT-L, and FACT-P. A random-effects meta-analysis was performed with moderate heterogeneity being present in the model (I-squared=60%). The p-value for Egger's regression was 0.638, which indicated no publication bias. The pooled correlation coefficient was moderate (*r*=0.49, 95%CI: 0.44-0.54) (Figure II.3).

Figure II.3. Meta-analysis on the correlations between financial toxicity (COST) and HRQoL scores



Abbreviations
COST: Comprehensive Score for Financial Toxicity; FACT: Functional Assessment of Cancer Therapy; FACT-B: FACT - Breast; FACT-G: FACT - General; FACT-G7: FACT-G 7-Item Version; FACT-L: FACT - Lung; FACT-P: FACT - Prostate; HRQoL: health-related quality of life

II.4 DISCUSSION

This is the first systematic review to summarise the published literature on the association of HRQoL and subjective financial toxicity using the COST measure in cancer patients and survivors, as well as the first to conduct a meta-analysis on these outcomes. We included 31 studies in the qualitative synthesis and 10 studies in the meta-analysis. Overall, these studies involved more than 13,000 patients and survivors from nine countries of four continents diagnosed with more than 25 types of cancer. All included studies had a generally good methodological quality and were published in the past five years, with more than two-thirds published in 2021-22.

The studies used 19 validated HRQoL instruments, of which the most common was the cancer-specific FACT-G used in nine studies. All but one included studies reported that higher financial toxicity was significantly associated with worse HRQoL. We demonstrated a moderate correlation between financial toxicity and overall HRQoL through meta-analysis. We identified 10 HRQoL domains that were related to financial toxicity, namely mental health, daily functioning, social health, physical health, physical

functioning, global health, pain, fatigue, cognitive functioning, and sleep. This aligns well with findings of previous studies that reported an association between financial toxicity and a range of clinical symptoms known to be related to the mental and physical domains of HRQoL, such as depression, anxiety, and pain severity.[31] Further, health utilities were estimated in three out of five studies that measured HRQoL using EQ-5D instruments.[59-61] Findings of these studies suggest that there is a significant association between financial toxicity and utility loss, and therefore, it may be possible that the mitigation of financial toxicity improves quality-adjusted life year gains in cancer patients and survivors.

The linear regression models used in numerous studies indicated financial toxicity as a predictor of HRQoL. As both financial toxicity and HRQoL are influenced by socio-demographic factors, one may conclude that the association identified between the two constructs is attributable to these variables. However, in our review, there were nine studies reporting HRQoL to be significantly predicted by financial toxicity after adjusting for several socio-demographic characteristics. Future research is warranted to further explore for the potential effect of these individual characteristics.

There are some distinctive findings from the included studies. First, one study in the US failed to detect a significant association between financial toxicity and HRQoL in colorectal patients, using FACT-C.[68] Despite the results being insignificant, the association between COST and FACT-C was as expected indicating a decline in HRQoL with higher financial toxicity outcomes. Interestingly, this was the only study to focus on young adults with a mean age of 32 (range=20-42). Second, four studies regressed financial toxicity on HRQoL outcomes and not *vice versa*. Among them there were two studies that aimed to validate COST, i.e., a test of construct validity in Australia or the US.[58,69] Third, among the studies carried out in patients that completed treatment, one study in South Korea exclusively recruited recovered breast cancer patients.[74] This indicates that COST may also be used outside its original target population and sheds light on possible further implications such as experiencing financial toxicity after remission.

Our systematic review pointed out gaps in the existing literature. Most of the included studies were from the US and the most common languages used for COST administration were English and Mandarin Chinese, whereas there were only two studies from Europe and two from Africa. More evidence is needed from other countries to better

represent different populations. Additionally, only two longitudinal studies were identified. More longitudinal investigations are required to understand the dynamics of financial toxicity during the disease course and its impact on HRQoL. Interestingly, our included studies showed that the correlation strengths between financial toxicity and overall HRQoL were slightly stronger in studies that utilised English instruments (median=0.53, range=0.33-0.73),[57,58,60,62,64,66,73,81] compared to those in other languages, e.g., Mandarin Chinese, Italian, and Arabic (median=0.43, range=0.34-0.52),[51,55,67,72,79,80] and conducted in countries with universal health coverage (median=0.49, range=0.34-0.73),[55,58,66,72,79,80] compared to those without (median=0.42, range=0.33-0.63).[51,57,60,62,64,67,73,81] However, we had inadequate number of studies to further examine (e.g., performing subgroup analysis) the potential impact of instrument language or universal health coverage on the association between financial toxicity HRQoL.[46] Exploring the role of universal health coverage and mitigation strategies in alleviating financial toxicity and improving HRQoL may be an important future research direction. Some possible strategies include coverage for direct and indirect healthcare costs, patient assistance programs through industry or charity, and financial navigation programs.[82] In addition, previous investigations suggest that income loss due to cancer may be explained by the decline of productivity or job loss,[83-86] which also occurs in countries with universal health coverage and may even lead to widening economic inequalities.[87,88] Considering that subjective financial toxicity is contingent upon its objective counterpart, improvements may also be made by compensating the negative income effects of cancer. One plausible way to achieve this is by developing income protection and employment reintegration programs for patients and survivors.

This systematic review has a few limitations. Even though we provided evidence of moderate correlation between financial toxicity and HRQoL, the moderate heterogeneity calls for a more cautious interpretation of the meta-analysis results. The generalisability of our findings may be limited to the observed patient groups in the included studies. Some very likely sources of heterogeneity in our pooled model include a variety of individual (e.g., age, ethnicity, and cancer type and stage) as well as country-related characteristics (e.g., health insurance system and social support availability). Ideally, techniques such as meta-regression or subgroup analysis would be further conducted to precisely identify the cause of heterogeneity. However, they were not feasible due to the low number of studies.[46] The covariates of interests (e.g., income and

ethnicity) for modelling were also unevenly distributed and insufficiently reported across the included studies. Future research may focus on the association between financial toxicity and HRQoL by considering cross-country differences, e.g., health payment system and cultural specificity, while also accounting for socio-demographic variables and the use of different HRQoL measures.

II.5 CONCLUSIONS

To conclude, we provided a summary of the increasing body of literature on financial toxicity and its association with HRQoL in cancer patients and survivors. Several HRQoL domains, including physical, mental, and social health, were found to be related to financial toxicity. Through meta-analysis, we demonstrated financial toxicity to be moderately correlated with overall HRQoL. Our findings contribute to the understanding of the burden cancer patients experience and confirm financial toxicity as a relevant adverse outcome of cancer care.

References

1 Bray F, Laversanne M, Weiderpass E et al. The ever-increasing importance of cancer as a leading cause of premature death worldwide. *Cancer.* 2021;127(16):3029-3030.

2 Kocarnik JM, Compton K, Dean FE et al. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis for the global burden of disease study 2019. *JAMA.* 2021. Online ahead of print. https://doi.org/10.1001/jamaoncol.2021.6987.

3 Vos T, Lim S, Abbafati C et al. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet.* 2020;396(10258):1204-1222.

4 Sung H, Ferlay J, Siegel RL et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209-249.

5 Landrigan PJ, Fuller R, Acosta NJR et al. The Lancet Commission on pollution and health. *Lancet.* 2018;391(10119):462-512.

6 Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: understanding and stepping-up action on the financial toxicity of cancer treatment. *CA Cancer J Clin.* 2018;68(2):153-165.

7 Gordon LG, Merollini KMD, Lowe A et al. A systematic review of financial toxicity among cancer survivors: we can't pay the co-pay. *Patient.* 2017;10(3):295-309.

8 Longo CJ, Fitch MI, Banfield L et al. Financial toxicity associated with a cancer diagnosis in publicly funded healthcare countries: a systematic review. *Support Care Cancer.* 2020;28(10):4645-4665.

9 Zafar SY, Abernethy AP. Financial toxicity, part I: a new name for a growing problem. *Oncology (Williston Park).* 2013;27(2):80-81,149.

10 Park J, Look KA. Relationship between objective financial burden and the health-related quality of life and mental health of patients with cancer. *J Oncol Pract.* 2018;14(2):e113-e121.

11 Chino F, Peppercorn J, Taylor DH, Jr. et al. Self-reported financial burden and satisfaction with care among patients with cancer. *Oncologist.* 2014;19(4):414-420.

12 Baddour K, Fadel M, Zhao M et al. The cost of cure: examining objective and subjective financial toxicity in head and neck cancer survivors. *Head Neck.* 2021;43(10):3062-3075.

13 Prawitz A, Garman ET, Sorhaindo B et al. InCharge Financial distress/Financial Well-Being scale: development, administration, and score interpretation. *J Financial Couns Plan.* 2006;17(1):34-50.

14 Given B, Given C, Stommel M. Family and out-of-pocket costs for women with breast cancer. *Cancer Pract.* 1994;2(3):187-193.

15 Head BA, Faul AC. Development and validation of a scale to measure socioeconomic well-being in persons with cancer. *J Support Oncol.* 2008;6(4):183-192.

16 de Souza JA, Yap BJ, Hlubocky FJ et al. The development of a financial toxicity patient-reported outcome in cancer: the COST measure. *Cancer.* 2014;120(20):3245-3253.

17 Hueniken K, Douglas CM, Jethwa AR et al. Measuring financial toxicity incurred after treatment of head and neck cancer: development and validation of the Financial Index of Toxicity questionnaire. *Cancer.* 2020;126(17):4042-4050.

18 Sitlinger A, Zafar SY. Health-related quality of life: the impact on morbidity and mortality. *Surg Oncol Clin N Am.* 2018;27(4):675-684.

19 Calman KC. Quality of life in cancer patients--an hypothesis. *J Med Ethics.* 1984;10(3):124-127.

20 Donovan K, Sanson-Fisher R, Redman S. Measuring quality of life in cancer patients. *J Clin Oncol.* 1989;7(7):959-968.

21 Bottomley A. The cancer patient and quality of life. *Oncologist.* 2002;7(2):120-125.

22 Boby JM, Rajappa S, Mathew A. Financial toxicity in cancer care in India: a systematic review. *Lancet Oncol.* 2021;22(12):e541-e549.

23 Smith GL, Lopez-Olivo MA, Advani PG et al. Financial burdens of cancer treatment: a systematic review of risk factors and outcomes. *J Natl Compr Canc Netw.* 2019;17(10):1184-1192.

24 Bhanvadia SK, Psutka SP, Burg ML et al. Financial toxicity among patients with prostate, bladder, and kidney cancer: a systematic review and call to action. *Eur Urol Oncol.* 2021;4(3):396-404.

25 Zhu Z, Xing W, Zhang X et al. Cancer survivors' experiences with financial toxicity: A systematic review and meta-synthesis of qualitative studies. *Psycho-Oncology.* 2020;29(6):945-959.

26 Casilla-Lennon MM, Choi SK, Deal AM et al. Financial toxicity among patients with bladder cancer: reasons for delay in care and effect on quality of life. *J Urol.* 2018;199(5):1166-1173.

27 Ting CY, Teh GC, Yu KL et al. Financial toxicity and its associations with health-related quality of life among urologic cancer patients in an upper middle-income country. *Support Care Cancer.* 2020;28(4):1703-1715.

28 Netemeyer RG, Warmath D, Fernandes D et al. How am I doing? Perceived financial well-being, its potential antecedents, and its relation to overall well-being. *J Consum Res.* 2017;45(1):68-89.
29 Brüggen EC, Hogreve J, Holmlund M et al. Financial well-being: a conceptualization and research agenda. *J Bus Res.* 2017;79:228-237.
30 Mols F, Tomalin B, Pearce A et al. Financial toxicity and employment status in cancer survivors: a systematic literature review. *Support Care Cancer.* 2020;28(12):5693-5708.
31 Chan RJ, Gordon LG, Tan CJ et al. Relationships between financial toxicity and symptom burden in cancer survivors: a systematic review. *J Pain Symptom Manage.* 2019;57(3):646-660.e641.
32 Xu B, Hu L, Cheng Q et al. A systematic review of financial toxicity among cancer patients in China. *Asia-Pac J Oncol Nurs.* 2022. Online ahead of print. https://doi.org/10.1016/j.apjon.2022.04.010.
33 Witte J, Mehlis K, Surmann B et al. Methods for measuring financial toxicity after cancer diagnosis and treatment: a systematic review and its implications. *Ann Oncol.* 2019;30(7):1061-1070.
34 Zhu Z, Xing W, Lizarondo L et al. Psychometric properties of self-reported financial toxicity measures in cancer survivors: a systematic review protocol using COSMIN methodology. *BMJ Open.* 2020;10(5):e036365.
35 Moher D, Liberati A, Tetzlaff J et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.* 2009;6(7):e1000097.
36 National Library of Medicine. Search Strategy Used to Create the PubMed Cancer Filter. NLM, 2019. Available at https://www.nlm.nih.gov/bsd/pubmed_subsets/cancer_strategy.html. Accessed October 6, 2021.
37 Arber M, Garcia S, Veale T et al. Performance of Ovid Medline search filters to identify health state utility studies. *Int J Technol Assess Health Care.* 2017;33(4):472-480.
38 van Roij J, Fransen H, van de Poll-Franse L et al. Measuring health-related quality of life in patients with advanced cancer: a systematic review of self-administered measurement instruments. *Qual Life Res.* 2018;27(8):1937-1955.
39 Downes MJ, Brennan ML, Williams HC et al. Development of a critical appraisal tool to assess the quality of cross-sectional studies (AXIS). *BMJ Open.* 2016;6(12):e011458.
40 Critical Appraisal Skills Programme. CASP Cohort Study Checklist. 2018. Available at https://casp-uk.net/casp-tools-checklists/. Accessed January 6, 2022.
41 Rovito MJ, Bruzzone A, Lee E et al. Assessing health-related quality of life among survivors of testicular cancer: a systematic review. *Am J Mens Health.* 2021;15(1):1557988320982184.
42 Fisher RA. Frequency distribution of the values of the correlation coefficient in samples from an indefinitely large population. *Biometrika.* 1915;10(4):507-521.
43 Hedges LV, Olkin I. Nonparametric estimators of effect size in meta-analysis. *Psychol Bull.* 1984;96(3):573.
44 Evans JD. Straightforward statistics for the behavioral sciences: Thomson Brooks/Cole Pub Co, Pacific Grove, 1996.
45 Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med.* 2002;21(11):1539-1558.
46 Deeks JJ, Higgins JP, Altman DG et al. Analysing data and undertaking meta-analyses. Cochrane Handbook for Systematic Reviews of Interventions, 2019; 241-284.
47 Viechtbauer W. Bias and efficiency of meta-analytic variance estimators in the random-effects model. *J Educ Behav Stat.* 2005;30(3):261-293.
48 Langan D, Higgins JP, Jackson D et al. A comparison of heterogeneity variance estimators in simulated random-effects meta-analyses. *Res Synth Methods.* 2019;10(1):83-98.
49 Sterne JAC, Sutton AJ, Ioannidis JPA et al. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. *BMJ.* 2011;343:d4002.
50 The Jamovi Project. The Jamovi (Version 1.6). 2021. Available at https://www.jamovi.org. Accessed January 4, 2022.
51 Akin-Odanye EO, Ogo CN, Sulaiman FA et al. Examining the influence of illness perception and financial toxicity on the quality of life of prostate cancer patients. *Afr J Urol.* 2021;27(1):1-8.
52 Belcher SM, Lee H, Nguyen J et al. Financial hardship and quality of life among patients with advanced cancer receiving outpatient palliative care: a pilot study. *Cancer Nurs.* 2021. Online ahead of print. https://doi.org/10.1097/ncc.0000000000001052.
53 Benedict C, Fisher S, Schapira L et al. Greater financial toxicity relates to greater distress and worse quality of life among breast and gynecologic cancer survivors. *Psychooncology.* 2022;31:9-20.
54 Bouberhan S, Shea M, Kennedy A et al. Financial toxicity in gynecologic oncology. *Gynecol Oncol.* 2019;154(1):8-12.

55 Chan DNS, Choi KC, Ng MSN et al. Translation and validation of the Traditional Chinese version of the Comprehensive Score for Financial Toxicity-Functional Assessment of Chronic Illness Therapy (Version 2). *Health Qual Life Outcomes.* 2021;19(1):17.
56 Coroneos CJ, Lin YL, Sidey-Gibbons C et al. Correlation between financial toxicity, quality of life, and patient satisfaction in an insured population of breast cancer surgical patients: a single-institution retrospective study. *J Am Coll Surg.* 2021;232(3):253-263.
57 de Souza JA, Yap BJ, Wroblewski K et al. Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the Comprehensive Score for Financial Toxicity (COST). *Cancer.* 2017;123(3):476-484.
58 Durber K, Halkett GK, McMullen M et al. Measuring financial toxicity in Australian cancer patients - Validation of the Comprehensive Score for Financial Toxicity (FACT COST) measuring financial toxicity in Australian cancer patients. *Asia Pac J Clin Oncol.* 2021;17(4):377-387.
59 Ehlers M, Bjurlin M, Gore J et al. A national cross-sectional survey of financial toxicity among bladder cancer patients. *Urol Oncol.* 2021;39(1):76e71-76e77.
60 Esselen KM, Stack-Dunnbier H, Gompers A et al. Crowdsourcing to measure financial toxicity in gynecologic oncology. *Gynecol Oncol.* 2021;161(2):595-600.
61 Gordon LG, Elliott TM, Wakelin K et al. The economic impact on Australian patients with neuroendocrine tumours. *Patient.* 2020;13(3):363-373.
62 Hazell SZ, Fu W, Hu C et al. Financial toxicity in lung cancer: an assessment of magnitude, perception, and impact on quality of life. *Ann Oncol.* 2020;31(1):96-102.
63 Kalra D, Menon N, Singh GK et al. Financial toxicities in patients receiving systemic therapy for brain tumors: a cross-sectional study. *Cancer Res Stat Treat.* 2020;3(4):724-729.
64 Liang MI, Summerlin SS, Blanchard CT et al. Measuring financial distress and quality of life over time in patients with gynecologic cancer-making the case to screen early in the treatment course. *JCO Oncol Pract.* 2021;17(10):e1576-e1583.
65 Mady LJ, Lyu L, Owoc MS et al. Understanding financial toxicity in head and neck cancer survivors. *Oral Oncol.* 2019;95:187-193.
66 McLean L, Hong W, McLachlan SA. Financial toxicity in patients with cancer attending a public Australian tertiary hospital: a pilot study. *Asia Pac J Clin Oncol.* 2021;17(3):245-252.
67 Mejri N, Rachdi H, Mnif A et al. Translation and validation of the Comprehensive Score of Financial Toxicity for cancer patients into Arabic. *J Nurs Meas.* 2021. Online ahead of print. https://doi.org/10.1891/JNM-D-20-00140.
68 Miller KA, Stal J, Gallagher P et al. Time from diagnosis and correlates of health-related quality of life among young adult colorectal cancer survivors. *Cancers (Basel).* 2021;13(16):4045.
69 Pavela G, Fifolt M, Tison S et al. Re-validation of the Comprehensive Score for Financial Toxicity (COST): assessing the scale's utility in chronic disease populations. *Health Serv Insights.* 2021;14:1-7.
70 Petruzzi LJ, Prezio E, Phillips F et al. An exploration of financial toxicity among low-income patients with cancer in Central Texas: a mixed methods analysis. *Palliat Support Care.* 2022;1-11.
71 Phillips F, Prezio E, Miljanic M et al. Patient reported outcomes affecting quality of life in socioeconomically disadvantaged cancer patients. *J Psychosoc Oncol.* 2021;1-16.
72 Ripamonti CI, Chiesi F, Di Pede P et al. The validation of the Italian version of the Comprehensive Score for Financial Toxicity (COST). *Support Care Cancer.* 2020;28(9):4477-4485.
73 Rosenzweig M, West M, Matthews J et al. Financial toxicity among women with metastatic breast cancer. *Oncol Nurs Forum.* 2019;46(1):83-91.
74 Shim S, Kang D, Kim N et al. Validation of Korean version of the Comprehensive Score for Financial Toxicity (COST) among breast cancer survivors. *Cancer Res Treat.* 2021. Online ahead of print. https://doi.org/10.4143/crt.2021.784.
75 Thom B, Mamoor M, Lavery JA et al. The experience of financial toxicity among advanced melanoma patients treated with immunotherapy. *J Psychosoc Oncol.* 2021;39(2):285-293.
76 Urek D, Ugurluoglu O. Predictors of financial toxicity and its associations with health-related quality of life and treatment non-adherence in Turkish cancer patients. *Support Care Cancer.* 2022;30(1):865-874.
77 Ver Hoeve ES, Ali-Akbarian L, Price SN et al. Patient-reported financial toxicity, quality of life, and health behaviors in insured US cancer survivors. *Support Care Cancer.* 2021;29(1):349-358.
78 Xu RH, Wang L-l, Zhou L-m et al. Urban-rural differences in financial toxicity and its effect on cancer survivors' health-related quality of life and emotional status: a latent class analysis. *Support Care Cancer.* 2022. Online ahead of print. https://doi.org/10.1007/s00520-021-06762-0.
79 Xu T, Xu L, Xi H et al. Assessment of financial toxicity among patients with advanced lung cancer in Western China. *Front Public Health.* 2021;9:754199.

80 Yu HH, Yu ZF, Li H et al. The Comprehensive Score for Financial Toxicity in China: validation and responsiveness. *J Pain Symptom Manage.* 2021;61(6):1297-1304.e1291.
81 Yusuf M, Pan J, Rai SN et al. Financial toxicity in women with breast cancer receiving radiation therapy: final results of a prospective observational study. *Pract Radiat Oncol.* 2021. Online ahead of print. https://doi.org/10.1016/j.prro.2021.11.003.
82 Arastu A, Hamilton A, Chen EY-s. Interventions to alleviate financial toxicity among patients with cancer: A systematic review. *J Clin Oncol.* 2021;39(15_suppl):e18841-e18841.
83 Andersen I, Kolodziejczyk C, Thielen K et al. The effect of breast cancer on personal income three years after diagnosis by cancer stage and education: a register-based cohort study among Danish females. *BMC Public Health.* 2015;15:50.
84 Zajacova A, Dowd JB, Schoeni RF et al. Employment and income losses among cancer survivors: estimates from a national longitudinal survey of American families. *Cancer*. 2015;121(24):4425-4432.
85 Kong YC, Wong LP, Ng CW et al. Understanding the financial needs following diagnosis of breast cancer in a setting with universal health coverage. *Oncologist.* 2020;25(6):497-504.
86 Blinder VS, Gany FM. Impact of cancer on employment. *J Clin Oncol.* 2020;38(4):302-309.
87 Bhoo-Pathy N, Ng CW, Lim GC et al. Financial toxicity after cancer in a setting with universal health coverage: a call for urgent action. *J Oncol Pract.* 2019;15(6):e537-e546.
88 Alleaume C, Bendiane MK, Peretti-Watel P et al. Inequality in income change among cancer survivors five years after diagnosis: Evidence from a French national survey. *PLoS One.* 2019;14(10):e0222832.

CHAPTER III

Financial Toxicity Experiences of Patients With Cancer in Indonesia: An Interpretive Phenomenological Analysis

Published as:
Pangestu, S., Harjanti, E.P., Pertiwi, I.H., Rencz, F., & Nurdiyanto, F.A. (2024). Financial Toxicity Experiences of Patients With Cancer in Indonesia: An Interpretive Phenomenological Analysis. *Value in Health Regional Issues*, 41C, 25-31. https://doi.org/10.1016/j.vhri.2023.11.007

ABSTRACT

Objectives: Financial toxicity is an important adverse effect of cancer. Recent systematic reviews have shown that financial toxicity may lead to treatment non-adherence and impaired health-related quality of life; both of which may adversely influence the survival rates of patients. However, less is known about how patients endure financial toxicity, particularly in low- and middle-income countries. The purpose of this study was to explore how patients with cancer experience and cope with financial toxicity in Indonesia.

Methods: Semi-structured in-depth interviews were conducted to explore the experiences of Indonesian patients with cancer. Qualitative data were analyzed using interpretive phenomenological analysis approach. We purposefully recruited eight patients undergoing active treatment (aged 27-69) who had been diagnosed with cancer over five years before and possessed health insurance at the time of diagnosis.

Results: We identified two main themes: i) the experienced financial burden, with subthemes: underinsurance, out-of-pocket non-healthcare cancer-related costs, and negative income effect from employment disruption; and ii) the financial coping strategies, with subthemes: reallocating household budget, seeking family support, rationalizing treatment decisions, and topping up insurance for family members.

Conclusions: This is the first interpretive phenomenological study on financial toxicity in the literature and the first qualitative financial toxicity study in Indonesia. Our findings provide insight into the occurrence of financial toxicity and coping strategies used by Indonesian patients with cancer. The subjective experiences of patients may be considered to further improve oncology care, support the need for measurement of financial toxicity, and the provision of mitigation programs for patients.

III.1 INTRODUCTION

Financial burden is an important problem experienced by patients with cancer. The oncological care needed for survival may cause catastrophic out-of-pocket health spending to patients, which is referred to as 'financial toxicity' (FT).[1] FT arises from objective financial burden (e.g., out-of-pocket medical costs) and subjective financial distress (i.e., the perceived level of distress reported by the patients.[2,3] FT impedes individuals of achieving financial well-being, where one can sustain an adequate standard of living and financial freedom.[4]

Recent systematic reviews have shown that FT may lead to treatment non-adherence and the impairment of health-related quality of life,[5,6] an important construct that may even be associated with the survival rate of patients.[7] The issue of FT has been reported by patients with health coverage from both developed and developing countries,[8,9] even in those with universal health coverage.[10] This is attributable to the unanticipated proportion of medical expenses that were not covered by the health plan providers.

The lack of awareness and readiness in facing FT, which could affect the physical, psychological, and socio-economic well-being of patients with cancer, was highlighted in a meta-synthesis of 14 qualitative studies.[11] As a result, patients may be forced to adapt both financially and emotionally. A key psychological strategy that mediates between FT and health outcomes is coping.[12-16] However, very few qualitative studies focusing on coping mechanisms for FT have been conducted: a German study performing content analysis, a US study utilizing constructivist grounded theory approach, and an Australian study conducting thematic analysis, all of which conducted semi-structured interviews.[9,12,17] So far, FT studies have mostly been performed in high-income and English-speaking countries, e.g., United States, United Kingdom, and Australia.[5,18] Investigations in middle- and low-income countries are needed to enable the proper understanding of FT cases,[11,18,19] and to enable the development of valid measures and mitigation strategies according to cultural specificity and socio-demographic context.

In Indonesia, a middle income country,[20] cancer is the second highest cause of mortality after cardiovascular disease.[21] Its prevalence was 1.49% in 2018 and estimated to rise in the future.[22] Cancer is also the second most costly chronic disease financed by the public healthcare system, the *Jaminan Kesehatan Nasional* (National Health Insurance program or JKN) program administered by the BPJS Kesehatan (The Health Social Security Agency).[23] The JKN was introduced in 2014 to ensure social health security for

Indonesians and achieve universal health coverage. The inception of this single-payer insurance program is relatively recent and approximately, 90% of the population have been enrolled as members.[23,24] Even though JKN members with any type of cancer can seek treatment (e.g., surgery, chemotherapy, and radiotherapy) at the designated healthcare facilities, there is still a wide gap in the distribution of general practitioners, specialist physicians, and medical devices across the country.[23] This signifies that even the insured population may not be impervious to FT as they potentially need to incur more costs to obtain the necessary care. In essence, the proportion of uninsured population and the inequality of health delivery quality suggest the relevance of FT in Indonesian patients with cancer.

Further, the FT literature in Indonesia is extremely limited.[19] One study measured FT and how it affected the risk attitude of 194 patients with cancer and survivors.[25] Another study reported the FT of 109 patients with cancer which was associated with household income and number of dependents.[26] More explorations are warranted to understand the FT dynamics in Indonesia, particularly how patients with cancer manage their lives under FT. Therefore, the purpose of this qualitative study is to comprehend how patients with cancer in Indonesia experience and cope with FT arising from cancer diagnosis and treatment.

III.2 METHODS

The study design, data analysis, and reporting of findings followed the Consolidated criteria for reporting qualitative studies (COREQ) checklist.[27] The approach to the data collection and analysis was entirely inductive.

III.2.1 Design and participants

Semi-structured in-depth phenomenological interviews were conducted to explore the subjective experience of FT in patients with cancer. Qualitative data were analyzed using interpretive phenomenological analysis. To achieve richness of data, patient recruitment for the interviews was conducted until reaching saturation. The inclusion criteria for patients were: i) at least 23 years of age, ii) spoke Indonesian language, iii) had a diagnosis of any type of cancer, iv) diagnosed with cancer at least five years prior to the interview, v) possessed health insurance at the time of diagnosis, vi) actively undergoing cancer treatment, and vii) signed informed consent for the study. The minimum five-year diagnosis criterion was determined to fittingly capture the

experience of cancer burden. This resulted in the minimum patient age of 23 years old, that is five years after the adult age of 18. The recruitment of patients was done through snowball sampling.

III.2.2 Data collection

An in-depth phenomenological interview guide was created by S.P. and F.A.N. The interviews focused on the experience of financial burden and the influence of cancer on the financial aspects of their lives. Example questions included "*How did you realize that you have cancer?*", "*What burden did you experience from cancer?*", "*Did your cancer disrupt your finances?*", "*If the cancer disrupted your finances, in what ways did it affect you?*", "*Were there any financial adjustments that you had to make?*", and "*Is there anything else that you would like to add?"*

The one-on-one in-depth video-interviews were conducted between January and May 2022. Video-based qualitative interviews were chosen in response to the regulations on social restrictions during the COVID-19 pandemic. The interviews were scheduled after the patients provided informed consent. In consideration of the potentially frail physical condition of patients who were undergoing active treatment, the interviewers offered dividing the interview into two sessions. Prior to the interview, every patient completed a brief questionnaire about their cancer history (e.g., cancer type by site, year of diagnosis) and socio-demographic background (e.g., age, sex, education, individual monthly net income). The interviews took place virtually on Zoom (Zoom Video Communications, Inc). All interviews were audio recorded with the patients' permission. There were three interviewers (E.P.H., I.H.P., and F.A.N.), all of whom had previous interviewing experience. Notes were written during and after the interview sessions. Biweekly panels were held to reflect on data collection process. After the completion of all interviews, the patients were offered an optional compensation of IDR 200,000 (approximately US$ 12.7) for Internet costs or mobile phone credit, which was accepted by six patients (75%).

III.2.3 Interpretive phenomenological analysis (IPA)

The IPA was followed to analyze the qualitative data. This approach involved a detailed examination of the participants' lifeworlds and their personal lived experiences.[28] Therefore, we were able to understand deeply how the patients uniquely perceived and interpreted the dynamics of their FT experience.[29] The IPA was performed by F.A.N.,

E.P.H., I.H.P., and S.P. All interviews were transcribed verbatim by trained research assistants and verified by F.A.N and S.P. First, the research team read the transcripts multiple times. To inductively derive emerging themes, exploratory notes were coded and clarified independently by E.P.H. and I.H.P. Afterward, the potential themes were refined and labeled through panel discussions. Discrepancies were resolved through a consensus process within the team led by S.P. Ultimately, all synthesized themes were central, relevant, and related to one another. Data analysis and management were performed in Microsoft Excel (Microsoft Corporation).

III.2.4 Ethics

All included patients were given comprehensive information about the description of the research, potential risks of triggering psychological trauma, voluntary participation, and possibility of withdrawing participation. All patients agreed to engage in the study by signing informed consent electronically. The protocol of this qualitative research was reviewed and granted ethical approval by the Research Ethics Committee of Gadjah Mada University (no. KE/UGM/001/EC/2022, granted on January 11, 2022).

III.3 RESULTS

A total of nine patients with cancer history were recruited. One interview was annulled because the patient did not fulfill the minimum disease duration criterion, resulting in a final sample of eight patients. Three patients (P1, P2, and P6) expressed their interests after receiving the patient recruitment poster on social media and were recruited through telephone. The other five patients (P3-P5, P7, and P8) were recruited through referrals of patients P1, P2, and P6. None of the research team members had any prior relationship with the patients before the interviews.

The interviews were conducted in Indonesian language with an average length of 123 minutes per patient. Six patients were interviewed in a single session, whereas two patients completed the interview in two sessions with a one-week lag in between interviews.

The included patients had a median age of 36 years (range=27-69). They were mostly female (n=5), part-time workers (n=4), and had completed tertiary education (n=6). The ethnic group of the patients were Javanese (n=4), Chinese (n=2), Papuan (n=1), and Sundanese (n=1). The cancer types were lung (n=4), thyroid (n=3), and throat

(n=1). The median of duration since cancer diagnosis was 6.5 years (range=6-10 years). The characteristics of the eight patients included in our study are presented in Table III.1.

Table III.1. Characteristics of included patients

Characteristic	Description	Median (range) or n (%)
Age	(in years)	36 (27-69)
Sex	Female	5 (62.5%)
	Male	3 (37.5%)
Highest level of education	Bachelor's degree	4 (50%)
	Master's degree	2 (25%)
	Associate's degree	2 (25%)
Cancer type by site	Thyroid	4 (50%)
	Lung	3 (37.5%)
	Throat	1 (12.5%)
Disease duration	(in years)	6.5 (6-10)
Ethnicity	Javanese	4 (50%)
	Chinese	2 (25%)
	Papuan	1 (12.5%)
	Sundanese	1 (12.5%)
Province of residence	West Java	4 (50%)
	East Java	1 (12.5%)
	Jakarta	1 (12.5%)
	Papua	1 (12.5%)
	Yogyakarta	1 (12.5%)
Personal monthly net income	<1,000,000 IDR	3 (37.5%)
	2,000,000-4,000,000 IDR	2 (25%)
	4,000,001-8,000,000 IDR	2 (25%)
	>8,000,000 IDR	1 (12.5%)
Marital status	Married	7 (87.5%)
	Single	1 (12.5%)
Occupation	Part-time worker	4 (50%)
	Full-time employee	2 (25%)
	Business owner	1 (12.5%)
	Unemployed	1 (12.5%)

Note. US $1 = 15 731 IDR (based on the 30 December 2022 middle exchange rate). IDR indicates Indonesian Rupiah

The analysis resulted in six subthemes that were classified into two main themes: 1) the experienced financial burden, and 2) the financial coping strategies.

III.3.1 The experienced financial burden

Three subthemes in were identified: i) underinsurance, ii) out-of-pocket non-healthcare cancer-related costs, and iii) negative income effect from employment disruption. These subthemes explained the factors that influence the occurrence of financial toxicity.

1. Underinsurance

None of the included patients were diagnosed at an early stage. All patients professed about the lengthy overall process for a definitive conclusion from the physicians. However ultimately, all patients received the medical treatment that they needed. Even though covered by health insurance, all patients expressed their grievances about the insufficiency of their coverage, which was perceived to be the main cause of their FT. The issue of underinsurance was brought up because the policies were inadequate to cover all cancer treatment costs. One patient said:

"I kept using JKN. It helped a lot even though it did not cover every medical treatment."
(P1, male, 62, lung cancer)

As a result, all patients had to pay out-of-pocket for healthcare costs that included medication and diagnostic tests. Two patients said:

"At that time, I could not afford a complete lab work. It was still very expensive then and it was not covered by my health insurance."
(P5, 36, female, thyroid cancer)

"There were some drugs that were not covered by my insurance. For me, my most expensive medication was the nasal spray."
(P7, 27, male, throat cancer)

Further, all patients expressed frustration with the costs that they may have to deal with for the rest of their lives due to the risk of relapse. Two patients mentioned:

"There is nothing cheap about cancer because the treatment has no end to it."
(P1, 62, male, lung cancer)

"After I was operated and the thyroid cancer along with the glands was removed, I had to take medication for the rest of my life."
(P6, 35, female, thyroid cancer)

2. Out-of-pocket non-healthcare cancer-related costs

To obtain treatment and examination, all patients also had to disburse on non-healthcare costs, which included transportation, accommodation, and wages for domestic helper (e.g., caregiver, housekeeper, nanny, and driver). P3 shared his experience:

> *"It was.. 2016 and 2017. I went to Singapore every three weeks. So, in those two years, I went to Singapore probably 35 times. I spent 10 million rupiah every time I went to Singapore for flights and hotel rooms."*
> (P3, 62, male, lung cancer)

For all patients, transportation was highlighted to be their main non-healthcare costs. Five patients (P2, P4, P5, P6, and P7) had to travel out of town due to the unavailability of certain medical procedures in their residence city or town. For example, P4 had to travel 400 kilometers from Malang to Yogyakarta for every round of treatment:

> *"JKN is really good. Even poor people are covered. We don't have to think much about the treatments, but we have to think about transport, accommodation, and others. As a patient, it is really a burden. Every three months I have to prepare funds, mostly allocated for transportation and accommodation."*
> (P4, 36, female, thyroid cancer)

3. Negative income effect from employment disruption

After being diagnosed with cancer, all patients experienced disrupted livelihood and loss of income. In treating cancer, they had to make lifestyle alterations which impacted their work behavior. They recognized the need to improve their work-life balance in favor of maintaining a healthy diet, fending off fatigue, and allocating time for follow-up examinations and treatments. All patients viewed cancer as a change that negatively influenced their work performance and career, such as loss of clients and potential job promotion with higher pay. One patient described:

"Being a cancer survivor, [my co-workers] became sympathetic toward me. They reduced my workload and told me not to get too tired. I find this discriminatory. I was seldomly involved in decision-making process."

"[At the time] I was supposed to become a permanent employee. I could have shined in that company and become a young executive. I was making [tens of millions of rupiah]."
(P2, 30, female, thyroid cancer)

Further, five patients (P2, P4, P5, P6, and P7) felt to have inconvenienced their colleagues due to treatment scheduling that required partial or full days of leave and treatment side effects. P5 was bothered by the attitude of her colleagues:

"At work, I felt that they were lacking awareness. I mean, they could not really accept that I had to take days of leave. They could not really tolerate that. It was unpleasant becoming the talk of the office, a gossip."
(P5, 36, female, thyroid cancer)

Six patients (P2, P3, P4, P5, P6, and P8) had to leave their occupations, where four became homemakers with part-time work, one started a business, and one became unemployed. Two patients reflected on this change:

"Yes, clearly I switched jobs because of cancer. I was working in a corporation with a high workload with at least eight hours of work, and sometimes doing overtime. My body does not agree with this."
(P2, 30, female, thyroid cancer)

"Praise the Lord, I had high income before I got cancer. But what can I do about it? God's plan for men is different from the plans of the men themselves."
(P7, 27, male, throat cancer)

III.3.2 The financial coping strategies

Four subthemes were identified: i) reallocating household budget, ii) seeking family support, iii) rationalizing treatment decisions, and iv) topping up insurance for family members. These subthemes expressed how the patients adjusted their financial conditions in coping with the experienced financial toxicity.

1. Reallocating household budget

Financial sacrifices were made to allow for cancer treatment. All patients expressed that cancer-related expenditures had become a fixed component of the household financial budget. As cancer is a life-threatening disease, healthcare budgeting became the financial priority in the family. Portions of regular monthly income and lifetime savings had to be re-allocated to finance treatment costs and supplements during post-treatment recovery. Basic living expenses (e.g., housing, food, clothing, transportation) were economized and luxury wants (e.g., vacation, hobbies) were either delayed or canceled. The funds saved from these cost-cutting measures were channeled to pay for the on-going cancer treatments or in anticipation of future ones. P5 shared her experience in economizing costs:

"At the end, we sacrificed the needs that were not so urgent. These were actual needs! But we had to pay for the treatment, so, it's okay, we postponed them."

"I had to adjust my budget to afford the transport to the hospital. At first, my husband and I took the train and bus which cost 70.000 rupiah. Then, I told my husband that we would save money if we biked from Bogor to Jakarta and back. The fuel cost did not exceed 50.000 rupiah per trip."
(P5, 36, female, thyroid cancer)

To increase personal cash flow and sustain their treatment, three patients (P1, P3, and P8) sold tangible assets. Two patients shared their experiences:

"I sold [real estate] property, it was enough for the drug costs"
(P1, 62, male, lung cancer)

"By chance, my husband had invested in land which was then sold. My husband then purchased [Singaporean] dollars to pay for the treatment."
(P8, 69, female, lung cancer)

After entering remission or upon improvement of health, the patients still had to allocate budget for medical tests, supplements, and dietary needs. Learning from the years of experience in undergoing treatment and the utilization of health insurance, the patients and their family were able to estimate the amount of funds needed for each round of examination and treatment. Afterwards, the amount was budgeted along with the identification of the source of the funds. Household expenditures were mapped and sorted according to priority or nature of urgency. All patients increased their healthcare budget. One patient described:

"I divide my income into sets of funds. When I was single, I saved money frequently. I thought if I fell sick, it would implode my finances. And turns out I was right. So, I divided my money into living, investments, zakat [Muslim charity], and entertainment. Only now my healthcare funds have larger portion. It even goes to 40%!"
(P2, 30, female, thyroid cancer)

2. Seeking family support

Due to high costs, not all patients were able to gather sufficient funds for treatment. In addition to cutting back on expenses and using their savings, three patients (P4, P5, and P7) had to seek external financial support from family members. Initially, P4's cancer treatment costs were financed by her father because she did not have a steady flow of income prior to getting married. After becoming a married woman, she obtained financial support from both her father and husband. Spouses, parents, and other relatives were not only materially helpful, but also emotionally supportive and even had a role in healthcare decisions. The patients felt that family support enabled them to mitigate FT and focus more on undergoing treatment and recovering. In the case of P8, her husband had a central role in making treatment decisions and financing out-of-pocket costs. She regarded this as the social role and responsibility of her husband:

"My husband handles every treatment. I gave the [control] to him. If he says that there is no money left and this is where I should get treated, then I would obey him. I am not the kind of wife who questions whether we have money or not, even though I know how much my husband has in the bank. Money management is my husband's responsibility."
(P8, 69, female, lung cancer)

3. Rationalizing treatment decisions

An interplay of factors was considered by the patients when making healthcare decisions, e.g., the potential risks and benefits of the treatment, how to gather the funds needed for treatment, and how the treatment choice would financially affect the family. Being constrained, the patients rationalized their decisions as a response. Faced with options recommended by the physicians, every patient selected the alternative that matched their financial capacities. When the patients perceived that a condition improvement or an increase in chances of recovery were possible, they showed their willingness to disburse more money for treatment. Four patients (P1, P3, P4, and P8) opted for costlier treatments which they assumed to be more effective. For example, in treating her thyroid cancer, P4 opted for brand-name instead of generic drugs, even though certain brand-name drugs were not covered by the JKN insurance scheme. P1 also selected a costlier alternative which he needed to pay out-of-pocket:

"After discussing with my family about costs, we chose the more expensive medicine because it is said that my hair would not fall, no nausea, no tinglings, no baldness. The cheaper one, they say, has more side effects"
(P1, male, 62, lung cancer)

Three patients (P1, P3, and P8) opted for treatment overseas in Singapore and Malaysia, thereby incurring higher transportation and accommodation costs. They learned about the potentially better quality of healthcare overseas through the experience of others. After discussing with his family, P3 decided to participate in a clinical trial of a new cancer drug in Singapore:

"The doctor in Singapore spoke with my brother. My friend suggested him to get a second opinion. I heard that some hospitals in Singapore were backed by pharmaceutical companies and if lucky, we could get free trials as part of their [research and] development."
(P3, 62, male, lung cancer)

Three patients (P1, P5, and P6) also sought for complementary alternative treatments to sustain their conditions in the forms of herbal medicine and spiritual healing. Three patients shared their experiences:

"So the herbal medicine was made by boiling. A liter cost 800 thousand rupiah. Each day I had to finish a liter. I bought eight liters at a time and I stored it in the fridge."
(P1, 62, male, lung cancer)

"I was referred by a pharmacology lecturer about this lotus pill. I had consumed it before I decided to get surgery. The pill was expensive, and I took 15 pills a day."
(P6, 35, female, thyroid cancer)

"I traveled to Pemalang to pursue an alternative treatment. They rubbed my neck with cotton dipped in holy water. I personally do not understand these things. They prayed while rubbing my neck. Abracadabra, the cotton was suddenly drenched in blood. They said my cancer was gone."
(P2, 30, female, thyroid cancer)

Further, all patients expressed their willingness to pay for certain expenses out-of-pocket if they could afford them to save time. They learned this from their experience in navigating claims process and doctor referrals that consumed considerable time. Two patients conveyed their stress:

"Turns out some laboratories in East Java were not under the JKN scheme. They do 100% in Yogyakarta and Semarang, but, in Surabaya is not that simple. The queue is long, and the process is complex!"

(P5, female, 36, thyroid cancer)

"The rules are just really complicated. I mean it's convoluted in my opinion. I ended up paying more.."
(P4, female, 36, thyroid cancer)

All patients highlighted the importance of earlier assessment to obtain a faster medical referral and timelier treatment to prevent the spread of cancer. The patients indicated that getting earlier assessment would have enabled them to prevent a higher level of FT. They believed that by being early, they could have been more thorough in consulting with the doctors and navigating the insurance administration flow. Two patients shared their experiences:

"All this time, I have been paying for blood work with my own money. I don't use JKN for this, it's faster. It's fine because it's only every six months. But, I do use JKN for scans because they are expensive!"
(P6, 35, female, thyroid cancer)

"I planned to make a biopsy appointment at xxx laboratory, but I had heard that the waiting list for this was long. It would take two, even three months before one could get in. After samples are taken, the results would also take one or two months. This is way too long. They have way too many patients"
(P1, 62, male, lung cancer)

All patients also rationalized in earning the money to finance for treatments. Although every patient was aware that working while undergoing treatment might delay the recovery process, they persisted. One patient described:

"I am a cancer patient who must work to pay for my treatment. Praise the Lord, I still work to support myself. It's true that my husband earns [an income], but that is for daily needs. But for my treatment, I have to keep earning [money] to sustain it."
(P2, 30, female, thyroid cancer)

4. Topping up insurance for family members

All patients emphasized the importance and benefits of health insurance when accessing medical care. One patient expressed his appreciation:

"I was lucky to be insured. It helped me cover my costs."
(P1, male, 62, lung cancer)

However, people with cancer history are unlikely to obtain a new private health insurance policy post-diagnosis. As a result, patients had to either utilize public insurance or finance the entire treatment using personal assets. Four patients (P1, P2, P3, and P6) compensated by signing up family members into health insurance programs or topping up their existing premiums to cover critical illnesses (e.g., cardiovascular disease, stroke, and cancer), even though prospective insurance claims would never be channeled to the patients. This was done to enhance household financial planning and prevent possible future FT within the family members. P3, who was an insurance agent prior to getting cancer, expressed his regret on not financially protected against cancer. He compensated by upgrading this family members' protection:

"Now, after I got cancer, the insurance did not want to cover me. It is possible for heart diseases, but when it comes to cancer, they suddenly have all these provisions."

"Even when I had insurance [in the past], it was never 100% [covered]. For myself, I could not top up my insurance anymore because of my [cancer] history. What I can do is to maintain my health, eat well and do enough sports, but for my young children.. I tell them to get enough exercise and I also added their insurance protection."
(P3, 62, male, lung cancer)

In addition, two patients (P2 and P6) who had the financial capacity financed their family members to get cancer screening, motivated by prudence and perceived unpredictability of cancer diagnosis. P6 shared her experience:

"We are regulars at xxx lab and they have these cancer risk assessments. But my husband did not want to [do them], oh well.. But for my children.. I was pregnant after I had the cancer, so this may affect them. So, we routinely did the assessments for them. My doctor said that my cancer is not [a] genetic [disease], not passable to my children, but I still do this just for my peace of mind, just to be sure."

(P6, 35, female, thyroid cancer)

III.4 DISCUSSION

This is the first qualitative study to explore how Indonesian patients with cancer experience FT and, to our knowledge, the first interpretive phenomenology study on FT in the literature. Our analysis of qualitative data resulted in two themes: 'the experienced financial burden' and 'the financial coping strategies.' The former elaborates the perceived contributing factors to the experience of FT, and the latter discusses the coping strategies implemented by the patients.

Overall, our subtheme findings correspond with previous FT studies. We found three contributing factors in the occurrence of FT: out-of-pocket healthcare and non-healthcare cancer-related expenditures,[11] being underinsured,[30] and employment disruption that caused negative income effects.[31,32] In coping with FT, four financial adjustment strategies were identified: expenditure reduction and budget reallocation,[12,33] seeking financial support,[12,33] rationalizing treatment,[34] and topping up insurance.[11] Interestingly, none of our included patients applied for formal loans to pay for their treatment, which was a coping strategy found in German patients with cancer.[12] This indicates Indonesian patients' preference for interpersonal over institutional support from corporations or financial institutions. In Indonesia, family may have a considerable influence in health decisions.[35,36] We found that family members (e.g., spouse, parent, and sibling of a parent) had a nuanced role, which was even framed as a responsibility. Not only did they provide financial and emotional support, but also; for some, family members determined healthcare decisions for the patient. This is a cultural distinction illustrated by collectivistic behavior.

Indonesia is making meaningful progress toward achieving universal health care (UHC).[37] However, the patients' experiences of hardship in obtaining cancer care (i.e., from diagnosis to treatment) indicated inequalities in access to healthcare. The results of

this study challenge the way we look at 'financial toxicity', which has been defined as the consequence of cancer treatment. It may be possible that patients with cancer have experienced subjective FT even before undergoing treatment due to lack of healthcare access and quality. Therefore, Indonesia must accelerate their efforts in advancing the necessary infrastructure and facilities; including but not limited to skilled health professionals. Further, in adherence to the World Health Organization, the goal of UHC is to ensure every person has access to health services without financial hardship.38 Presently, the issue of FT has received little to no attention in Indonesia. There are initiatives that may be considered to tackle this issue. First, communicating to patients about FT. Patients can be educated by health professionals about the financial and other psychosocial consequences of treatment, even under insurance coverage. Second, properly detecting subjective FT in patients using a valid and reliable scale. Concurrently, mitigation programs can be provided to patients to prevent and combat FT. Interventions like non-healthcare cost coverages (e.g., transportation and accommodation related to treatment) and provision of financial navigation programs have been shown to ameliorate FT.[39] To anticipate the negative income effects of cancer, employment reintegration programs may also be provided. Future investigations may be directed toward the measurement of FT and the development of mitigation programs that may alleviate FT for the Indonesian population.

This study has limitations. First, we focused on the subjective experience of the patients through interpretive phenomenological analysis. The use of this approach enables researchers to interpret the unique and subjective lived experience of the participants, instead of making empirical generalizations. Therefore, applying the findings of this study in other contexts calls for a more careful judgment. Second, while the relatively small sample size may be a potential limitation of the present study, data saturation was reached as no important new themes emerged by the fourth interview. All our patients had survived their cancer for at least six years and half of them were patients with thyroid cancer. We believe this attained sufficient richness in shared perspective upon the phenomenon of FT to derive representative conclusions. Third, the levels of FT in patients were not objectively assessed prior to the interview. This was chosen because we wanted to explore the phenomenon of FT in an entirely inductive approach. To be more resource efficient, future studies may consider using a validated scale (e.g., the Comprehensive Score for Financial Toxicity) to screen patients with FT. Fourth, our inclusion criteria did not allow us from capturing the FT experiences of patients who were in end-of-life care,

specifically from being unable to afford cancer treatment. This perspective has yet to be explored and may be considered for future FT studies. Fifth, conducting virtual interviews might have excluded prospective patients who did not possess the technological access. However, the use of videos was essential to capturing facial expressions and body language cues.

III.5 CONCLUSIONS

In summary, we provided an insight into the experience of FT and coping strategies used in patients with cancer in Indonesia. Our interpretive phenomenological analysis revealed the perceived factors contributing to the experience of FT: underinsurance, out-of-pocket non-healthcare cancer-related costs, and negative income effect from employment disruption. In response, financial coping strategies were implemented through household budget reallocation, family support obtainment, treatment rationalization, and the purchase of health insurance for family members. We expect that the findings of this qualitative study may help policymakers in healthcare in Indonesia and other countries with similar characteristics.

References

1. Zafar SY, Abernethy AP. Financial toxicity, part I: a new name for a growing problem. *Oncology (Williston Park, NY)*. 2013;27(2):80.
2. Baddour K, Fadel M, Zhao M, et al. The cost of cure: Examining objective and subjective financial toxicity in head and neck cancer survivors. *Head & neck*. 2021;43(10):3062-3075.
3. Witte J, Mehlis K, Surmann B, et al. Methods for measuring financial toxicity after cancer diagnosis and treatment: a systematic review and its implications. *Annals of Oncology*. 2019;30(7):1061-1070.
4. Brüggen EC, Hogreve J, Holmlund M, Kabadayi S, Löfgren M. Financial well-being: A conceptualization and research agenda. *Journal of Business Research*. 2017/10/01/ 2017;79:228-237. doi:10.1016/j.jbusres.2017.03.013
5. Pangestu S, Rencz F. Comprehensive Score for Financial Toxicity and Health-Related Quality of Life in Patients With Cancer and Survivors: A Systematic Review and Meta-Analysis. *Value in Health*. 2022;doi:10.1016/j.jval.2022.07.017
6. Bhanvadia SK, Psutka SP, Burg ML, et al. Financial toxicity among patients with prostate, bladder, and kidney cancer: a systematic review and call to action. *European Urology Oncology*. 2021;4(3):396-404.
7. Jones GL, Ledger W, Bonnett TJ, Radley S, Parkinson N, Kennedy SH. The impact of treatment for gynecological cancer on health-related quality of life (HRQoL): a systematic review. *American journal of obstetrics and gynecology*. 2006;194(1):26-42.
8. Ürek D, Uğurluoğlu Ö. Predictors of financial toxicity and its associations with health-related quality of life and treatment non-adherence in Turkish cancer patients. *Supportive Care in Cancer*. 2022;30(1):865-874.
9. Head B, Harris L, Kayser K, Martin A, Smith L. As if the disease was not enough: coping with the financial consequences of cancer. *Supportive care in cancer*. 2018;26(3):975-987.
10. Longo CJ, Fitch MI, Banfield L, Hanly P, Yabroff KR, Sharp L. Financial toxicity associated with a cancer diagnosis in publicly funded healthcare countries: a systematic review. *Supportive Care in Cancer*. 2020;28(10):4645-4665.
11. Zhu Z, Xing W, Zhang X, Hu Y, So WK. Cancer survivors' experiences with financial toxicity: A systematic review and meta-synthesis of qualitative studies. *Psycho-Oncology*. 2020;29(6):945-959.
12. Schröder SL, Schumann N, Fink A, Richter M. Coping mechanisms for financial toxicity: a qualitative study of cancer patients' experiences in Germany. *Supportive Care in Cancer*. 2020;28(3):1131-1139.
13. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. *CA Cancer J Clin*. 2018;68(2):153-165. doi:10.3322/caac.21443
14. Kale HP, Carroll NV. Self-reported financial burden of cancer care and its effect on physical and mental health-related quality of life among US cancer survivors. *Cancer*. 2016;122(8):283-9. doi:10.1002/cncr.29808
15. Ramsey SD, Bansal A, Fedorenko CR, et al. Financial Insolvency as a Risk Factor for Early Mortality Among Patients With Cancer. *J Clin Oncol*. 2016;34(9):980-6. doi:10.1200/jco.2015.64.6620
16. Banegas MP, Dickerson JF, Kent EE, et al. Exploring barriers to the receipt of necessary medical care among cancer survivors under age 65 years. *J Cancer Surviv*. 2018;12(1):28-37. doi:10.1007/s11764-017-0640-1
17. Ross XS, Gunn KM, Olver I. Understanding the strategies rural cancer patients and survivors use to manage financial toxicity and the broader implications on their lives. *Supportive Care in Cancer*. 2021;29(9):5487-5496. doi:10.1007/s00520-021-06086-z
18. Zhu Z, Xing W, Wen H, et al. Psychometric properties of self-reported financial toxicity measures in cancer survivors: a systematic review. *BMJ open*. 2022;12(6):e057215.
19. Donkor A, Atuwo-Ampoh VD, Yakanu F, et al. Financial toxicity of cancer care in low-and middle-income countries: A systematic review and meta-analysis. *Supportive Care in Cancer*. 2022:1-32.
20. The World Bank. The World Bank In Indonesia. Accessed December 12, 2022. https://www.worldbank.org/en/country/indonesia/overview
21. CDC in Indonesia [Fact Sheet]. 2021. Accessed December 12, 2022. https://www.cdc.gov/globalhealth/countries/indonesia/pdf/indonesia-fs.pdf
22. Indonesian Ministry of Health. *Beban Kanker di Indonesia*. 2019. Accessed July 10, 2023. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwiqzfvbupf5AhUQxosKHaj3DiQQFnoECAkQAQ&url=https%3A%2F%2Fpusdatin.kemkes.go.id%2Fdownload.

php%3Ffile%3Ddownload%2Fpusdatin%2Finfodatin%2FInfodatin-Kanker-2019.pdf&usg=AOvVaw2Bfvrd60YCmsoC8XJL3A1r
23. Kosen S. Coverage and implementation of healthcare delivery for cancer under national health insurance, experience of Indonesia. *The Lancet Regional Health - Southeast Asia*. 2022;6doi:10.1016/j.lansea.2022.100065
24. Firmansyah M. BPJS Kesehatan Claims Nearly 91% Indonesians Covered by JKN-KIS. *Tempo*. 2023. Accessed September 25, 2023. https://en.tempo.co/read/1702469/bpjs-kesehatan-claims-nearly-91-indonesians-covered-by-jkn-kis
25. Pangestu S, Karnadi EB. Financial toxicity in Indonesian cancer patients & survivors: How it affects risk attitude. *Cogent Medicine*. 2018;5(1):1525887.
26. Susilowati M, Afiyanti Y. The socio-demographic factors correlated with financial toxicity among patients with breast cancer in Indonesia. *Journal of Public Health Research*. 2021;10(s1)
27. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International journal for quality in health care*. 2007;19(6):349-357.
28. Smith JA, Shinebourne P. Interpretative phenomenological analysis. *APA handbook of research methods in psychology, Vol 2: Research designs: Quantitative, qualitative, neuropsychological, and biological*. American Psychological Association; 2012:73-82. *APA handbooks in psychology®*.
29. Neubauer BE, Witkop CT, Varpio L. How phenomenology can help us learn from the experiences of others. *Perspectives on Medical Education*. 2019;8(2):90-97. doi:10.1007/s40037-019-0509-2
30. Petermann V, Zahnd WE, Vanderpool RC, et al. How cancer programs identify and address the financial burdens of rural cancer patients. *Supportive Care in Cancer*. 2022;30(3):2047-2058. doi:10.1007/s00520-021-06577-z
31. Mols F, Tomalin B, Pearce A, Kaambwa B, Koczwara B. Financial toxicity and employment status in cancer survivors. A systematic literature review. *Support Care Cancer*. 2020;28(12):5693-5708. doi:10.1007/s00520-020-05719-z
32. Carlson MA, Fradgley EA, Bridge P, et al. The dynamic relationship between cancer and employment-related financial toxicity: an in-depth qualitative study of 21 Australian cancer survivor experiences and preferences for support. *Supportive Care in Cancer*. 2022;30(4):3093-3103. doi:10.1007/s00520-021-06707-7
33. Lueckmann SL, Schumann N, Hoffmann L, et al. 'It was a big monetary cut'—A qualitative study on financial toxicity analysing patients' experiences with cancer costs in Germany. *Health & Social Care in the Community*. 2020;28(3):771-780.
34. Thom B, Benedict C. The Impact of Financial Toxicity on Psychological Well-Being, Coping Self-Efficacy, and Cost-Coping Behaviors in Young Adults with Cancer. *J Adolesc Young Adult Oncol*. 2019;8(3):236-242. doi:10.1089/jayao.2018.0143
35. Pradnyani N, Suariyani N. Family role in decision making of health seeking behavior on elderly in Tabanan Regency, Bali, Indonesia. *Epidemiology (sunnyvale)*. 2016;6(218):2161-1165.1000218.
36. Thomas D, Contreras D, Frankerberg E. Distribution of power within the household and child health. *MPRA Paper*. 2002.
37. Agustina R, Dartanto T, Sitompul R, et al. Universal health coverage in Indonesia: concept, progress, and challenges. *The Lancet*. 2019;393(10166):75-102. doi:10.1016/S0140-6736(18)31647-7
38. Cotlear D, Nagpal S, Smith O, Tandon A, Cortez R. *Going Universal*. The World Bank Group; 2015.
39. Arastu A, Hamilton A, Chen EY-s. Interventions to alleviate financial toxicity among patients with cancer: A systematic review. *Journal of Clinical Oncology*. 2021;39(15_suppl):e18841-e18841. doi:10.1200/JCO.2021.39.15_suppl.e18841

CHAPTER IV

Validity, Test-Retest Reliability, and Responsiveness of the Indonesian Version of FACIT-COST Measure for Subjective Financial Toxicity

Published as:
Pangestu, S., Purba, F.D., Setyowibowo, H., Mukuria, C., & Rencz, F. Validity, Test-Retest Reliability, and Responsiveness of the Indonesian Version of FACIT-COST Measure for Subjective Financial Toxicity. *Health and Quality of Life Outcomes*. 2024;22(1):89. https://doi.org/10.1186/s12955-024-02303-5

ABSTRACT

Background: Financial toxicity describes the impairment of financial well-being in patients due to the burden of cancer diagnosis and care. The COST: A Functional Assessment of Chronic Illness Therapy Measure of Financial Toxicity (FACIT-COST) is the most widely used cancer-specific measure of subjective financial toxicity, having been validated in multiple languages, but not in Indonesian. This study aimed to validate the Indonesian version of FACIT-COST in a breast cancer sample.

Methods: A single-center prospective cohort study was performed in Indonesia. Female breast cancer patients aged ≥18 undergoing treatment at baseline were invited to participate and followed for up to six months. The survey included the official Indonesian version of FACIT-COST (v2) which was administered to the patients by interviewers. Clinical information (e.g., metastasis status, disease duration) was provided based on medical records. The following measurement properties of FACIT-COST were tested: distributional characteristics, structural validity (principal component [PCA] and confirmatory factor analyses [CFA]), internal consistency reliability (Cronbach's alpha and McDonald's omega), known-groups validity (Mann-Whitney U or Kruskal-Wallis H test), test-retest reliability, and responsiveness to change.

Results: Overall, 300 female patients participated at baseline. No patients reported the best or worst possible FACIT-COST total scores. The PCA proposed a two-factor model structure for the instrument, which was confirmed by the CFA (RMSEA=0.042, SRMR=0.049, CFI=0.99, TLI=0.99). The internal consistency reliability of the two factors was considered adequate (Cronbach's alpha=0.774-0.882, McDonald's omega=0.786-0.888). The FACIT-COST total score significantly discriminated across the following known-groups: age, education, residential setting, income, employment, metastasis status, number of symptoms, and financial coping strategies. The FACIT-COST demonstrated excellent test-retest reliability (intraclass correlation coefficient=0.96) and satisfactory responsiveness to change (standardized response mean and effect size ranges=|0.39| to |0.92|).

Conclusions: This is the first study to validate the FACIT-COST in patients with breast cancer and to present the measurement properties of the Indonesian version of FACIT-

COST. The Indonesian FACIT-COST demonstrates acceptable psychometric performance and shows potential as a valid measure of subjective financial toxicity. The instrument may serve as a valuable tool for informing health policies that focus on providing resource support to improve cancer care in Indonesia.

IV.1 INTRODUCTION

Financial toxicity is the impairment of financial well-being in patients arising from the burden of cancer diagnosis and care. Experienced by patients with cancer around the world, unmitigated financial toxicity may lead to adverse consequences that include treatment non-adherence, impaired health-related quality of life, and poorer survival outcomes.[1-4] To better understand the burden of cancer, valid measurement of financial toxicity is essential. Generally, financial toxicity can be categorized into two forms: objective and subjective.[5-7] Objective financial toxicity is typically assessed using metrics, such as nominal of out-of-pocket cancer-related costs or its percentage to household income, and questions on financial coping mechanisms, e.g., borrowing money and selling possessions. Meanwhile, subjective financial toxicity (SFT) can be measured by assessing the perceived distress regarding the patient's cancer-related financial burden.

Recent systematic reviews revealed the heterogeneity of measures used, including the use of measures that had not been validated in assessing SFT in cancer.[5,7,8] The measures can either be generic or cancer-specific. Some generic measures that have been used to capture SFT include the InCharge Personal Financial Well-being, Personal Financial Wellness, and the Financial Distress Questionnaire [1,8]. Additionally, there are cancer-specific measures that were developed to capture SFT, such as the Patient-Reported Outcome for Fighting Financial Toxicity (PROFFIT), Subjective Financial Distress Questionnaire (SFDQ), and Financial Index of Toxicity (FIT).[9-11] So far, the most widely validated cancer-specific measure of SFT is the COST: A Functional Assessment of Chronic Illness Therapy Measure of Financial Toxicity (FACIT-COST).[1,8,12]

Standardized questionnaires that are translated and cross-culturally adapted from their source language necessitate psychometric testing before their use.[13,14] In the case of SFT, differences in healthcare system, socioeconomic, and cultural contexts may affect the interpretation of the item content of the measure. While many studies have validated various language versions of the FACIT-COST in different countries or cultures (e.g., United States, Italy, Australia, China, and Japan), evidence for the Indonesian version is not yet available.[15-24] Indonesia is the fourth most populous country in the world, where cancer is a major cause of mortality and financial toxicity is very understudied. Cancer also ranks as the second most expensive chronic disease financed by the country's public healthcare system [25]. The considerable disparities in healthcare delivery quality, including the distribution of general practitioners, specialists, and medical equipment, further

highlight the importance of measuring and addressing financial toxicity in Indonesia, as additional out-of-pocket costs may still incur despite existing national insurance coverage. Furthermore, factor structure differences of FACIT-COST have been found across validation studies of different language versions of the instrument.[15,17,18,24] Certain psychometric properties (e.g., responsiveness) have also been rarely investigated in the financial toxicity literature.[15-24,26]

Therefore, the purpose of this study is to assess the psychometric properties of the official Indonesian version of FACIT-COST, including its distributional characteristics (floor and ceiling), structural and known-groups validity, internal consistency reliability, test-retest reliability, and responsiveness to change. This study focuses on breast cancer, which is the most prevalent cancer type both worldwide and in Indonesia.[27]

IV.2 METHODS

IV.2.1 Study design and patients

An observational prospective cohort study was conducted from September 2023 to March 2024 at the oncology department of Hasan Sadikin General Hospital, a primary referral center in Bandung, West Java province, Indonesia. The study was approved by the Research Ethics Committee of the hospital (LB.02.01/X.6.5/284/2023). Soft quotas were applied to allow for diverse stages of cancer and treatment cycle. The inclusion criteria were as follows: female of at least 18 years of age with a breast cancer diagnosis of any type and stage, undergoing any type of treatment (e.g., immunotherapy and chemotherapy), had the cognitive capacity to complete the questionnaire, fluent in the Indonesian language, and signed a written informed consent. The recruitment of patients was performed by three trained research assistants under the oversight of the oncologist and team of nurses. Patients were recruited in the clinic waiting area prior to their treatment session. The first half of the recruited patients consisted of patients in active treatment cycle (‘T1’ follow-up group) and the remaining half comprised patients in their last round of treatment cycle (‘T2’ follow-up group).

IV.2.2 Data collection

The target sample size for this study was 300, which met the requirements for the planned main statistical analyses.[28,29] Two structured paper questionnaires were prepared for this study, one to be completed by the patients and the other by the nurses. At all time points, the patient questionnaire was distributed by research assistants in the Indonesian

language to the patients, who then completed it themselves using paper-and-pencil. The research assistants were available to provide explanations during the completion process when needed. For the T1 group, the follow-up questionnaire was completed during their subsequent treatment cycle, while the T2 group completed the follow-up during their post-treatment consultation. A pilot test was performed to assess the feasibility and comprehensibility of the questionnaire. Five patients with breast cancer (aged 35-60 with diverse types of treatment) were involved and no modifications were made to the questionnaire afterward. All patients received a compensation of IDR 100,000 (equivalent to approximately USD 6.3) after completing each of the baseline and follow-up questionnaires. Meanwhile, the oncology nurses' questionnaire was self-completed by the nurses to provide additional clinical information on the patients obtained from the computerized hospital records, namely disease duration and metastasis status.

IV.2.3 Patient questionnaire

The questionnaire included the FACIT-COST and an extensive set of other outcome measures, as part of a study comparing the psychometric performance of preference-accompanied measures in breast cancer. The measures were presented in a fixed order, with all items being required to be responded by the patients: EQ Health and Wellbeing (EQ-HWB), EQ-5D-5L, FACIT-COST, Warwick Edinburgh Mental Wellbeing Scale (WEMWBS) and Functional Assessment of Cancer Therapy – General (FACT-G). Results of the outcome measures other than the FACIT-COST will be reported elsewhere. Patients also responded to questions on socio-demographic characteristics (age, education level, employment status, classification of residence, number of children aged <17 living in the same household, net monthly household income, and health insurance use), symptoms experienced during the last week (e.g., fatigue, weight loss, and hair loss), and a question on financial coping strategies. The financial coping strategy referred to the economic actions performed by the patients to mitigate cancer-related costs: incurring debt, withdrawing savings or pension, selling assets, and closing business or declaring bankruptcy.

IV.2.4 FACIT-COST

The official Indonesian version of FACIT-COST (v2) was used to measure SFT.[30] The current second version has 12 items with 0-4 response scale: 'not at all' (0), 'a little bit' (1), 'somewhat' (2), 'quite a bit' (3), and 'very much' (4). The items relate to financial

adequacy, worry, and control, among others. The difference between the 11-item v1 and 12-item v2 FACIT-COST is the addition of the twelfth item (FT12), 'financial hardship to my family and me.' FT12, a global summary item, is not included in the total score calculation.[30] Following the current scoring guideline, the FACIT-COST total score is calculated by summing items 1 through 11, where items 2, 3, 4, 5, 8, 9, 10 are scored in reverse. Therefore, the possible theoretical score for both v1 and v2 is between 0 and 44, where lower scores indicate worse SFT.

IV.2.5 Statistical analyses

The analysis strategy was guided by previous studies on the validation of the translated FACIT-COST.[17-19] All variables were descriptively summarized using frequency and percentage for categorical variables, and mean and standard deviation for continuous variables. Baseline characteristics for patients that belonged to the T1 and T2 follow-up groups were compared using chi-square test. All analyses were performed using Stata 18 (StataCorp LLC), unless indicated otherwise, with a p-value of <0.05 being considered statistically significant.

1. Distributional characteristics

The response distribution of each FACIT-COST item was detailed along with their corresponding ceiling and floor. Ceiling or floor effects were considered present if more than 15% of the patients scored the highest or lowest possible FACIT-COST total score.[31]

2. Structural validity

Structural validity of the FACIT-COST was first assessed using the principal component analysis (PCA). The appropriateness of PCA was assessed using the Kaiser-Meyer-Olkin (KMO) test and Bartlett's test of sphericity, with a KMO value of at least 0.80 and $p<0.05$ for the Bartlett's test indicating suitability for analysis.[29] The number of retained principal components was determined using the parallel analysis technique.[32] Rotation was performed using the oblique Promax method to allow for potential correlations among components. Factor loadings, which indicate how strongly the items were associated with the construct they are intended to measure, were interpreted as: ≤ 0.32 (unacceptable), 0.33-0.44 (poor), 0.45-0.54 (fair), 0.55-0.62 (good), 0.63-0.70 (very good), and ≥ 0.71 (excellent).[33] Item communalities

(i.e., the extent to which an item correlates with all other items) of ≥0.5 were deemed acceptable.[29] Afterward, the structure of the instrument was further evaluated using the confirmatory factor analysis (CFA). Prior to testing the two-factor model proposed by the PCA output, we also experimented with other models (e.g., one-factor and bifactor models). The two-factor model was ultimately selected based on goodness-of-fit statistics and item loading sizes. CFA parameters were estimated using diagonally weighted least squares method due to the ordinal nature of item responses in FACIT-COST.[34] Modification indices (MIs) were inspected to identify error covariances, and correlations were allowed between pairs of items with MIs >3.84.[35] The goodness-of-fit of the model was evaluated using multiple criteria: i) Root mean square error of approximation (RMSEA), ii) Standardized root mean square residual (SRMR), iii) comparative fit index (CFI), and iv) Tucker-Lewis index (TLI). In addition, 95% confidence intervals were computed around the goodness-of-fit values using 1000 bootstrap resampling. The model fit was deemed good with values of: RMSEA <0.06, SRMR <0.08, and CFI and TLI, each >0.95.[36] The PCA and CFA were conducted using the 'lavaan' R package in RStudio (Posit Software, PBC).[37]

3. Internal consistency reliability

Item discrimination or the extent to which individual items contributed to the overall scale, was assessed by calculating Cronbach's alpha (α) and McDonald's omega (ω) values if the item was removed.[38,39] The internal consistency reliability of the identified FACIT-COST factors was also evaluated using Cronbach's α and McDonald's ω, with internal consistency considered adequate if α or ω was between 0.70 and 0.90, inclusive.[40,41]

4. Known-groups validity

Known-groups validity was evaluated by comparing the average FACIT-COST scores of patient groups based on their socio-demographic, clinical characteristics, financial coping strategies, and responses of FT12 item, which was not included in the computation of FACIT-COST total score. The FACIT-COST total scores were compared across subgroups using the Mann-Whitney or Kruskal-Wallis test. We hypothesized that patients who were younger, low-educated, living in a rural area, had lower income, not actively working, had metastatic cancer, and experienced more

symptoms to have lower FACIT-COST total score (or higher SFT).[15,18,19,42] We also predicted that patients who used more financial coping strategies and scored higher (i.e., worse) on FT12 of FACIT-COST would have lower FACIT-COST score.

5. Evaluation of changes in SFT status

The FT12 item, which asked whether illness had been a financial hardship to study participants and their families, was adopted to evaluate changes in the patients' SFT and further utilized as an anchor for test-retest reliability and responsiveness analyses. To determine the appropriateness of the FT12 as anchor, a Spearman's rank correlation of ≥0.30 between FT12 and FACIT-COST total score was required.[43] Changes in FT12 were classified into three subgroups: i) 'unchanged,' if baseline FT12 item score was equal to the follow-up, ii) 'improved,' if baseline FT12 item score was greater than the follow-up, and iii) 'worsened,' if baseline FT12 item score was lower than the follow-up. The test-retest reliability analysis included only patients with an 'unchanged' status, while the responsiveness analysis considered patients with 'improved' and 'worsened' statuses.

6. Combining the T1 and T2 group responses for test-retest reliability and responsiveness analyses

Initially, different follow-up time points were used to increase the likelihood that one group (T1) would remain stable, serving for test-retest reliability analysis, while the other group (T2) would experience change, designated for responsiveness analysis. However, ultimately, the responses from T1 and T2 were combined due to minimal differences between the groups' responses, as well as to increase statistical power.

7. Test-retest reliability and responsiveness

Test-retest reliability was evaluated using Gwet's AC2 coefficient for the items and intraclass correlation coefficient for the instrument.[44,45] The coefficients were interpreted as: slight agreement (0-0.20), fair agreement (0.21-0.40), moderate agreement (0.41-0.60), strong agreement (0.61-0.80), and almost-perfect agreement (0.81-1.00).[46]

Responsiveness to change was assessed using standardized response mean (SRM) and effect size (SES). The SRM was estimated as the mean change in FACIT-COST

total scores between baseline and follow-up and divided by the standard deviation of the score change. The SES was computed as the mean change between baseline and follow-up scores divided by the standard deviation of the baseline score. The SRM and SES results were interpreted as small (<0.50), moderate (0.50-0.79), and large (≥0.80).[47]

IV.3 RESULTS

IV.3.1 Patient characteristics

A total of 300 female patients with breast cancer (mean age 51±10) participated completed the baseline questionnaire (response rate=96.8%). Out of 300 patients, 150 were in active treatment cycles at baseline and invited to the T1 follow-up, which was completed by 148 patients (mean follow-up duration=5.8±3.0 weeks, range=1.9-13.0 weeks). The remaining 150 patients, consisting of those in their final round of treatment cycle, were invited to the T2 follow-up, with all 150 completing the follow-up questionnaire (mean follow-up duration=11.6±4.0 weeks, range=4.0-25.9 weeks). Two patients died during the study period. There were no statistically significant differences in socio-demographic or clinical characteristics between the patients in T1 and T2 groups except for disease duration (Table IV.1)

IV.3.2 Distributional characteristics

The FACIT-COST items with the highest ceiling (i.e., no SFT) were ‘frustrated about unable to continue/work as usual’ (54.7%), ‘concerned about keeping income’ (45.7%), and ‘out-of-pocket expenses were more than thought’ (42.3%), while the items with highest floor (i.e., highest SFT) were ‘have enough money to cover treatment’ (37.7%), ‘satisfied with current finances’, and ‘in control of finances’ (19.0% each) (Table IV.2). Complete FACIT-COST responses are presented in Table IV.2 (baseline) and Appendix IV.1 (follow-up). The mean FACIT-COST total scores were 24.29±8.66 and 24.50±8.68 at baseline and follow-up, respectively. No patients reported the best or worst possible total score (i.e., both ceiling and floor were 0%).

IV.3.3 Structural validity

The PCA resulted in a two-component model, with the first and second components accounting for 37.3% and 23.3% of the variance in FACIT-COST, respectively (Table IV.3).

Table IV.1. Baseline characteristics of the patients

Characteristic	Overall sample (n=300)		T1 follow-up group (n=148)		T2 follow-up group (n=150)		p-value
	N	%	N	%	N	%	
Socio-demographic characteristic							
Age							
<50 years	132	44.0%	67	45.3%	64	42.7%	0.642
50 years and above	168	56.0%	81	54.7%	86	57.3%	
Education							
Primary or less	92	30.7%	46	31.1%	45	30.0%	0.893
Secondary	157	52.3%	78	52.7%	78	52.0%	
Tertiary	51	17.0%	24	16.2%	27	18.0%	
Employment status							
Employed	55	18.3%	32	21.6%	23	15.3%	0.400
Homemaker	221	73.7%	104	70.3%	115	76.7%	
Unemployed and job-seeking	4	1.3%	2	1.4%	2	1.4%	
Retired	20	6.7%	10	6.8%	10	6.7%	
Residential setting							
Rural	179	59.7%	91	61.5%	86	57.3%	0.410
Urban	121	40.3%	57	38.5%	64	42.7%	
Children (aged <17) living in the same household							
0	144	48.0%	65	43.9%	78	52.0%	0.235
1	80	26.7%	40	27.0%	40	26.7%	
2 or more	76	25.3%	43	29.1%	32	21.3%	
Net monthly household income[a]							
Up to 5 million IDR	270	90.0%	131	88.5%	137	91.3%	0.441
>5 million IDR	30	10.0%	17	11.5%	13	8.7%	
Health insurance coverage	299	99.7%	147	99.3%	150	100.0%	0.317
Clinical characteristic							
Disease duration							
1 year or less	144	48.0%	60	40.5%	83	55.3%	0.011*
>1 year	156	52.0%	88	59.5%	67	44.7%	
Current metastasis status[b]							
No	276	92.0%	136	91.9%	140	93.3%	0.395
Yes	24	8.0%	12	8.1%	10	6.7%	
Number of symptoms experienced during the past week[c]							
None	17	5.7%	12	8.1%	5	3.3%	0.311
1-5 symptoms	119	39.7%	61	41.2%	58	38.7%	
6-10 symptoms	93	31.0%	43	29.1%	49	32.7%	
>10 symptoms	71	23.7%	32	21.6%	38	25.3%	

Notes. T1 follow-up= completed during the subsequent treatment cycle, T2 follow-up= completed during the post-treatment consultation. There were no missing responses as all questions were mandatory. Total of the percentages may not add up to 100% due to rounding.

*Chi-square (χ^2) test $p<0.05$

[a]IDR= Indonesian Rupiah, 324.34 USD = 5 million IDR (based on the closing 2023 middle exchange rate, Bank Indonesia)

[b]Most common sites were bone, lung, and liver

[c]Most commonly self-reported symptoms included fatigue, dizziness, muscle pain, sleep problem, and anxiety

.

Table IV.2. FACIT-COST item distribution at baseline

Code	FACIT-COST item[§]	Baseline responses, n=300 (n, %)					Ceiling (n, %)	Floor (n, %)
		Not at all	A little bit	Somewhat	Quite a bit	Very much		
FT1	Have enough money to cover treatment	113 (37.7%)	86 (28.7%)	80 (26.7%)	19 (6.3%)	2 (0.7%)	2 (0.7%)	113 (37.7%)
FT2[r]	Out-of-pocket expenses are more than thought	127 (42.3%)	53 (17.7%)	56 (18.7%)	47 (15.7%)	17 (5.7%)	127 (42.3%)	17 (5.7%)
FT3[r]	Worry about future financial problems	86 (28.7%)	50 (16.7%)	76 (25.3%)	52 (17.3%)	36 (12.0%)	86 (28.7%)	36 (12.0%)
FT4[r]	No choice about money spent	104 (34.7%)	48 (16.0%)	68 (22.7%)	57 (19.0%)	23 (7.7%)	104 (34.7%)	23 (7.7%)
FT5[r]	Frustrated about inability to contribute/work as usual	164 (54.7%)	52 (17.3%)	52 (17.3%)	24 (8.0%)	8 (2.7%)	164 (54.7%)	8 (2.7%)
FT6	Satisfied with current finances	57 (19.0%)	62 (20.7%)	135 (45.0%)	39 (13.0%)	7 (2.3%)	7 (2.3%)	57 (19.0%)
FT7	Able to meet monthly expenses	45 (15.0%)	64 (21.3%)	141 (47.0%)	43 (14.3%)	7 (2.3%)	7 (2.3%)	45 (15.0%)
FT8[r]	Feel financially stressed	70 (23.3%)	65 (21.7%)	93 (31.0%)	41 (13.7%)	31 (10.3%)	70 (23.3%)	31 (10.3%)
FT9[r]	Concerned about keeping income	137 (45.7%)	58 (19.3%)	50 (16.7%)	38 (12.7%)	17 (5.7%)	137 (45.7%)	17 (5.7%)
FT10[r]	Reduced financial satisfaction due to treatment/disease	89 (29.7%)	57 (19.0%)	84 (28.0%)	46 (15.3%)	24 (8.0%)	89 (29.7%)	24 (8.0%)
FT11	In control of finances	57 (19.0%)	79 (26.3%)	118 (39.3%)	37 (12.3%)	9 (3.0%)	9 (3.0%)	57 (19.0%)
FT12	Financial hardship to my family and me	101 (33.7%)	47 (15.7%)	67 (22.3%)	53 (17.7%)	32 (10.7%)	101 (33.7%)	32 (10.7%)

FACIT-COST= COST: A FACIT Measure of Financial Toxicity
[§]Labeled by the authors based on the FACIT-COST items
[r]Items coded in reverse for the FACIT-COST total score computation

Table IV.3. Principal component analysis results

Code	FACIT-COST item[§]	Component loadings		Communalities
		Component 1	Component 2	
FT4	No choice about money spent	0.896	-	0.740
FT3	Worry about future financial problems	0.828	-	0.701
FT9	Concerned about keeping income	0.787	-	0.652
FT10	Reduced financial satisfaction due to treatment/disease	0.755	-	0.654
FT5	Frustrated about inability to contribute/work as usual	0.698	-	0.540
FT2	Out-of-pocket expenses are more than thought	0.672	-	0.603
FT8	Feel financially stressed	0.633	-	0.380
FT7	Able to meet monthly expenses	-	0.818	0.728
FT6	Satisfied with current finances	-	0.792	0.690
FT11	In control of finances	-	0.756	0.540
FT1	Have enough money to cover treatment	-	0.697	0.436
Component characteristic		**Promax rotation**		
		Eigenvalue		**Proportion variance**
Component 1		4.102		37.3%
Component 2		2.560		23.3%
PCA appropriateness check				
Kaiser-Meyer-Olkin overall measure		0.883		
Bartlett's test for sphericity		$\chi 2$ =1542.459 (df = 55), p<0.001		

FACIT-COST= COST: A FACIT Measure of Financial Toxicity
[§]Labeled by the authors based on the FACIT-COST items

Component 1 consisted of the seven negatively worded items related to adverse reactions to financial burden, whereas Component 2 comprised the four positively worded items related to the perceived ability to manage financial burden. Overall, seven items exhibited excellent factor loadings (range=0.755-0.896), while the rest were very good (0.633-0.698). Two items did not pass the threshold for acceptable communalities in relation to the factor on which they loaded, i.e., 'have enough money to cover treatment (0.436) and 'feel financially stressed' (0.380).

The results of the CFA confirmed a good fit for the two-factor model, reflecting the underlying construct of subjective financial toxicity, as indicated by the following indices: RMSEA=0.042 (95%CI=0.019-0.063), SRMR=0.049 (95%CI=0.048-0.074), CFI=0.998 (95%CI=0.990-0.999), and TLI=0.997 (95%CI=0.987-0.997) (Table IV.4). Three covariance parameters were added to this model. Items with the highest factor loadings included 'able to meet monthly expenses' (0.899), 'satisfied with current finances' (0.847), and 'reduced financial satisfaction due to treatment/disease' (0.846), while 'have enough money to cover treatment' and 'out-of-pocket expenses are more than thought' items had the lowest factor loadings at 0.509 and 0.474, respectively.

IV.3.4 Internal consistency reliability

The two factors of the FACIT-COST demonstrated adequate internal consistency reliability (Appendix IV.2). For the first factor (i.e., the seven negatively worded items),

Cronbach's α was 0.882 (95%CI: 0.861-0.901) and McDonald's ω was 0.888 (95%CI: 0.868-0.907). The second factor (i.e., the four positively worded items) yielded lower reliability coefficients, with α=0.774 (95%CI: 0.729-0.813) and ω=0.786 (95%CI: 0.747-0.825). Trivial improvements were observed in the first factor's reliability if FT2 was removed (α=0.893, ω=0.896), and in the second factor if FT1 was removed (α=0.795, ω=0.800).

Table IV.4. Confirmatory factor analysis results

Factor loadings				
Factor	**FACIT-COST item[§]**		**Estimate**	**p-value**
Factor 1	FT2	Out-of-pocket expenses are more than thought	0.474	p<0.001
	FT3	Worry about future financial problems	0.819	p<0.001
	FT4	No choice about money spent	0.791	p<0.001
	FT5	Frustrated about inability to contribute/work as usual	0.739	p<0.001
	FT8	Feel financially stressed	0.808	p<0.001
	FT9	Concerned about keeping income	0.810	p<0.001
	FT10	Reduced financial satisfaction due to treatment/disease	0.846	p<0.001
Factor 2	FT1	Have enough money to cover treatment	0.509	p<0.001
	FT6	Satisfied with current finances	0.847	p<0.001
	FT7	Able to meet monthly expenses	0.899	p<0.001
	FT11	In control of finances	0.641	p<0.001
Factor 1 ↔ Factor 2 covariance = -0.577				
Correlations in the model				
FT5 ↔ FT9			0.178	
FT2 ↔ FT4			0.178	
FT3 ↔ FT4			0.146	
Goodness-of-fit statistics (95% confidence interval)				
RMSEA	**SRMR**	**CFI**	**TLI**	
0.042 (0.019-0.063)	0.049 (0.048-0.074)	0.998 (0.990-0.999)	0.997 (0.987-0.997)	

CFI= Comparative Fit Index, FACIT-COST= COST: A FACIT Measure of Financial Toxicity, RMSEA= Root mean square error of approximation, SRMR= Standardized root mean square residual, TLI= Tucker-Lewis Index

[§]Labeled by the authors based on the FACIT-COST items

IV.3.5 Known-groups validity

As hypothesized, patients who were younger, lower-educated, resided in a rural area, earned lower income, not actively employed, suffered from metastatic cancer, and reported more symptoms had significantly lower FACIT-COST total scores (i.e. higher SFT) (Table IV.5). Significant differences were found in FACIT-COST total scores across patients who implemented financial coping strategies as follows: incurring debt, selling assets, and closing business. The FACIT-COST also significantly discriminated across the responses of FT12 item. However, the FACIT-COST score did not discriminate across known-groups based on the number of children, disease duration, and withdrawing savings/pension to cope with financial challenges.

Table IV.5. Differences in FACIT-COST scores across known-groups

Characteristics	n	%	Mean (SD) FACIT-COST total score	p-value
Socio-demographic grouping				
Age				
<50 years	132	44.0%	22.1 (8.6)	p<0.001
50 years and above	168	56.0%	25.9 (8.3)	
Education				
Primary or less	92	30.7%	21.8 (7.9)	p<0.001
Secondary	157	52.3%	24.0 (8.5)	
Tertiary	51	17.0%	29.4 (8.3)	
Residential setting				
Rural	179	59.7%	22.5 (8.5)	p<0.001
Urban	121	40.3%	26.8 (8.2)	
Net monthly household income				
Up to 5 million IDR	270	90.0%	23.3 (8.4)	p<0.001
>5 million IDR	30	10.0%	32.5 (5.8)	
Children (aged <17) living in the same household				
0	144	48.0%	24.8 (8.9)	p=0.082
1	80	26.7%	22.4 (8.5)	
2 or more	76	25.3%	25.1 (8.2)	
Employment status				
Employed	55	18.3%	25.9 (8.5)	p=0.002
Homemaker (incl. n=4 seeking for work)	225	75.0%	23.4 (8.6)	
Retired	20	6.7%	28.9 (7.4)	
Clinical grouping				
Disease duration (in years)				
1 year or less	144	48.0%	25.2±8.4	p=0.079
> 1 year	156	52.0%	23.3±8.8	
Metastasis (current)				
No	276	92.0%	24.5 (8.7)	p=0.042
Yes	24	8.0%	20.8 (7.6)	
Number of symptoms in the past 7 days				
None	17	5.7%	26.82 (87.84)	p<0.001
1-5 symptoms	119	39.7%	26.29 (8.39)	
6-10 symptoms	93	31.0%	24.15 (7.96)	
>10 symptoms	71	23.7%	20.31 (8.88)	
Financial coping strategies:				
Debt				
Incurred loan	90	30.0%	18.6 (7.8)	p<0.001
Did not incur loan	210	70.0%	26.6 (7.8)	
Savings/pension withdrawal				
Withdrew pension/savings	77	25.7%	24.6 (9.3)	p=0.645
Did not withdraw pension/savings	223	74.3%	24.1 (8.4)	
Asset sale				
Sold assets	33	11.0%	19.7 (9.2)	p=0.002
Did not sell assets	267	89.0%	24.8 (8.4)	
Closing business				
Closed business	10	3.3%	18.8 (9.1)	p=0.047
Did not close business	290	96.7%	24.4 (8.6)	
Number of financial coping strategies used				
0	147	49.0%	26.4 (7.9)	p<0.001
1	116	38.7%	23.3 (8.8)	
2	21	7.0%	21.8 (7.0)	
3-4	16	5.3%	12.7 (5.7)	
FACIT-COST item 12 responses				
0: Not at all	101	33.7%	32.1 (6.1)	p<0.001
1: A little bit	47	15.7%	25.5 (4.0)	
2: Somewhat	67	22.3%	23.2 (4.2)	
3: Quite a bit	53	17.7%	16.7 (6.0)	
4: Very much	32	10.7%	12.2 (5.0)	

FACIT-COST= COST: A FACIT Measure of Financial Toxicity
Note. Total of the percentages may not add up to 100% due to rounding.

IV.3.6 Changes in SFT status

Overall, 45 (15%), 66 (22%), and 187 (63%) patients experienced improved, worsened, and unchanged SFT based on the FT12 item, respectively (Table IV.6). A strong correlation (Spearman's rho=0.80) was found between the FT12 item and FACIT-COST total score at baseline, therefore supporting its use as an anchor for test-retest reliability and responsiveness analyses

IV.3.7 Test-retest reliability and responsiveness

Strong agreement was found for all items (Gwet's AC2 range=0.64-0.79), with 'concerned about keeping income' as the best-performing item (Table IV.6). At the instrument level, the FACIT-COST indicated excellent agreement, with an ICC of 0.96. Furthermore, it demonstrated responsiveness with large SRM and SES in the 'improved' subgroup (n=45, SRM=0.92, SES=0.75). While in the 'worsened' subgroup, small to borderline moderate SRM and SES were found (n=66, SRM=-0.50, SES=-0.39). The Gwet's AC2, ICC, SRM, and SES for each follow-up group are presented in Appendix IV.3.

IV.4 DISCUSSION

The study evaluated the measurement properties of the Indonesian version of FACIT-COST. Our findings show that the FACIT-COST is a psychometrically valid and reliable measure, as indicated by the absence of ceiling and floor effects at the scale level, good structural validity, adequate internal consistency reliability, discriminatory power across multiple key known-groups, excellent instrument-level test-retest reliability, and evidence of responsiveness to change. The absence of ceiling and floor effects suggests a good coverage of the FACIT-COST items across the whole range of the underlying construct.

Our findings suggest a two-factor structure for the Indonesian version of FACIT-COST (v2). The factors and their corresponding items align with the structures found in the Simplified Chinese, Arabic, and Vietnamese (v1) versions, which were validated across various types of cancer.[18,20,48] The two-factor model suggests that financial toxicity encompasses both the negative experiences of financial burden and the ability to manage one's finances. This model provides healthcare providers with a better understanding of patients' financial toxicity and supports more targeted interventions, such as providing

Table IV.6. Test-retest reliability and responsiveness of the FACIT-COST

Code	FACIT-COST item[§]	Gwet's AC2 for T1 and T2 follow-up groups combined (n=187)
FT1	Have enough money to cover treatment	0.72
FT2	Out-of-pocket expenses are more than thought	0.71
FT3	Worry about future financial problems	0.71
FT4	No choice about money spent	0.71
FT5	Frustrated about inability to contribute/work as usual	0.76
FT6	Satisfied with current finances	0.69
FT7	Able to meet monthly expenses	0.64
FT8	Feel financially stressed	0.69
FT9	Concerned about keeping income	0.79
FT10	Reduced financial satisfaction due to treatment/disease	0.68
FT11	In control of finances	0.65

Patient subgroups	n	%	Mean (SD) FACIT-COST total score			ICC (95% CI)	SRM (95% CI)	SES (95% CI)
			Baseline	Follow-up	Change			
T1 and T2 combined	*298*	*100%*	24.29 (8.66)	24.50 (8.68)	0.21 (4.96)			
Improved in FT12	45	*15%*	19.47 (6.85)	24.60 (6.25)	5.13 (5.59)	-	0.92 (0.67, 1.18)	0.75 (0.51, 1.01)
Worsened in FT12	*66*	*22%*	24.17 (6.54)	21.62 (6.64)	-2.55 (5.13)	-	-0.50 (-0.77, -0.22)	-0.39 (-0.59, -0.19)
Unchanged in FT12	*187*	*63%*	25.49 (9.31)	25.49 (9.57)	0.00 (3.75)	0.96 (0.95, 0.97)	-	-

CI= confidence interval, FACIT-COST= COST: A FACIT Measure of Financial Toxicity, FT12=twelfth item of the FACIT-COST ('financial hardship to my family and me'), ICC= intraclass correlation coefficient, SD= standard deviation, SEM= standard error of measurement, SES= standardized effect size, SRM= standardized response mean

[§]Labeled by the authors based on the FACIT-COST items

Notes.

1. T1 follow-up= completed during the subsequent treatment cycle, T2 follow-up= completed during the post-treatment consultation.
2. Gwet's AC2 was computed for patients with unchanged FT12 response at the follow-up compared to the baseline.
3. Test-retest reliability (Gwet's AC2) for item FT12 was not computed because it was used as an anchor.
4. Improved in FT12= baseline item score greater than follow-up, worsened= follow-up item score greater than baseline, unchanged= baseline item score equaled to follow-up.

resources to reduce financial burden or financial navigation programs to improve financial management skills.[49-55] The results of our internal consistency reliability analysis align with the range observed in previous validations of translated FACIT-COST instruments with two-factor solutions (α=0.77-0.92),[18,20,48] even though some of these figures are lower than those reported in the original US validation study, which used a one-factor solution (α=0.92).[15]

Structural variations in FACIT-COST have been observed, including a one-factor model for the original US (v1) and Italian (v2) versions, and a three-factor model for the Persian (v1) version.[17,24,56] Interestingly, a study in Hong Kong failed to confirm either a one- or two-factor structure for the Traditional Chinese (v2) version.[19] Originating in the US, the FACIT-COST may not universally apply due to differences in health systems, socioeconomic factors, and cultural contexts. In the case of the Indonesian FACIT-COST, two items—'have enough money to cover treatment' and 'out-of-pocket expenses are more than thought'—did not fit the model well, while also showing high item floor/ceiling. This outcome could be attributable to the public referral hospital setting of our study. Moreover, the women in our sample were predominantly not the primary earners in their families and may have perceived financial hardship differently from the main income provider. Nevertheless, we support the use of the two-factor structure based on the good model fit. Factorial structure differences are not uncommon in outcome measures, both in original and translated versions.[57-60] Therefore, future translations and cross-cultural adaptations can consider qualitative testing to inform the further development of the instrument.

Patients who were younger, living in a rural area, had lower income, and not actively employed were shown to have higher SFT. These differences in socio-demographic factors have been well-documented.[1,18,42,61] Younger patients or those who are not actively employed could be more susceptible to have financial toxicity due to lower or no earning capacity. Meanwhile, those living in rural area may incur higher transportation costs to reach the medical facility for treatment.[62] Higher SFT was also reported by patients with metastatic cancer and experiencing more symptoms. Studies have shown that financial toxicity was related to cancer symptom burden,[63,64] and that patients with more advanced stage of cancer experienced higher financial burden due to their more complex treatment.[65] Furthermore, as hypothesized, patients who implemented more coping strategies had higher SFT, as their high cancer-related costs may have

required them to prepare more funds through actions such as making loans, which could be associated with higher perceived SFT.

The excellent instrument-level test-retest reliability of the Indonesian FACIT-COST (ICC=0.96) was similar to that of the Chinese (ICCs=0.80-0.89) and Japanese (ICC=0.85) versions,[18,66] and higher than the US version (ICC=0.80), which was assessed in a small sample size of 20.[15] In comparison, the responsiveness that we observed (SRM= |0.50| to |0.92|) was larger than what was reported in the Chinese validation study (SRM=0.2-0.3) in patients with lung, stomach, colorectal, and breast cancer.[18] However, it should be noted that the Chinese study had a longer follow-up period of six months and involved all patients without using an anchor for assessing change in the patients.

We acknowledge some limitations of our study. First, the sample comprised exclusively female patients with one type of cancer. Second, the study was performed at a public referral hospital where almost all patients (99.7%) were covered by insurance, which may explain why there were no worst possible scores. However, it is important to note that public health insurance coverage did not guarantee exemption from financial toxicity, as certain expenses such as transportation, specific medical procedures and supplies, may not have been covered. Moreover, patients may have also experienced productivity loss due to treatment. The use of financial coping strategies reported by patients further supported the presence of financial toxicity. Third, some analyses may have been underpowered due to the limited sample size of subgroups. Future studies can consider larger sample size, involving other or multiple cancer types, and populations from private hospitals where patients may incur higher out-of-pocket cancer expenditures. Longer follow-up periods (e.g., 6-12 months) can also be considered for future testing.

IV. 5 CONCLUSIONS

This study is the first to validate the FACIT-COST solely in a breast cancer population and to report on the measurement properties of the Indonesian version of FACIT-COST. We conclude that the Indonesian version of FACIT-COST (v2) shows acceptable psychometric performance and may be applied for assessing patient financial toxicity. Healthcare providers can use this instrument to better understand and address the financial challenges their patients may face during treatment, integrating these considerations into personalized care plans. This can be help prevent serious consequences of financial toxicity, such as treatment non-adherence. Additionally,

patients identified as experiencing high financial toxicity can be referred to existing social aid resources for further support.

References

1. Pangestu S, Rencz F. Comprehensive Score for Financial Toxicity and Health-Related Quality of Life in Patients With Cancer and Survivors: A Systematic Review and Meta-Analysis. *Value Health*. 2023;26(2):300-316. doi:10.1016/j.jval.2022.07.017
2. Bhanvadia SK, Psutka SP, Burg ML, et al. Financial Toxicity Among Patients with Prostate, Bladder, and Kidney Cancer: A Systematic Review and Call to Action. *Eur Urol Oncol*. 2021;4(3):396-404. doi:10.1016/j.euo.2021.02.007
3. Ritter J, Allen S, Cohen PD, et al. Financial hardship in families of children or adolescents with cancer: a systematic literature review. *Lancet Oncol*. 2023;24(9):e364-e375. doi:10.1016/s1470-2045(23)00320-0
4. Sitlinger A, Zafar SY. Health-Related Quality of Life: The Impact on Morbidity and Mortality. *Surg Oncol Clin N Am*. Oct 2018;27(4):675-684. doi:10.1016/j.soc.2018.05.008
5. Witte J, Mehlis K, Surmann B, et al. Methods for measuring financial toxicity after cancer diagnosis and treatment: a systematic review and its implications. *Ann Oncol*. 2019;30(7):1061-1070. doi:10.1093/annonc/mdz140
6. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. *CA Cancer J Clin*. 2018;68(2):153-165. doi:10.3322/caac.21443
7. Gordon LG, Merollini KMD, Lowe A, Chan RJ. A Systematic Review of Financial Toxicity Among Cancer Survivors: We Can't Pay the Co-Pay. *Patient*. 2017;10(3):295-309. doi:10.1007/s40271-016-0204-x
8. Jiang H, Lyu J, Mou W, Jiang Q, Du J. Association between financial toxicity and health-related quality of life in cancer survivors: A systematic review. *Asia Pac J Clin Oncol*. 2023;19(4):439-457. doi:10.1111/ajco.13901
9. Riva S, Arenare L, Di Maio M, et al. Cross-sectional study to develop and describe psychometric characteristics of a patient-reported instrument (PROFFIT) for measuring financial toxicity of cancer within a public healthcare system. *BMJ Open*. 2021;11(10):e049128. doi:10.1136/bmjopen-2021-049128
10. Dar MA, Chauhan R, Murti K, Trivedi V, Dhingra S. Development and Validation of Subjective Financial Distress Questionnaire (SFDQ): A Patient Reported Outcome Measure for Assessment of Financial Toxicity Among Radiation Oncology Patients. *Front Oncol*. 2021;11:819313. doi:10.3389/fonc.2021.819313
11. Hueniken K, Douglas CM, Jethwa AR, et al. Measuring financial toxicity incurred after treatment of head and neck cancer: Development and validation of the Financial Index of Toxicity questionnaire. *Cancer*. 2020;126(17):4042-4050. doi:10.1002/cncr.33032
12. Zhu Z, Xing W, Zhang X, Hu Y, So WKW. Cancer survivors' experiences with financial toxicity: A systematic review and meta-synthesis of qualitative studies. *Psychooncology*. 2020;29(6):945-959. doi:10.1002/pon.5361
13. Eremenco SL, Cella D, Arnold BJ. A comprehensive method for the translation and cross-cultural validation of health status questionnaires. *Eval Health Prof*. 2005;28(2):212-32. doi:10.1177/0163278705275342
14. Acquadro C, Conway K, Hareendran A, Aaronson N. Literature review of methods to translate health-related quality of life questionnaires for use in multinational clinical trials. *Value Health*. 2008;11(3):509-21. doi:10.1111/j.1524-4733.2007.00292.x
15. de Souza JA, Yap BJ, Wroblewski K, et al. Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the COmprehensive Score for financial Toxicity (COST). *Cancer*. 2017;123(3):476-484. doi:10.1002/cncr.30369
16. Durber K, Halkett GK, McMullen M, Nowak AK. Measuring financial toxicity in Australian cancer patients - Validation of the COmprehensive Score for financial Toxicity (FACT COST) measuring financial toxicity in Australian cancer patients. *Asia Pac J Clin Oncol*. 2021;17(4):377-387. doi:10.1111/ajco.13508
17. Ripamonti CI, Chiesi F, Di Pede P, et al. The validation of the Italian version of the COmprehensive Score for financial Toxicity (COST). *Support Care Cancer*. 2020;28(9):4477-4485. doi:10.1007/s00520-019-05286-y
18. Yu HH, Yu ZF, Li H, Zhao H, Sun JM, Liu YY. The COmprehensive Score for financial Toxicity in China: Validation and Responsiveness. *J Pain Symptom Manage*. 2021;61(6):1297-1304.e1. doi:10.1016/j.jpainsymman.2020.12.021

19. Chan DNS, Choi KC, Ng MSN, et al. Translation and validation of the Traditional Chinese version of the COmprehensive Score for financial Toxicity-Functional Assessment of Chronic Illness Therapy (Version 2). *Health Qual Life Outcomes*. 2021;19(1):17. doi:10.1186/s12955-020-01646-z
20. Mejri N, Rachdi H, Mnif A, et al. Translation and Validation of the Comprehensive Score of Financial Toxicity for Cancer Patients Into Arabic. *J Nurs Meas*. 2022;30(4):673-682. doi:10.1891/jnm-d-20-00140
21. Honda K, Gyawali B, Ando M, et al. Prospective Survey of Financial Toxicity Measured by the Comprehensive Score for Financial Toxicity in Japanese Patients With Cancer. *J Glob Oncol*. 2019;5:1-8. doi:10.1200/jgo.19.00003
22. Fradelos EC, Prapa PM, Tsaras K, et al. The Validation of the COmprehensive Score for Financial Toxicity (COST) Scale in Greek Language. *Adv Exp Med Biol*. 2023;1425:191-197. doi:10.1007/978-3-031-31986-0_18
23. de Alcantara Nogueira L, Koller FJ, Marcondes L, et al. Validation of the comprehensive score for financial toxicity for Brazilian culture. *Ecancermedicalscience*. 2020;14:1158. doi:10.3332/ecancer.2020.1158
24. Pahlevan Sharif S, Moshtagh M, Sim OF, Naghavi N, Sharif Nia H. Psychometric evaluation of the comprehensive score for financial toxicity scale among Iranian cancer patients. *J Cancer Policy*. 2021;30:100308. doi:10.1016/j.jcpo.2021.100308
25. Kosen S. Coverage and implementation of healthcare delivery for cancer under national health insurance, experience of Indonesia. *Lancet Reg Health Southeast Asia*. 2022;6:100065. doi:10.1016/j.lansea.2022.100065
26. Fiala MA, Leblanc MR, Coccia KW, et al. Mixed-Methods Study on the Responsiveness of the Comprehensive Score for Financial Toxicity Among People With Multiple Myeloma. *JCO Oncol Pract*. 2024:Op2300645. doi:10.1200/op.23.00645
27. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-249. doi:10.3322/caac.21660
28. Mokkink LB, Prinsen CAC, Patrick DL, et al. *COSMIN Study Design checklist for Patient-reported outcome measurement instruments (Version July 2019)*. 2019. https://www.cosmin.nl/wp-content/uploads/COSMIN-study-designing-checklist_final.pdf
29. Hair JF, Babin BJ, Black WC, Anderson RE. *Multivariate Data Analysis*. Cengage; 2019.
30. FACIT. FACIT-COST. Accessed March 31, 2024, https://www.facit.org/measures/facit-cost
31. Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol*. 2007;60(1):34-42. doi:10.1016/j.jclinepi.2006.03.012
32. Franklin SB, Gibson DJ, Robertson PA, Pohlmann JT, Fralish JS. Parallel analysis: a method for determining significant principal components. *Journal of Vegetation Science*. 1995;6(1):99-106.
33. Comrey AL, Lee HB. *A first course in factor analysis*. Psychology press; 2013.
34. Li CH. The performance of ML, DWLS, and ULS estimation with robust corrections in structural equation models with ordinal variables. *Psychol Methods*. 2016;21(3):369-87. doi:10.1037/met0000093
35. Whittaker TA. Using the modification index and standardized expected parameter change for model modification. *The Journal of Experimental Education*. 2012;80(1):26-44.
36. Schermelleh-Engel K, Moosbrugger H, Müller H. Evaluating the fit of structural equation models: Tests of significance and descriptive goodness-of-fit measures. *Methods of psychological research online*. 2003;8(2):23-74.
37. Rosseel Y. lavaan: An R Package for Structural Equation Modeling. *Journal of Statistical Software*. 2012;48(2):1 - 36. doi:10.18637/jss.v048.i02
38. Cronbach LJ. Coefficient alpha and the internal structure of tests. *psychometrika*. 1951;16(3):297-334.
39. Hayes AF, Coutts JJ. Use omega rather than Cronbach's alpha for estimating reliability. But…. *Communication Methods and Measures*. 2020;14(1):1-24.
40. McNeish D. Thanks coefficient alpha, we'll take it from here. *Psychol Methods*. 2018;23(3):412-433. doi:10.1037/met0000144
41. Tavakol M, Dennick R. Making sense of Cronbach's alpha. *Int J Med Educ*. 2011;2:53-55. doi:10.5116/ijme.4dfb.8dfd
42. Xu RH, Wang LL, Zhou LM, Wong EL, Wang D. Urban-rural differences in financial toxicity and its effect on cancer survivors' health-related quality of life and emotional status: a latent class analysis. *Support Care Cancer*. 2022;30(5):4219-4229. doi:10.1007/s00520-021-06762-0
43. Revicki D, Hays RD, Cella D, Sloan J. Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol*. 2008;61(2):102-9. doi:10.1016/j.jclinepi.2007.03.012

44. Gwet KL. *Handbook of inter-rater reliability: The definitive guide to measuring the extent of agreement among raters*. Advanced Analytics, LLC; 2014.
45. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med*. 2016;15(2):155-63. doi:10.1016/j.jcm.2016.02.012
46. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. Mar 1977;33(1):159-74.
47. Cohen J. *Statistical power analysis for the behavioral sciences*. Academic press; 2013.
48. Tran BT, Le DD, Nguyen TG, et al. Validation of the COmprehensive Score for Financial Toxicity (COST) in Vietnamese patients with cancer. *PLoS One*. 2024;19(6):e0306339. doi:10.1371/journal.pone.0306339
49. Carrera PM, Curigliano G, Santini D, et al. ESMO expert consensus statements on the screening and management of financial toxicity in patients with cancer. *ESMO Open*. 2024;9(5):102992. doi:10.1016/j.esmoop.2024.102992
50. Khan HM, Ramsey S, Shankaran V. Financial Toxicity in Cancer Care: Implications for Clinical Care and Potential Practice Solutions. *J Clin Oncol*. 2023;41(16):3051-3058. doi:10.1200/jco.22.01799
51. Liang MI, Harrison R, Aviki EM, Esselen KM, Nitecki R, Meyer L. Financial toxicity: A practical review for gynecologic oncology teams to understand and address patient-level financial burdens. *Gynecol Oncol*. 2023;170:317-327. doi:10.1016/j.ygyno.2023.01.035
52. Yuan X, Zhang X, He J, Xing W. Interventions for financial toxicity among cancer survivors: A scoping review. *Crit Rev Oncol Hematol*. 2023;192:104140. doi:10.1016/j.critrevonc.2023.104140
53. Aviki EM, Thom B, Braxton K, et al. Patient-reported benefit from proposed interventions to reduce financial toxicity during cancer treatment. *Support Care Cancer*. 2022;30(3):2713-2721. doi:10.1007/s00520-021-06697-6
54. Fitch MI, Sharp L, Hanly P, Longo CJ. Experiencing financial toxicity associated with cancer in publicly funded healthcare systems: a systematic review of qualitative studies. *J Cancer Surviv*. 2022;16(2):314-328. doi:10.1007/s11764-021-01025-7
55. Smith GL, Banegas MP, Acquati C, et al. Navigating financial toxicity in patients with cancer: A multidisciplinary management approach. *CA Cancer J Clin*. 2022;72(5):437-453. doi:10.3322/caac.21730
56. de Souza JA, Yap BJ, Hlubocky FJ, et al. The development of a financial toxicity patient-reported outcome in cancer: The COST measure. *Cancer*. 2014;120(20):3245-53. doi:10.1002/cncr.28814
57. Bridger Staatz C, Kelly Y, Lacey RE, Hardy R. Investigating the factorial structure and measurement invariance of the parent-reported strengths and difficulties questionnaire at 11 years of age from the UK Millennium Cohort Study. *Eur Child Adolesc Psychiatry*. 2024;33(1):255-266. doi:10.1007/s00787-023-02156-1
58. Boothroyd L, Dagnan D, Muncer S. PHQ-9: One factor or two? *Psychiatry Res*. 2019;271:532-534. doi:10.1016/j.psychres.2018.12.048
59. Jiang R, Plunkett SW, Ainsworth AT. Factor structure and validity of the Affective Style Questionnaire. *J Health Psychol*. 2020;25(12):1805-1815. doi:10.1177/1359105318772650
60. Smith W, Vitoratou S, McCrone P, Patel A. Exploring the factor structure of the Health of the Nation Outcomes Scale (HoNOS) in a sample of patients with schizophrenia, schizotypal and delusional disorders. *Health Qual Life Outcomes*. 2017;15(1):141. doi:10.1186/s12955-017-0701-1
61. Corrigan KL, Fu S, Chen YS, et al. Financial toxicity impact on younger versus older adults with cancer in the setting of care delivery. *Cancer*. 2022;128(13):2455-2462. doi:10.1002/cncr.34220
62. Pangestu S, Harjanti EP, Pertiwi IH, Rencz F, Nurdiyanto FA. Financial Toxicity Experiences of Patients With Cancer in Indonesia: An Interpretive Phenomenological Analysis. *Value Health Reg Issues*. 2023;41:25-31. doi:10.1016/j.vhri.2023.11.007
63. Perni S, Azoba C, Gorton E, et al. Financial Toxicity, Symptom Burden, Illness Perceptions, and Communication Confidence in Cancer Clinical Trial Participants. *JCO Oncol Pract*. 2022;18(9):e1427-e1437. doi:10.1200/op.21.00697
64. Chan RJ, Gordon LG, Tan CJ, et al. Relationships Between Financial Toxicity and Symptom Burden in Cancer Survivors: A Systematic Review. *J Pain Symptom Manage*. 2019;57(3):646-660.e1. doi:10.1016/j.jpainsymman.2018.12.003
65. Rotter J, Spencer JC, Wheeler SB. Financial Toxicity in Advanced and Metastatic Cancer: Overburdened and Underprepared. *J Oncol Pract*. 2019;15(4):e300-e307. doi:10.1200/jop.18.00518
66. Kajimoto Y, Shibutani T, Nagao S, et al. Validity of the COmprehensive Score for financial Toxicity (COST) in patients with gynecologic cancer. *Int J Gynecol Cancer*. 2022;doi:10.1136/ijgc-2022-003410

CHAPTER V

The Psychometric Properties of the EQ-HWB and EQ-HWB-S in Patients With Breast Cancer: A Comparative Analysis with EQ-5D-5L, FACT-8D, and SWEMWBS

Published as:
Pangestu, S., Purba, F.D., Setyowibowo, H., Azhar, Y., Mukuria, C., & Rencz, F. The Psychometric Properties of the EQ-HWB and EQ-HWB-S in Patients With Breast Cancer: A Comparative Analysis with EQ-5D-5L, FACT-8D and SWEMWBS. *Value in Health*. 2025;28(3):449-459. https://doi.org/10.1016/j.jval.2024.12.003

ABSTRACT

Objectives: The EQ Health and Well Being is a new generic measure that captures constructs beyond health-related quality of life, with a 25-item long form (EQ-HWB) and a shorter 9-item version (EQ-HWB-S). This study aims to assess the psychometric performance of both versions in breast cancer, which is the most prevalent cancer globally, and compare them to other instruments.

Methods: A longitudinal survey in Indonesia (2023-24) with 300 female patients used the EQ-HWB, EQ-5D-5L, Functional Assessment of Cancer Therapy-General (FACT-G, from which FACT-8D was derived), Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS, from which SWEMWBS was derived). Distributional characteristics, convergent validity, known-group validity (Student's t-test or ANOVA), test-retest reliability, and responsiveness were assessed.

Results: All patients reported problems on at least one EQ-HWB item. The EQ-HWB-S index (11%) had a lower ceiling than the EQ-5D-5L (35%) and SWEMWBS (15.3%), but not the FACT-8D (5%). EQ-HWB-S index values correlated strongly with EQ-5D-5L (r=0.73) and FACT-8D (r=0.70) index values, while EQ-HWB level sum scores correlated strongly with FACT-G (r=0.69) and moderately with WEMWBS (r=0.49). The EQ-HWB and EQ-HWB-S discriminated across known-groups comparably to the EQ-5D-5L and FACT-8D with large effect sizes according to EQ VAS groups, number of symptoms, and general health, and exhibited excellent instrument-level test-retest reliability (intraclass correlations=0.79-0.83) and acceptable responsiveness (standardized response means=|0.24| to |0.97|).

Conclusions: This study represents one of the first validations of the EQ-HWB and EQ-HWB-S in any clinical population. Both instrument versions demonstrate robust psychometric performance. The EQ-HWB-S can be recommended to inform resource allocation decisions of breast cancer treatments.

V.1 INTRODUCTION

EQ Health and Wellbeing (EQ-HWB) is a recently developed generic instrument that goes beyond traditional measures of health-related quality of life (HRQoL) to encompass carer-related and social care-related quality of life.[1] The EQ-HWB underwent a rigorous development process, including conceptual and domain identification using literature reviews, face validation of candidate items using interviews with a wide range of stakeholders (i.e., patients, social care users, caregivers, and health technology assessment experts), psychometric testing, and final item selection through consultation rounds and pilot valuation.[1-5] Two versions of the measure have been constructed: a long 25-item version (EQ-HWB) and a short 9-item version (EQ-HWB-S). The EQ-HWB is a profile measure, while the EQ-HWB-S is a preference-accompanied measure comprising a subset of EQ-HWB items, primarily designed as a self-classifier for economic evaluations in healthcare, social care, and public health interventions.[1]

Currently, the EQ-HWB and EQ-HWB-S are experimental instruments, and so far, only a few studies have reported on their measurement performance. The content validity of EQ-HWB and EQ-HWB-S has been documented in various populations from four countries, namely patients with cancer, caregivers, older adults and other general populations.[6-8] Six studies from Australia, China, Italy, and US have validated the EQ-HWB and EQ-HWB-S in surgery patients, caregivers, social care users, and general populations with/without chronic conditions, with all assessing distributional characteristics, and convergent and known-group validity.[8-13] In some of these validation studies, the psychometric performance of EQ-HWB/EQ-HWB-S has been compared to various other preference-accompanied measures such as the Adult Social Care Outcomes Toolkit for Carers (ASCOT-Carer), Care-Related Quality of Life (CarerQol-7D), and EQ-5D-5L.[9-12] Furthermore, one study from Australia has provided test-retest reliability and responsiveness evidence on the EQ-HWB-S from a caregiver population.[8]

Little is known about the psychometric performance of EQ-HWB in clinical populations, particularly with longitudinal designs and in-person administration. Nearly all validation studies have been conducted on online panel samples or using cross-sectional design.[9-11,13,14] Further psychometric evidence is necessary, including test-retest reliability, responsiveness, comparisons with condition-specific measures, and validations across diverse patient populations, countries, and cultures. The instruments' performance in languages beyond those of its development countries (i.e., English, Spanish, Mandarin Chinese, and German) is also underexplored. Additional evidence

from other Asian countries is warranted, as the face validation and psychometric testing stages of the instrument's development in Asia were only conducted in China.[12]

The purpose of this study is therefore to assess the psychometric performance of the EQ-HWB and EQ-HWB-S in Indonesian patients with breast cancer, which is the most common form of cancer in 157 countries, including Indonesia.[15,16] A previous qualitative study, primarily involving patients with breast cancer, validated the content of EQ-HWB-S for cancer outcomes, highlighting its relevance for capturing patients' experiences.[7] A secondary aim is to compare their psychometric properties with other measures widely used in cancer populations, specifically the generic EQ-5D-5L, Warwick Edinburgh Mental Wellbeing Scale (WEMWBS), from which Short WEMWBS (SWEMWBS) can be derived, and the cancer-specific Functional Assessment of Cancer Therapy – General (FACT-G), from which FACT-8D can be derived.

V.2 METHODS

V.2.1 Study design and patients

A longitudinal data collection was conducted from September 2023 to March 2024 at the Oncology Division of Hasan Sadikin General Hospital in Bandung, Indonesia, following approval from the hospital's Research Ethics Committee (LB.02.01/X.6.5/284/2023). Under the oversight of the chief oncologist and nurses, a team of three graduate research assistants recruited patients in the hospital's oncology clinic waiting area. The participant inclusion criteria were: i) female patients aged 18 or older, ii) diagnosed with any type or stage of breast cancer, iii) undergoing active treatment, iv) cognitively able to complete the survey, v) fluent in Indonesian, and vi) provided informed consent. Patients undergoing their first cycle of therapy were not included. Our aim was for the first half of the recruited patients to be in active treatment cycle at baseline and to be invited to complete a follow-up questionnaire during their next cycle (Group 1). The remaining half were in their final treatment cycle at baseline and were invited to complete the follow-up at their post-treatment consultation (Group 2). Every patient was compensated IDR100,000 (approximately USD6.3) after completing each of the baseline and follow-up questionnaires.

V.2.2 Survey instruments

Two distinct paper questionnaires were prepared for data collection: one for the patients and the other for the nurses. The patients' questionnaire used the paper-and-pencil, self-completion version of standardized measures in the official Indonesian versions presented in a fixed order: EQ-HWB, EQ-5D-5L, Comprehensive Score for Financial Toxicity (FACIT-COST), WEMWBS, and FACT-G. The FACIT-COST responses have been reported elsewhere.[17] All questions or items from the outcome measures were mandatory, except for the FACT-G 'satisfied with sex life' item. Patients were also asked about their socio-demographic characteristics (age, marital status, education, employment, household size, and net monthly household income), caregiver use, general health, and symptoms experienced over the past seven days. Self-reported symptoms were queried using a binary (yes/no) format, featuring 30 predefined symptoms (e.g., nausea, fatigue, and hair loss) alongside an open-ended 'other' option. In the follow-up questionnaire, patients were asked to rate the change in their health status using the Global Rating of Change (GRC) scale. To assess the questionnaire's feasibility and comprehensibility, a pilot test was performed with five patients and no further changes were made thereafter. During data collection, the research assistants distributed the questionnaire to patients and provided explanations during completion when needed. Oncology nurses provided the following clinical information on patients based on the hospital's electronic records: stage and type of breast cancer, cancer duration, metastasis status and sites, comorbidities (e.g., hypertension), and current treatment(s) (e.g., immunotherapy and chemotherapy).

V.2.3 Health and well-being measures

1. **EQ Health and Wellbeing (EQ-HWB)**

   The EQ-HWB is a 25-item profile measure with seven high-level domains: activity, feelings and emotions, cognition, relationships, autonomy, self-identity, and physical sensations.[1] The items five-level response scales, which describe i) frequency: none of the time (1), only occasionally (2), sometimes (3), often (4), most or all of the time (5); ii) severity: no (1), mild (2), moderate (3), severe (4), very severe (5); or iii) difficulty: no difficulty (1), slight difficulty (2), some difficulty (3), a lot of difficulty (4), unable (5). The recall period is 'in the last seven days.' The 25-item EQ-HWB was administered, from which we derived the EQ-HWB-S responses. Level sum scores (LSSs) were computed for both the EQ-HWB and EQ-HWB-S by

summing the responses from the 25 and nine items, respectively. The theoretical LSS ranges of 25-125 (EQ-HWB) and 9-45 (EQ-HWB-S) were linearly rescaled to a 0-100 range, with higher scores indicating better health and well-being. Further, an index value was computed for the EQ-HWB-S by using the UK pilot value set, with higher scores indicating better health and well-being.[4]

2. EQ-5D-5L

The EQ-5D-5L is a generic preference-accompanied measure of HRQoL consisting of a descriptive system and a visual analogue scale (VAS), both with a "today" recall period.[18] The descriptive system has five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression), each with five levels: no problems (1), slight problems (2), moderate problems (3), severe problems (4), and extreme problems/unable to (5). LSSs were calculated by summing the five digits of the health state profile. The theoretical LSS range of 5-25 was linearly rescaled to 0-100 range for analysis similarly to the EQ-HWB. Further, an index value was assigned to each health state profile by using the Indonesian value set.[19] Higher scores in both the LSS and index value indicate better HRQoL. The EQ VAS enables respondents to indicate their overall health status using a vertical line ranging from 100 ('the best health you can imagine') to 0 ('the worst health you can imagine').

3. FACT-G

The FACT-G is a cancer-specific HRQoL measure with four domains: physical, social, emotional, and functional.[20] It has 27 items, a recall period of seven days and five response options for each item: not at all (0), a little bit (1), somewhat (2), quite a bit (3), and very much (4). The FACT-G was scored in two ways. First, a total score calculated from the sum of all responses which was rescaled to a scale of 0-100. Imputation was undertaken as recommended to score those missing the 'satisfied with sex life' item.[21,22] Second, from nine items of the FACT-G (nausea, pain, fatigue, sleep work, worry about worsening health, sadness, and support from family and friends), index values were computed using the FACT-8D Australian value set.[23] Both the FACT-G total score and FACT-8D index value indicated better HRQoL with higher scores.

4. WEMWBS

The WEMWBS is a 14-item generic measure of mental well-being, focusing on subjective well-being and psychological functioning.[24] The instrument has a recall period of 'over the last two weeks' and five response options for each item: none of the time (1), rarely (2), some of the time (3), often (4), and all of the time (5). The WEMWBS total score was computed by summing all the responses and rescaled to a range of 0-100 for analysis. Next, from the responses of the 14 items, we derived the 7-item SWEMWBS and assigned an index value using the UK value set.[25] Higher WEMWBS total score and SWEMWBS index value reflected better mental well-being.

5. GRC

The GRC scale was used in the follow-up questionnaire for patients to evaluate changes in their health status compared to their previous hospital visit (i.e., baseline).[26] The scale comprised a seven-point horizontal numeric rating system with the following points: much worse (-3), moderately worse (-2), a little worse (-1), unchanged (0), a little better (1), moderately better (2), and much better (3). Three patient subgroups were defined using the GRC responses: improved (1-3), worsened (-1 to -3), and unchanged (0) health. Patients from the Group 1 with unchanged health status were considered for the test-retest reliability analysis, while all patients from the Group 2 were included in the responsiveness analysis, which was conducted for each of the three subgroups of patients based on GRC.

V.2.4 Statistical analyses

Descriptive characteristics were used to summarize the characteristics of the patient population, and responses and scores on all instruments. Measurement properties were assessed for both the EQ-HWB and EQ-HWB-S, comparing them to the EQ-5D-5L, FACT-G, FACT-8D, WEMWBS, and SWEMWBS where relevant. The analytical framework followed earlier work on psychometric testing of preference-accompanied measures.[27-30] All analyses were conducted using Stata 18.0. Results were deemed statistically significant at $p<0.05$.

1. Distributional characteristics

Ceiling and floor effects were determined by assessing the proportion of patients achieving the best and worst responses on i) each item and ii) LSSs, total scores or index values of the measures. Thresholds of 70% were used at the item-level following previous EQ-HWB studies,[5,31] and 15% at the instrument level.[32] Due to the broader domains included, we predicted that EQ-HWB-S would have lower ceiling than EQ-5D-5L and SWEMWBS,[1,10] but not necessarily in comparison to the cancer-specific FACT-8D.

2. Convergent and divergent validity

Convergent validity was tested to assess the strength of relationship between items or domains aiming to measure a similar construct as well as between different instruments.[32] Divergent validity was used to identify where EQ-HWB items captured aspects not covered in other measures. We used Spearman's rank-order correlations between individual items or domains, whereas at the instrument level, Pearson's correlation was used for index values and LSSs or total scores. For individual items, raw responses were recoded to indicate better condition in the HRQoL or well-being domain with higher scores, where applicable. Absolute correlation coefficients were interpreted as none (r=0.00-0.09), weak (r=0.10-0.29), moderate (r=0.30-0.49), or strong (r=0.50 and above).[33] We hypothesized at least moderate correlations between conceptually-overlapping items, e.g., i) EQ-HWB personal care and EQ-5D-5L self-care, ii) EQ-HWB sleep and FACT-8D sleeping well, iii) EQ-HWB-S cognition and WEMWBS thinking clearly, iv) EQ-HWB-S anxiety and EQ-5D-5L anxiety/depression and FACT-G nervous.[1,9-12] At the instrument level, due to overlapping HRQoL and well-being constructs, we expected strong correlations between i) EQ-HWB-S, EQ-5D-5L and FACT-8D index values,[9,10] ii) EQ-HWB and EQ-5D-5L LSS, EQ VAS, and FACT-G total score,[9,10] and moderate correlations between i) EQ-HWB-S and SWEMWBS index values, and ii) EQ-HWB LSS and WEMWBS total score.[5] Meanwhile, moderate, weak, or no correlations were expected across the non-overlapping items.

3. Known-group validity

Known-group validity tests were used to examine the ability of EQ-HWB LSS and EQ-HWB-S index value at distinguishing between groups of patients compared to the other measures. The known groups were defined by cancer stage, EQ VAS

(≥80),[5] number of comorbidities, number of self-reported symptoms, and general health. For general health, the five-point scale response was recategorized into three subgroups: poor/fair, good, and very good/excellent. Student's t-test or ANOVA was used to compare mean differences between the known-groups. Effect sizes (ESs) and their 95% confidence intervals were calculated: Cohen's d for t-tests and eta-squared (η^2) for ANOVA. ESs were interpreted as trivial (d=0–0.19, η^2<0.01), small (d=0.20–0.49, η^2=0.01–0.05), moderate (d=0.50–0.79, η^2=0.06–0.13), or large (d≥0.80, η^2≥0.14).[33,34] We hypothesized that patients with higher cancer stage at diagnosis, EQ VAS <80, higher number of comorbidities and self-reported symptoms, and those rated their health as poorer would report lower scores on EQ-HWB/EQ-HWB-S, EQ-5D-5L, FACT-G/FACT-8D, and WEMWBS/SWEMWBS.

4. Test-retest reliability

The test-retest reliability of EQ-HWB/EQ-HWB-S, EQ-5D-5L, FACT-G/FACT-8D, and WEMWBS/SWEMWBS items were assessed using Gwet's AC2,[35] where values of 0.0-0.19, 0.20-0.39, 0.40-0.59, 0.60-0.79, and ≥0.80 were interpreted as slight, fair, moderate, strong, and almost-perfect agreement.[36] Further, intraclass correlation coefficients (ICCs), using two-way mixed effects model with absolute agreement, and their corresponding 95% confidence intervals were computed for the instrument-level analysis: EQ-HWB-S, EQ-5D-5L, FACT-8D, SWEMWBS index values, EQ-HWB, EQ-5D-5L LSSs, EQ VAS, FACT-G total and WEMWBS total scores.[37] ICC values of 0.0-0.39, 0.40-0.59, 0.60-0.74, and 0.75-1.0 were interpreted as poor, fair, good, and excellent test-retest reliability.[38]

5. Responsiveness to change

Responsiveness of the EQ-HWB-S, EQ-5D-5L, FACT-8D, SWEMWBS index values, EQ-HWB, EQ-5D-5L LSSs, EQ VAS, FACT-G total, and WEMWBS total scores were assessed using the standardized response means (SRMs) and their associated 95% confidence intervals. The SRM was estimated as the mean change in scores (or indices) between baseline and follow-up divided by the change's standard deviation. The SRM values were interpreted as small (<0.50), moderate (0.50-0.79), or large (≥0.80).[33]

V.3 RESULTS

V.3.1 Characteristics of the patient population

Out of 310 patients approached, 10 declined participation due to time constraints. The final sample included 300 female patients with breast cancer aged 51.3±10.3 (Table V.1). Most were married (77.7%), completed secondary education or less (83.0%), were homemakers (73.7%), and had low household income (90.0%). The majority were diagnosed with stage 2 breast cancer (62.0%), an average of 2.45±3.19 years ago, with invasive lobular (46.7%) or invasive ductal (39.0%) carcinoma. At the time of survey, most patients were receiving immunotherapy (84.3%) or chemotherapy (13.0%). The most commonly self-reported symptoms in the past week were fatigue (58.3%), dizziness (47.7%), and muscle pain (44.3%).

Follow-up questionnaires were completed by 298 patients (response rate=99.3%): 148 from the Group 1 (mean follow-up=5.8±3.0 weeks, range=1.9-13.0 weeks) and 150 from Group 2 (mean follow-up=11.6±4.0 weeks, range=4.0-25.9 weeks). Two patients died and were excluded from the test-retest reliability and responsiveness analyses. Out of Group 1, 32 patients (21.6%) had unchanged health status based on the GRC scale. In Group 2, 75 (50.0%), 18 (12.0%), and 57 (38.0%) patients reported improved, worsened, and unchanged health, respectively.

V.3.2 Distributional characteristics

Seven EQ-HWB items exhibited ceiling effects, namely ‘hearing’ (85.7%), ‘getting around inside and outside’ (71.0%), ‘personal care’ (79.7%), ‘unsupported’ (88.3%), ‘nothing to look forward’ (81.3%), ‘no control over daily life’ (79.7%), and ‘coping’ (76.7%) (Table V.2). Additionally, ‘cognition’ also showed borderline ceiling effect (69.7%). Meanwhile, EQ-5D-5L exhibited ceiling effects for three items and FACT-G/FACT-8D for four items, while WEMWBS/SWEMWBS showed none (Appendix V.1).

Overall, the patients reported good health status at baseline. Comparable mean index values of EQ-HWB-S, EQ-5D-5L, and SWEMWBS were observed at 0.84±0.17, 0.85±0.21, and 0.86±0.15 respectively, while the mean FACT-8D index was lower at 0.72±0.23 (Appendix V.2). The EQ-5D-5L index showed a more skewed distribution with a few clusters, while EQ-HWB-S, FACT-8D, and SWEMWBS were less skewed and had greater variability. Interestingly, the observed ranges were similar across all

Table V.1. Patient characteristics at baseline

Characteristic	Total sample (n=300)		Group 1 (n=32*)		Group 2 (n=150†)	
	N or Mean	% or SD	N or Mean	% or SD	N or Mean	% or SD
Socio-demographic characteristics						
Age	51.26	10.29	49.34	8.93	52.35	10.54
< 50 years	132	44.0%	15	46.9%	64	42.7%
50 years and above	168	56.0%	17	53.1%	86	57.3%
Marital status	-	-	-	-	-	-
Married	233	77.7%	27	84.4%	32	21.3%
Single/divorced/widower	67	22.3%	5	15.6%	118	78.7%
Education	-	-	-	-	-	-
Primary or less	92	30.7%	9	28.1%	45	30.0%
Secondary	157	52.3%	18	56.3%	78	52.0%
Tertiary	51	17.0%	5	15.6%	27	18.0%
Employment status[a]	-	-	-	-	-	-
Employed	55	18.3%	8	25.0%	23	15.3%
Homemaker	221	73.7%	22	68.8%	115	76.7%
Unemployed (looking for work)	4	1.3%	1	3.1%	2	1.3%
Retired	20	6.7%	1	3.1%	10	6.7%
Household size	-	-	-	-	-	-
1-2	59	19.7%	9	28.1%	27	18.0%
3-4	140	46.7%	15	46.9%	78	52.0%
5 or more	101	33.7%	8	25.0%	45	32.0%
Net monthly household income[b]	-	-	-	-	-	-
5 million and below	270	90.0%	27	84.4%	137	91.3%
> 5 million IDR	30	10.0%	5	15.6%	13	8.7%
Use of caregiver	184	61.3%	15	46.9%	82	54.7%
Clinical characteristics						
Cancer stage at diagnosis[c]	-	-	-	-	-	-
1	26	8.7%	4	12.5%	8	5.3%
2	186	62.0%	20	62.5%	90	60.0%
3	81	27.0%	8	25.0%	49	32.7%
4	5	1.7%	0	0.0%	3	2.0%
Unknown	2	0.7%	0	0.0%	0	0.0%
Breast cancer type	-	-	-	-	-	-

Characteristic	Total sample (n=300)		Group 1 (n=32*)		Group 2 (n=150†)	
	N or Mean	% or SD	N or Mean	% or SD	N or Mean	% or SD
Invasive lobular carcinoma	140	46.7%	18	56.3%	76	50.7%
Invasive ductal carcinoma[d]	117	39.0%	12	37.5%	51	34.0%
Ductal carcinoma in situ	37	12.3%	2	6.3%	22	14.7%
Lobular carcinoma in situ	3	1.0%	-	-	1	0.7%
Inflammatory breast cancer	2	0.7%	0	0.0%	0	0.0%
Mucinous carcinoma	1	0.3%	0	0.0%	0	0.0%
Disease duration (in years)	2.45	3.19	3.09	3.61	2.90	3.26
Number of metastasis sites[e]	-	-	-	-	-	-
0	276	92.0%	29	90.6%	140	93.3%
1	19	6.3%	3	9.4%	9	6.0%
2	4	1.3%	0	0.0%	1	0.7%
3	1	0.3%	0	0.0%	0	0.0%
Current treatment[a]	-	-	-	-	-	-
Immunotherapy	253	84.3%	28	87.5%	135	90.0%
Chemotherapy	37	12.3%	6	18.8%	8	5.3%
Radiation therapy	11	3.7%	0	0.0%	7	4.7%
Stem cell or bone marrow	2	0.7%	0	0.0%	2	1.3%
Palliative care	23	7.7%	1	3.1%	14	9.3%
Unknown	2	0.7%	0	0.0%	0	0.0%
Number of comorbidities[f]	-	-	-	-	-	-
0	78	26.0%	8	25.0%	44	29.3%
1	123	41.0%	15	46.9%	53	35.3%
2-3	86	28.7%	8	25.0%	44	29.3%
4 or more	13	4.3%	1	3.1%	9	6.0%
Number of symptoms	-	-	-	-	-	-
0	17	5.7%	4	12.5%	5	3.3%
1-3	71	23.7%	10	31.3%	30	20.0%
4-6	68	22.7%	5	15.6%	42	28.0%
7-9	60	20.0%	6	18.8%	29	19.3%
10+	84	28.0%	7	21.9%	44	29.3%
Self-reported symptoms in the past week	-	-	-	-	-	-
Fatigue	175	58.3%	16	47.1%	100	66.7%
Dizziness	143	47.7%	16	47.1%	76	50.7%
Muscle pain	133	44.3%	18	52.9%	72	48.0%
Sleep problem	123	41.0%	9	26.5%	67	44.7%
Anxiety	122	40.7%	11	32.4%	67	44.7%

Characteristic	Total sample (n=300)		Group 1 (n=32*)		Group 2 (n=150†)	
	N or Mean	% or SD	N or Mean	% or SD	N or Mean	% or SD
Hair loss	120	40.0%	10	29.4%	64	42.3%
Skin itching	106	35.3%	13	38.2%	56	37.3%
Dry mouth	101	33.7%	10	29.4%	51	34.0%
Headache	101	33.7%	14	41.2%	51	34.0%
Weight loss	95	31.7%	8	23.5%	44	29.3%

Notes. Group 1 consisted of patients in active treatment cycle at baseline who were invited to complete the follow-up questionnaire during their next cycle. Group 2 consisted of those in their final treatment cycle at baseline and were invited to complete the follow-up at their post-treatment consultation. Totals may not equal 100% due to rounding adjustments.

*Included in the test-retest reliability analysis

†Included in the responsiveness analysis

[a]*Response may belong in one more category*

[b]*IDR= Indonesian Rupiah, 5 million IDR ≈ 324 USD*

[c]*0: non-invasive, pre-cancerous, 1: early stage, spread to other tissue in small area, 2: localized, tumor between 20-50mm and lymph nodes involved or tumor larger than 50 mm with no lymph nodes involved), 3: regional spread, tumor larger than 50mm with lymph nodes involved in larger region, may have spread to skin or chest wall, 4: metastatic, distant spread beyond the breast and nearby lymph nodes* (American Joint Committee on Cancer Staging Manual 8th ed. New York, NY: Springer; 2017:589)

[d]*Includes subtypes: triple negative breast cancer, luminal A, luminal B HER-2 negative, luminal B HER-2 positive, and HER-2 positive*

[e]*Most common sites were bone, lung, and liver*

[f]*Most common comorbidities: chronic gastritis, hypertension, obesity, and hyperlipidemia*

Table V.2. Response distribution of EQ-HWB/EQ-HWB-S items

No	EQ-HWB items	Responses at baseline, n (%)				
		No difficulty	***Slight difficulty***	***Some difficulty***	***Much difficulty***	***Unable***
1	Sight	138 (46.0%)	134 (44.7%)	21 (7.0%)	7 (2.3%)	-
2	Hearing	257 (85.7%)	30 (10.0%)	8 (2.7%)	4 (1.3%)	1 (0.3%)
3	Getting around inside and outside (s)	213 (71.0%)	61 (20.3%)	20 (6.7%)	5 (1.7%)	1 (0.3%)
4	Day-to-day activities (s)	201 (67.0%)	70 (23.3%)	15 (5.0%)	11 (3.7%)	3 (1.0%)
5	Personal care	239 (79.7%)	41 (13.7%)	12 (4.0%)	3 (1.0%)	1 (0.3%)
		None of the time	***Only occasionally***	***Sometimes***	***Often***	***Most of the time***
6	Sleep	123 (41.0%)	56 (18.7%)	77 (25.7%)	25 (8.3%)	19 (6.3%)
7	Exhaustion (s)	87 (29.0%)	74 (24.7%)	99 (33.0%)	30 (10.0%)	10 (3.3%)
8	Loneliness (s)	215 (71.7%)	29 (9.7%)	40 (13.3%)	11 (3.7%)	5 (1.7%)
9	Unsupported	265 (88.3%)	10 (3.3%)	18 (6.0%)	6 (2.0%)	1 (0.3%)
10	Memory	194 (64.7%)	59 (19.7%)	41 (13.7%)	6 (2.0%)	-
11	Cognition (s)	209 (69.7%)	43 (14.3%)	43 (14.3%)	5 (1.7%)	-
12	Anxiety (s)	158 (52.7%)	58 (19.3%)	66 (22.0%)	15 (5.0%)	3 (1.0%)
13	Unsafe	199 (66.3%)	54 (18.0%)	42 (14.0%)	4 (1.3%)	1 (0.3%)
14	Frustration	252 (84.0%)	23 (7.7%)	21 (7.0%)	3 (1.0%)	1 (0.3%)
15	Sadness or depression (s)	192 (64.0%)	57 (19.0%)	41 (13.7%)	8 (2.7%)	2 (0.7%)
16	Nothing to look forward	244 (81.3%)	31 (10.3%)	21 (7.0%)	3 (1.0%)	1 (0.3%)
17	No control over daily life (s)	239 (79.7%)	29 (9.7%)	23 (7.7%)	5 (1.7%)	4 (1.3%)
18	Coping	230 (76.7%)	36 (12.0%)	29 (9.7%)	3 (1.0%)	2 (0.7%)
19	Accepted by others (r)	24 (8.0%)	3 (1.0%)	29 (9.7%)	50 (16.7%)	194 (64.7%)
20	Feel good about self (r)	13 (4.3%)	14 (4.7%)	34 (11.3%)	56 (18.7%)	183 (61.0%)
21	Do things one wanted to do (r)	14 (4.7%)	13 (4.3%)	91 (30.3%	61 (20.3%)	121 (40.3%)
22	Pain (frequency)	113 (37.7%)	58 (19.3%)	89 (29.7%)	29 (9.7%)	11 (3.7%)
		No	***Mild***	***Moderate***	***Severe***	***Very severe***
23	Pain (severity) (s)	115 (38.3%)	104 (34.7%)	64 (21.3%)	13 (4.3%)	4 (1.3%)
		None of the time	***Only occasionally***	***Sometimes***	***Often***	***Most of the time***
24	Discomfort (frequency)	105 (35.0%)	73 (24.3%)	81 (27.0%)	33 (11.0%)	8 (2.7%)
		No	***Mild***	***Moderate***	***Severe***	***Very severe***
25	Discomfort (severity)	107 (35.7%)	114 (38.0%)	61 (20.3%)	17 (5.7%)	1 (0.3%)

Abbreviations. (s)= EQ-HWB-S items, (r)= reverse coded for the level sum scores
Note. Overall, 300 patients completed the baseline survey.

instruments, except for SWEMWBS which did not exhibit negative values in this sample (Figure V.1).

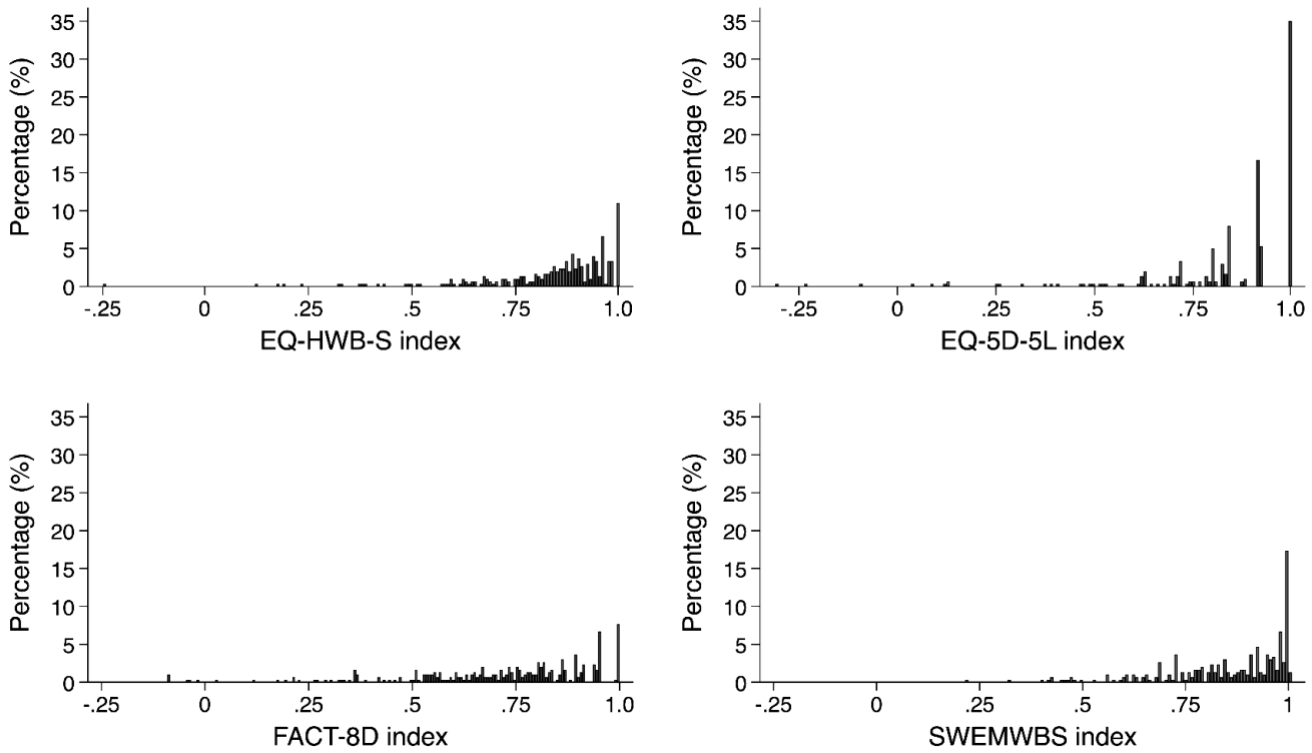
The EQ-HWB-S and FACT-8D indicated no ceiling effects at the instrument level (10.7% and 5.0%) (Appendix V.2). However, patients with no problems in any items of EQ-HWB-S reported some problems in seven of the FACT-8D dimensions, e.g., 'work' (62.0%), 'sleep' (46.0%), and 'fatigue' (22.0%) (Appendix V.3). Further, EQ-5D-5L and SWEMWBS demonstrated ceiling effects of 35.0% and 15.3%, respectively. The EQ-HWB LSS, FACT-G total, and WEMWBS total scores did not exhibit ceiling effects. The mean EQ-HWB LSS, EQ-5D-5L LSS, EQ VAS, FACT-G total and WEMWBS total scores were 83.52±11.76, 90.67±12.57, 81.18±15.63, 76.48±13.73, and 76.02±17.85, respectively (Appendix V.4).

V.3.3 Convergent and divergent validity

The correlations between EQ-HWB/EQ-HWB-S and corresponding items of EQ-5D-5L ranged from 0.31 to 0.64, with FACT-G/FACT-8D from 0.20 to 0.66, and with WEMWBS/SWEMWBS from 0.31 to 0.35 (Table V.3). The strongest correlations were observed between EQ-HWB sleep and FACT-8D sleeping well (r=0.66), EQ-HWB pain frequency and EQ-5D-5L pain/discomfort (r=0.64), and EQ-HWB personal care and EQ-5D-5L self-care (r=0.62). Some EQ-HWB items correlated varyingly with the composite domains of EQ-5D-5L, e.g., strong correlation between EQ-5D-5L anxiety/depression and EQ-HWB anxiety, but moderately with EQ-HWB sadness/depression, and strong correlation between EQ-5D-5L pain/discomfort and EQ-HWB pain (severity and frequency), but moderately with EQ-HWB discomfort (severity and frequency). Further, in most cases none or weak correlations were observed between non-overlapping items (Appendix V.5).

At the instrument level, strong correlations were observed between EQ-HWB-S index and EQ-5D-5L (r=0.73) and FACT-8D (r=0.70), and between EQ-HWB LSS and EQ-5D-5L LSS (r=0.65), EQ VAS (r=0.50), and FACT-G total score (r=0.69). Moderate correlations were shown between EQ-HWB-S and SWEMWBS index (r=0.34), and between EQ-HWB LSS and WEMWBS total score (r=0.49) (Table V.3).

Figure V.1. Distribution of the EQ-HWB-S, EQ-5D-5L, FACT-8D, and SWEMWBS index values



Abbreviations
EQ-HWB-S= EQ-HWB short form (9 items), EQ-5D-5L= EQ Five-level EQ-5D Version, FACT-8D= FACT Eight Dimension, SWEMWBS= Short WEMWBS.

Table V.3. Convergent validity results

	EQ-HWB-S index		**EQ-HWB-S sadness or depression**
EQ-5D-5L index	0.73	EQ-5D-5L anxiety/depression	0.40
FACT-8D index	0.70	FACT-8D sad	0.45
SWEMWBS index	0.34		**EQ-HWB discomfort (frequency)**
	EQ-HWB LSS	EQ-5D-5L pain/discomfort	0.41
EQ-5D-5L LSS	0.65	FACT-8D nausea	0.24†
EQ VAS	0.50	FACT-G bothered by side effects	0.33
FACT-G total	0.69	FACT-G feel ill	0.43
WEMWBS total	0.49		**EQ-HWB discomfort (severity)**
	EQ-HWB-S anxiety	EQ-5D-5L pain/discomfort	0.44
EQ-5D-5L anxiety/depression	0.51	FACT-8D nausea	0.20†
FACT-G nervous	0.57	FACT-G bothered by side effects	0.32
FACT-G worry about dying	0.34	FACT-G feel ill	0.45
FACT-8D worry about condition	0.42		**EQ-HWB feel good about self**
	EQ-HWB-S cognition	WEMWBS feeling good	0.31
WEMWBS thinking clearly	0.35		**EQ-HWB frustration**
	EQ-HWB-S day-to-day activities	EQ-5D-5L anxiety/depression	0.44
EQ-5D-5L usual activities	0.60		**EQ-HWB pain (frequency)**
FACT-8D work	0.40	EQ-5D-5L pain/discomfort	0.64
	EQ-HWB-S exhaustion	FACT-G pain	0.56
FACT-8D fatigue (lack of energy)	0.43	FACT-G feel ill*	0.51
	EQ-HWB-S getting around		**EQ-HWB personal care**
EQ-5D-5L mobility	0.60	EQ-5D-5L self-care	0.62
	EQ-HWB-S loneliness		**EQ-HWB sleep**
EQ-5D-5L anxiety/depression	0.41	FACT-8D sleeping well	0.66
	EQ-HWB-S pain (severity)		**EQ-HWB unsafe**
EQ-5D-5L pain/discomfort	0.60	EQ-5D-5L anxiety/depression	0.31
FACT-G pain	0.51		
FACT-G feel ill*	0.53		

Abbreviations. EQ-HWB= EQ Health and Wellbeing long form (25 items), EQ-HWB-S= EQ-HWB short form (9 items), FACT= Functional Assessment of Cancer Therapy, FACT-G= FACT-General, FACT-8D= FACT Eight Dimension, LSS= level summary scores, SWEMWBS= Short WEMWBS, WEMWBS= Warwick-Edinburgh Mental Wellbeing Scale

Note. Correlations are presented in absolute form. Correlations: weak (0.10-0.29), moderate (r=0.30-0.49), or strong (r=0.50 and above)

*In the Indonesian language, the word for "ill" is an umbrella term which may also include "pain"

†Weaker than hypothesized

V.3.4 Known-group validity

The EQ-HWB and EQ-HWB-S significantly distinguished known-groups, with large ESs for EQ VAS, general health, and number of symptoms, and small ESs for comorbidities and cancer stage (Table V.4).

All instruments, except SWEMWBS, performed similarly for EQ VAS known groups (large ESs) (Appendix V.6). EQ-HWB-S performed similarly to FACT-8D and outperformed EQ-5D-5L index and SWEMWBS for general health (large vs. moderate ESs). For number of symptoms, EQ-HWB-S performed comparably with EQ-5D-5L and FACT-8D, and better than SWEMWBS (large vs. moderate ESs). For cancer stage, EQ-HWB-S was comparable to EQ-5D-5L index and better than FACT-8D and SWEMWBS (borderline small vs. trivial ESs). EQ-HWB-S performed better than EQ-HWB in all comparisons except for the number of symptoms.

V.3.5 Test-retest reliability

Across EQ-HWB, 7 items demonstrated almost-perfect agreement, 10 strong agreement, 5 moderate agreement, and 3 fair agreement (Appendix V.7). The best-performing items included ‘unsupported’, ‘getting around inside and outside’, ‘personal care’, ‘frustration’, ‘nothing to look forward’, and ‘no control over daily life’ (Gwet’s AC2=0.87-0.97), while the lowest-performing in terms of test-retest reliability were ‘anxiety’, ‘exhaustion’, and ‘sleep’ (Gwet’s AC2=0.32-0.35). In comparison, the Gwet’s AC2 ranged from 0.64-0.97 for EQ-5D-5L, 0.24-0.90 for FACT-G, and 0.29-0.69 for WEMWBS.

At the instrument level, the EQ-HWB-S index and EQ-HWB LSS demonstrated excellent reliability with ICCs of 0.83 and 0.79, respectively (Table V.5). In comparison, the EQ-5D-5L had higher ICCs at 0.89 (LSS) and 0.88 (index value), while FACT-8D index and FACT-G total scores had lower at 0.77 and 0.76, respectively. Notably, SWEMWBS index and WEMWBS total score had the lowest ICCs among the instruments at 0.53 and 0.50, respectively.

V.3.6 Responsiveness

Small to moderate responsiveness to change was demonstrated by the EQ-HWB-S index in the improved (SRM=0.24), worsened (SRM=-0.68), and unchanged (SRM=0.35) subgroups of patients. Meanwhile, the EQ-HWB LSS performed better and

Table V.4. Known-group validity of EQ-HWB and EQ-HWB-S

Groups	n	EQ-HWB-S index		EQ-HWB LSS	
		Mean (SD)	**Effect size (95% CI)**	**Mean (SD)**	**Effect size (95% CI)**
Caregiver use					
Yes	184	0.84 (0.16)	d=0.04 (-0.19, 0.27)	83.53 (11.70)	d=0.00 (-0.23, 0.23)
No	116	0.84 (0.18)		83.51 (11.90)	
Cancer stage at diagnosis					
1-2	212	0.85 (0.15)	d=0.21 (-0.04, 0.46)	83.63 (11.71)	d=0.04 (-0.21, 0.29)
3-4	86	0.82 (0.20)		83.21 (12.07)	
EQ VAS score					
80 and above	219	0.89 (0.11)*	d=1.18 (0.91, 1.45)	86.67 (9.63)*	d=1.10 (0.83, 1.37)
<80	81	0.71 (0.23)*		75.02 (12.81)*	
Number of comorbidities					
0	78	0.87 (0.17)	η^2=0.031 (0.00, 0.08)	86.45 (11.67)	η^2=0.030 (0.00, 0.07)
1	123	0.85 (0.13)*		83.61 (10.29)	
2+	99	0.80 (0.20)*		81.11 (13.06)	
Number of symptoms					
0	17	0.94 (0.06)*	η^2=0.271 (0,19, 0.35)	92.18 (8.13)*	η^2=0.290 (0.20, 0.36)
1-3	71	0.92 (0.08)*		89.56 (8.02)*	
4-6	68	0.88 (0.11)*		86.71 (8.62)*	
7-9	60	0.86 (0.11)*		83.50 (9.81)*	
10+	84	0.70 (0.22)*		74.11 (12.58)*	
General health					
Very good/excellent	53	0.88 (0.13)*	η^2=0.154 (0.08, 0.23)	86.68 (9.37)*	η^2=0.145 (0.08, 0.22)
Good	166	0.88 (0.12)*		86.10 (9.88)*	
Poor/fair	81	0.73 (0.22)*		76.19 (13.55)*	

Abbreviations. CI= confidence interval, d= Cohen's D, EQ-HWB= EQ Health and Wellbeing long form (25 items), EQ-HWB-S= EQ-HWB short form (9 items), η^2= eta-squared, LSS= level summary score (linearly transformed to 0-100 scale)

*p<0.05

Table V.5. Test-retest reliability and responsiveness of index values, level summary scores, and EQ VAS

	Test-retest reliability			Responsiveness								
	Unchanged health subgroup (n=32)			Improved health subgroup (n=75)			Worsened health subgroup (n=18)			Unchanged health subgroup (n=57)		
	Mean (SD)		ICC (95% CI)	Mean (SD)		SRM (95% CI)	Mean (SD)		SRM (95% CI)	Mean (SD)		SRM (95% CI)
	Baseline	Follow-up		Baseline	Follow-up		Baseline	Follow-up		Baseline	Follow-up	
EQ-HWB-S index	0.87 (0.17)	0.88 (0.15)	0.83 (0.68 - 0.91)	0.88 (0.14)	0.90 (0.10)	0.24 (0.01, 0.47)	0.80 (0.15)	0.75 (0.15)	-0.68 (-0.99, -0.37)	0.83 (0.21)	0.84 (0.18)	0.35 (0.23, 0.46)
EQ-5D-5L index	0.87 (0.17)	0.90 (0.15)	0.94 (0.87 - 0.97)	0.91 (0.14)	0.92 (0.13)	0.16 (-0.03, 0.34)	0.83 (0.21)	0.70 (0.23)	-0.65 (-0.92, -0.39)	0.82 (0.22)	0.84 (0.23)	0.31 (0.12, 0.49)
FACT-8D index	0.78 (0.21)	0.75 (0.21)	0.77 (0.58 - 0.88)	0.77 (0.22)	0.81 (0.19)	0.23 (0.01, 0.44)	0.64 (0.19)	0.51 (0.18)	-1.72 (-2.33, -1.10)	0.72 (0.25)	0.72 (0.24)	0.06 (-0.21, 0.34)
SWEMWBS index	0.90 (0.10)	0.94 (0.07)	0.53 (0.07 - 0.76)	0.86 (0.15)	0.89 (0.13)	0.29 (0.07, 0.52)	0.82 (0.14)	0.79 (0.15)	-0.27 (-0.66, 0.12)	0.85 (0.15)	0.86 (0.15)	0.24 (0.08, 0.40)
EQ-HWB LSS[a]	86.38 (10.77)	86.28 (9.87)	0.79 (0.61 - 0.89)	86.32 (10.77)	88.37 (8.55)	0.29 (0.05, 0.53)	79.72 (10.87)	74.11 (12.25)	-0.97 (-1.36, -0.58)	83.14 (13.33)	84.74 (13.11)	0.59 (0.40, 0.78)
EQ-5D-5L LSS[a]	92.19 (11.43)	93.75 (10.16)	0.89 (0.79 - 0.95)	94.33 (9.02)	95.47 (7.59)	0.22 (-0.10, 0.53)	89.44 (13.49)	80.83 (14.78)	-1.13 (-1.80, -0.46)	89.39 (12.36)	90.18 (13.13)	0.18 (-0.11, 0.46)
EQ VAS	79.38 (20.31)	83.13 (15.75)	0.71 (0.48 - 0.85)	82.33 (14.41)	88.87 (7.56)	0.62 (0.40, 0.84)	76.67 (12.72)	62.50 (14.68)	-1.10 (-1.64, -0.57)	79.82 (16.85)	80.96 (15.63)	0.18 (-0.03, 0.40)
FACT-G total score[a]	79.51 (13.54)	80.77 (13.60)	0.76 (0.56 - 0.87)	80.74 (12.27)	82.16 (10.44)	0.17 (0.04, 0.31)	72.79 (14.06)	66.90 (15.09)	-0.74 (-1.51, 0.02)	77.46 (15.13)	77.96 (15.50)	0.18 (0.03, 0.33)
WEMWBS total score	80.41 (14.71)	85.49 (10.48)	0.50 (0.02 - 0.75)	77.50 (18.33)	78.98 (16.05)	0.15 (-0.05, 0.37)	69.74 (15.97)	65.58 (16.85)	-0.55 (-1.53, 0.42)	75.38 (18.13)	75.72 (18.02)	0.12 (-0.09, 0.33)

Abbreviations. CI= Confidence interval, EQ-HWB= EQ Health and Wellbeing, EQ-HWB-S= EQ Health and Wellbeing short form (9 items), FACT= Functional Assessment of Cancer Therapy, FACT-G= FACT-General, FACT-8D= FACT Eight Dimension, ICC= Intraclass correlation coefficient, two-way mixed effects model with absolute agreement, LSS= level summary score SD= standard deviation, SRM= standardized response means, SWEMWBS

[a]Linearly transformed to a scale of 0-100

Notes.

1. Test-retest reliability analysis was conducted on patients with unchanged health status from Group 1, i.e., patients in active treatment cycle at baseline who were invited to complete the follow-up questionnaire during their next cycle.
2. Responsiveness analysis was conducted on patients from Group 2, i.e., patients in their final treatment cycle at baseline who were invited to complete the follow-up at their post-treatment consultation.

exhibited small to large responsiveness: improved (SRM=0.29), worsened (SRM=-0.97), and unchanged (SRM=0.59) subgroups (Table V.5). In comparison, other measures also displayed small responsiveness in the improved health subgroup, except for EQ VAS which exhibited moderate responsiveness (SRM=0.62). In the worsened health subgroup, three other measures also exhibited large responsiveness: FACT-8D (SRM=-1.72), EQ-5D-5L LSS (SRM=-1.13), and EQ VAS (SRM=-1.10). In the unchanged health subgroup, all except EQ-HWB LSS exhibited small responsiveness.

V.4 DISCUSSION

This study is the first to validate the EQ-HWB and EQ-HWB-S in breast cancer and provide evidence on the test-retest reliability and responsiveness of both instruments in a clinical population. It is also the first study providing quantitative evidence of the Indonesian version of the measures. Ceiling effects were exhibited by seven EQ-HWB items, but not at the instrument level. The construct validity of EQ-HWB and EQ-HWB-S was supported by the high degree of convergence across multiple conceptually similar dimensions with EQ-5D-5L and FACT-8D. In known-group validity, both instrument versions discriminated with large effect sizes among patients grouped by their EQ VAS scores, general health, and number of symptoms, with the EQ-HWB-S displaying to be just effective as EQ-HWB. The EQ-HWB and EQ-HWB-S performed favorably in test-retest analysis, showing at least strong reliability for at almost 70% individual items and excellent reliability at the instrument level. Evidence of responsiveness was also observed, with particularly large effect by the EQ-HWB LSS in patients with worsened health.

The EQ-HWB and EQ-HWB-S performed well also compared to other commonly used measures in cancer - the EQ-5D-5L, FACT-G/FACT-8D, and WEMWBS/SWEMWBS. In cancer outcomes research, the EQ-5D has been shown to have limited sensitivity compared to cancer-specific preference-accompanied instruments.[7,39-41] The absence of ceiling effects in the EQ-HWB and EQ-HWB-S suggests that these instruments may be more sensitive than EQ-5D-5L, likely due to the inclusion of broader aspects and more dimensions. Furthermore, the varying degree of correlations between EQ-HWB and the composite domains of EQ-5D-5L suggests that EQ-HWB may provide better clarity at capturing patient problems.[10-12] Across various cancer types and treatments, patients often experience diminished HRQoL and well-

being, specifically marked by problems in exhaustion, sleep, nausea, interpersonal relationships, and personal appearances, which may not be sufficiently captured by the EQ-5D-5L.[42-44] These HRQoL areas included in the EQ-HWB may be considered candidates for bolt-ons to improve the performance of EQ-5D-5L in (breast) cancer populations.

Before our investigation, one Australian study demonstrated favorable test-retest reliability of EQ-HWB-S in a caregiver population, despite the limited sample size.[8] Our findings provide encouraging evidence about the test-retest reliability of both EQ-HWB and EQ-HWB-S. Importantly, the EQ-HWB and EQ-HWB-S showed slightly better test-retest reliability than the FACT-G/FACT-8D, which has been widely used in cancer clinical trials.[45] However, notably, three EQ-HWB items, of which two also belong to EQ-HWB-S, performed sub-optimally: 'sleep', 'exhaustion', and 'anxiety'. Similarly, the FACT-8D 'sleep' showed the poorest test-retest reliability among the FACT-G/FACT-8D items. The relatively long follow-up interval for the analysis may have influenced the results; however, we anchored this upon the patients' own self-reported unchanged health status. Additionally, patients reacting differently to treatments (i.e., adverse effects) may contribute to the heterogeneity.

Some limitations in this study need to be acknowledged. First, our sample predominantly consisted of less-educated Indonesians with lower economic status, who may tend to rate their health more favorably than wealthier and more-educated individuals (i.e., response heterogeneity).[46] Furthermore, Asian patients are often less inclined to report health problems, including physical and mental symptoms, compared to their Western counterparts, possibly resulting in better self-reported health.[47,48] Secondly, the use of the Australian and (pilot) UK value sets for the FACT-8D and EQ-HWB-S, and SWEMWBS may not precisely reflect the preferences of the Indonesian population. Thirdly, the measures in the survey were administered in a fixed order. While this could potentially introduce bias, previous studies suggest that presentation order is not likely to significantly responses, or may have only a small effect if present.[49,50] Fourthly, the use of GRC as anchor for responsiveness may not have fully captured the scope of changes experienced by patients, as the EQ-HWB extends beyond health constructs. Fifthly, varying recall periods among the instruments may have influenced our results, although the extent is unclear and needs further investigation.

V.5 CONCLUSIONS

This study provided psychometric evidence regarding the validity, reliability, and responsiveness of the EQ-HWB and EQ-HWB-S in a breast cancer population. The EQ-HWB and EQ-HWB-S performed comparably to the widely validated EQ-5D-5L, FACT-G, and FACT-8D, where the domains of exhaustion, pain, discomfort, and sleep may be particularly relevant in our sample. Our findings support the potential usefulness of EQ-HWB and EQ-HWB-S as patient-reported outcome measures for clinical and economic purposes in cancer populations, including their role in health technology assessments for breast cancer treatments.

References

1. Brazier J, Peasgood T, Mukuria C, et al. The EQ-HWB: Overview of the Development of a Measure of Health and Wellbeing and Key Results. *Value Health*. 2022;25(4):482-491. doi:10.1016/j.jval.2022.01.009
2. Peasgood T, Mukuria C, Carlton J, et al. What is the best approach to adopt for identifying the domains for a new measure of health, social care and carer-related quality of life to measure quality-adjusted life years? Application to the development of the EQ-HWB? *Eur J Health Econ*. 2021;22(7):1067-1081. doi:10.1007/s10198-021-01306-z
3. Mukuria C, Connell J, Carlton J, et al. Qualitative Review on Domains of Quality of Life Important for Patients, Social Care Users, and Informal Carers to Inform the Development of the EQ-HWB. *Value Health*. 2022;25(4):492-511. doi:10.1016/j.jval.2021.11.1371
4. Mukuria C, Peasgood T, McDool E, Norman R, Rowen D, Brazier J. Valuing the EQ Health and Wellbeing Short Using Time Trade-Off and a Discrete Choice Experiment: A Feasibility Study. *Value Health*. 2023;26(7):1073-1084. doi:10.1016/j.jval.2023.02.008
5. Peasgood T, Mukuria C, Brazier J, et al. Developing a New Generic Health and Wellbeing Measure: Psychometric Survey Results for the EQ-HWB. *Value Health*. 2022;25(4):525-533. doi:10.1016/j.jval.2021.11.1361
6. Engel L, Kosowicz L, Bogatyreva E, et al. Face Validity of Four Preference-Weighted Quality-of-Life Measures in Residential Aged Care: A Think-Aloud Study. *Patient*. 2023;16(6):655-666. doi:10.1007/s40271-023-00647-6
7. Gibson AEJ, Longworth L, Bennett B, Pickard AS, Shaw JW. Assessing the Content Validity of Preference-Based Measures in Cancer. *Value Health*. 2024;27(1):70-78. doi:10.1016/j.jval.2023.10.006
8. Bailey C, Dalziel K, Constable L, et al. The performance of the EQ-HWB-S as a measure of quality-of-life of caregivers in families that have experienced adverse events. *Eur J Health Econ*. 2024;doi:10.1007/s10198-024-01688-w
9. Kuharic M, Mulhern B, Sharp LK, Turpin RS, Pickard AS. Comparison of EQ Health and Well-Being Long and Short With Other Preference-Based Measures Among United States Informal Caregivers. *Value Health*. 2024;doi:10.1016/j.jval.2024.03.003
10. Kuharić M, Pickard AS, Mukuria C, Finch AP. The Measurement Properties of the EQ Health and Well-being and EQ Health and Well-Being Short Form in Italian Population: A Comparative Study With EQ-5D-5L. *Value Health*. 2024;doi:10.1016/j.jval.2024.03.002
11. Lee P, Engel L, Lubetkin E, Gao L. Exploring the Comparability Between EQ-5D and the EQ Health and Wellbeing in the General Australian Population. *Value Health*. 2024;27(4):508-517. doi:10.1016/j.jval.2024.01.004
12. Long C, Mao Z, Yang Z. A Head-to-Head Comparison of EQ Health and Wellbeing and EQ-5D-5L in Patients, Carers, and General Public in China. *Value Health*. 2024;doi:10.1016/j.jval.2024.02.012
13. Thai TM, C.;Engel, L. Head-to-head comparison of the EQ-HWB-S, ReQoL, EQ-5D-5Lmeasure in Australian general population and mental health wellbeing. presented at: The 4th EuroQol Early Career Researchers Meeting 2024; 2024 2024; Copenhagen, Denmark.
14. Bailey C, Dalziel K, Jones R, Hiscock H, Devlin NJ, Peasgood T. The Validity of the EuroQol Health and Wellbeing Short Version (EQ-HWB-S) Instrument in Parents of Children With and Without Health Conditions. *Pharmacoeconomics*. 2024;doi:10.1007/s40273-024-01351-5
15. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin*. 2021;71(3):209-249. doi:10.3322/caac.21660
16. Landrigan PJ, Fuller R, Acosta NJR, et al. The Lancet Commission on pollution and health. *Lancet*. 2018;391(10119):462-512. doi:10.1016/s0140-6736(17)32345-0
17. Pangestu S, Purba FD, Setyowibowo H, Mukuria C, Rencz F. Examining the Associations between Objective and Subjective Financial Toxicity and EQ-5D-5L Outcomes in Patients With Breast Cancer. presented at: The 4th EuroQol Early Career Researchers Meeting 2024; 2024; Copenhagen, Denmark.
18. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727-36. doi:10.1007/s11136-011-9903-x
19. Purba FD, Hunfeld JAM, Iskandarsyah A, et al. The Indonesian EQ-5D-5L Value Set. *Pharmacoeconomics*. 2017;35(11):1153-1165. doi:10.1007/s40273-017-0538-9
20. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol*. 1993;11(3):570-9. doi:10.1200/jco.1993.11.3.570

21. Fairclough DL, Cella DF. Functional Assessment of Cancer Therapy (FACT-G): non-response to individual questions. *Qual Life Res*. 1996;5(3):321-9. doi:10.1007/bf00433916
22. Cheung YB, Daniel R, Ng GY. Response and non-response to a quality-of-life question on sexual life: a case study of the simple mean imputation method. *Qual Life Res*. 2006;15(9):1493-501. doi:10.1007/s11136-006-0004-1
23. King MT, Norman R, Mercieca-Bebber R, et al. The Functional Assessment of Cancer Therapy Eight Dimension (FACT-8D), a Multi-Attribute Utility Instrument Derived From the Cancer-Specific FACT-General (FACT-G) Quality of Life Questionnaire: Development and Australian Value Set. *Value Health*. 2021;24(6):862-873. doi:10.1016/j.jval.2021.01.007
24. Tennant R, Hiller L, Fishwick R, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. *Health Qual Life Outcomes*. 2007;5:63. doi:10.1186/1477-7525-5-63
25. Yiu HHE, Buckell J, Petrou S, Stewart-Brown S, Madan J. Derivation of a UK preference-based value set for the Short Warwick-Edinburgh Mental Well-being Scale (SWEMWBS) to allow estimation of Mental Well-being Adjusted Life Years (MWALYs). *Soc Sci Med*. 2023;327:115928. doi:10.1016/j.socscimed.2023.115928
26. Kamper SJ, Maher CG, Mackay G. Global rating of change scales: a review of strengths and weaknesses and considerations for design. *J Man Manip Ther*. 2009;17(3):163-70. doi:10.1179/jmt.2009.17.3.163
27. Janssen MF, Pickard AS, Golicki D, et al. Measurement properties of the EQ-5D-5L compared to the EQ-5D-3L across eight patient groups: a multi-country study. *Qual Life Res*. 2013;22(7):1717-27. doi:10.1007/s11136-012-0322-4
28. McDool E, Mukuria C, Brazier J. A Comparison of the SF-6Dv2 and SF-6D UK Utility Values in a Mixed Patient and Healthy Population. *Pharmacoeconomics*. 2021;39(8):929-940. doi:10.1007/s40273-021-01033-6
29. Rencz F, Brodszky V, Janssen MF. A Direct Comparison of the Measurement Properties of EQ-5D-5L, PROMIS-29+2 and PROMIS Global Health Instruments and EQ-5D-5L and PROPr Utilities in a General Population Sample. *Value Health*. 2023;26(7):1045-1056. doi:10.1016/j.jval.2023.02.002
30. Nikl A, Janssen MF, Brodszky V, Rencz F. A head-to-head comparison of the EQ-5D-5L and 15D descriptive systems and index values in a general population sample. *Health Qual Life Outcomes*. 2023;21(1):17. doi:10.1186/s12955-023-02096-z
31. McDool E, Mukuria C, Peasgood T. Psychometric Performance of the EQ Health and Wellbeing Short in a United Kingdom Population Sample. *Value Health*. 2024;doi:10.1016/j.jval.2024.05.007
32. Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol*. 2007;60(1):34-42. doi:10.1016/j.jclinepi.2006.03.012
33. Cohen J. Quantitative methods in psychology: A power primer. *Psychol Bull*. 1992;112:1155-1159.
34. Richardson JT. Eta squared and partial eta squared as measures of effect size in educational research. *Educ Res Rev*. 2011;*6*(2):135-147. doi:10.1016/j.edurev.2010.12.001
35. Gwet KL. *Handbook of inter-rater reliability: The definitive guide to measuring the extent of agreement among raters*. Advanced Analytics, LLC; 2014.
36. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33(1):159-74.
37. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *J Chiropr Med*. 2016;15(2):155-63. doi:10.1016/j.jcm.2016.02.012
38. Cicchetti DV. Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. *Psychological assessment*. 1994;6(4):284.
39. Davies A, Waylen A, Leary S, et al. Assessing the validity of EQ-5D-5L in people with head & neck cancer: Does a generic quality of life measure perform as well as a disease-specific measure in a patient population? *Oral Oncol*. 2020;101:104504. doi:10.1016/j.oraloncology.2019.104504
40. Lin FJ, Longworth L, Pickard AS. Evaluation of content on EQ-5D as compared to disease-specific utility measures. *Qual Life Res*. 2013;22(4):853-74. doi:10.1007/s11136-012-0207-6
41. van Dongen-Leunis A, Redekop WK, Uyl-de Groot CA. Which Questionnaire Should Be Used to Measure Quality-of-Life Utilities in Patients with Acute Leukemia? An Evaluation of the Validity and Interpretability of the EQ-5D-5L and Preference-Based Questionnaires Derived from the EORTC QLQ-C30. *Value Health*. 2016;19(6):834-843. doi:10.1016/j.jval.2016.05.008
42. Bottomley A, Flechtner H, Efficace F, et al. Health related quality of life outcomes in cancer clinical trials. *Eur J Cancer*. 2005;41(12):1697-709. doi:10.1016/j.ejca.2005.05.007
43. Heidary Z, Ghaemi M, Hossein Rashidi B, Kohandel Gargari O, Montazeri A. Quality of Life in Breast Cancer Patients: A Systematic Review of the Qualitative Studies. *Cancer Control*. 2023;30:10732748231168318. doi:10.1177/10732748231168318

44. Hernández Alava M, Pudney SE, Wailoo AJ. Does EQ-5D Tell the Whole Story? Statistical Methods for Comparing the Thematic Coverage of Clinical and Generic Outcome Measures, With Application to Breast Cancer. *Value Health*. 2023;26(9):1398-1404. doi:10.1016/j.jval.2023.05.016
45. Giesinger JM, Efficace F, Aaronson N, et al. Past and Current Practice of Patient-Reported Outcome Measurement in Randomized Cancer Clinical Trials: A Systematic Review. *Value Health*. 2021;24(4):585-591. doi:10.1016/j.jval.2020.11.004
46. Hanandita W, Tampubolon G. Does reporting behaviour bias the measurement of social inequalities in self-rated health in Indonesia? An anchoring vignette analysis. *Quality of Life Research*. 2016;25(5):1137-1149. doi:10.1007/s11136-015-1152-y
47. Chen CH, Tang ST, Chen CH. Meta-analysis of cultural differences in Western and Asian patient-perceived barriers to managing cancer pain. *Palliat Med*. 2012;26(3):206-21. doi:10.1177/0269216311402711
48. Birtel MD, Mitchell BL. Cross-cultural differences in depression between White British and South Asians: Causal attributions, stigma by association, discriminatory potential. *Psychol Psychother*. 2023;96(1):101-116. doi:10.1111/papt.12428
49. Cheung Y-B, Wong L-C, Tay M-H, et al. Order effects in the assessment of quality of life in cancer patients. *Quality of Life Research*. 2004;13(7):1217-1223. doi:10.1023/B:QURE.0000037499.80080.07
50. Childs AL. Effect of order of administration of health-related quality of life interview instruments on responses. *Quality of Life Research*. 2005;14(2):493-500. doi:10.1007/s11136-004-0727-9

CHAPTER VI

Associations between Financial Toxicity, Health-Related Quality of Life, and Well-Being in Indonesian Patients With Breast Cancer

Published as:
Pangestu, S., Purba, F.D., Setyowibowo, H., Mukuria, C., & Rencz, F. Associations between Financial Toxicity, Health-Related Quality of Life, and Well-Being in Indonesian Patients With Breast Cancer. *Quality of Life Research*. 2025; Online ahead of print. 22(1):89. https://doi.org/10.1007/s11136-025-03925-y

ABSTRACT

Objectives: Financial toxicity (FT) is the impairment of financial well-being experienced by patients with cancer, categorized into subjective (SFT) and objective (OFT) forms. This study aimed to investigate the associations between FT, health-related quality of life, and overall well-being in patients with breast cancer.

Methods: We analyzed baseline data from a single-center longitudinal study in Indonesia. Patients completed the EQ-5D-5L, EQ Health and Wellbeing (EQ-HWB), COST: A FACIT Measure of Financial Toxicity (FACIT-COST, to measure SFT), and OFT-related questions. Ordinal logistic regression was used to examine the associations between FT and selected EQ-5D-5L and EQ-HWB items. Multivariable linear regression was used to assess the associations of FT and EQ-5D-5L and EQ-HWB-S index values. The main regression models were adjusted for socio-demographic and clinical factors such as age, income, metastasis, and symptoms.

Results: The survey included 300 female patients with breast cancer undergoing treatment (mean age=51). Overall, 21% experienced high SFT (FACIT-COST≤17.5) and 51% reported any OFT (e.g., incurring debt). Adjusted for covariates, higher SFT was associated with more problems in EQ-5D pain/discomfort and anxiety/depression, and in EQ-HWB exhaustion, anxiety, sadness/depression, frustration, pain, and discomfort. OFT was associated with more problems in exhaustion. Higher SFT was associated with lower EQ-5D-5L and EQ-HWB-S index values, with explained variances of 46.3% for EQ-HWB-S and 31.2% for EQ-5D-5L.

Conclusions: This study is the first to explore the associations between financial toxicity, EQ-5D-5L, and EQ-HWB outcomes in breast cancer. Our findings provide insight into the cancer burden and its link to health and well-being

VI.1 INTRODUCTION

Patients with cancer worldwide often face considerable financial burdens.[1] The experienced financial challenges can adversely impact their financial well-being, which is the perceived ability to sustain living standards and achieve financial freedom.[2] The term 'financial toxicity' (FT) describes the impairment of financial well-being of patients due to cancer diagnosis and its associated care.[3] FT has been reported across many countries, regardless of income levels or healthcare systems.[4,5] If unaddressed, FT can lead to treatment non-adherence, reduced health-related quality of life (HRQoL), and worse health and survival outcomes.[6-9]

In general, FT can be assessed both objectively and subjectively.[10-12] Objective FT (OFT) is measured using quantifiable financial metrics (e.g., out-of-pocket expenditure amount or its ratio to household income) or questions on financial coping strategies (e.g., incurring loan and liquidating assets). Meanwhile, subjective FT (SFT) is the perceived distress arising from the financial burden of their diagnosis and treatment. The measurement of SFT is typically self-reported by the patients using patient-reported outcome measures, such as the COST: A FACIT Measure of Financial Toxicity (FACIT-COST) and Socioeconomic Wellbeing Scale (SWBS).[13,14]

There is an increasing body of literature exploring the association between FT and HRQoL in patients and survivors of cancer.[15,16] Significant correlations were found between high levels of both OFT and SFT and reduced overall HRQoL. Specifically, FT has shown associations with a number of HRQoL domains (e.g., social and mental health), measured using instruments such as the European Organization for Research and Treatment of Cancer of Life Questionnaire Core 30 (EORTC QLQ-C30), EQ-5D-5L, Functional Assessment of Cancer Therapy – General (FACT-G), Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29), and 12-Item Short-Form Health Survey (SF-12).[15,16] However, most FT studies have been performed in high-income and English-speaking countries.[15,16] Further research is needed in low-and-middle-income countries (LMICs) to better understand FT in different cultures and socio-demographic settings.[10,17-20]

While there has been a surge of FT studies examining its associations with HRQoL, very little is known about the relationship between FT and well-being. There are various definitions of well-being; for example, the World Health Organization defines the well-being construct as a broader spectrum of dimensions compared to HRQoL,

which predominantly focuses on physical, psychological, and social domains of health.[21-24] In an earlier study, SFT was associated with the environment domain of well-being, measured using the World Health Organization Quality of Life Brief Version (WHOQOL-BREF) instrument.[25] Evidence suggests that the world is moving toward universal health coverage to ensure access to health care without financial hardship.[26] However, FT persists as a major challenge in oncology care across many countries. A better understanding of the relationships between FT, HRQoL, and well-being may offer valuable insights into how financial challenges relate to various health and well-being domains, helping to shape health and social policies that support patients and their households.

Breast cancer is the most prevalent cancer worldwide, including in Indonesia.[27] Recent findings also suggest that FT in breast cancer occurs in more than twice as many patients in LMICs compared with their high-income counterparts.[20] Indonesia is a middle-income country where cancer is a major cause of mortality and the second costliest chronic disease financed by the country's single-payer universal health system.[28] Despite the presence of a public health system, patients may face challenges such as underinsurance, which does not cover substantial non-healthcare, cancer-related costs (e.g., transportation to healthcare facilities and caregiver fees), and the uneven distribution of medical professionals and equipment.[15]

Therefore, this study aims to investigate the associations between FT, HRQoL, and well-being outcomes in female patients with breast cancer in Indonesia. We hypothesize that FT is negatively associated with HRQoL and well-being.

VI.2 METHODS

This study was conducted in accordance with the Indonesian Health Research and Development Ethical Guidelines and Standards.[29] Ethics approval was granted by the Research Ethics Committee of the Hasan Sadikin General Hospital (LB.02.01/X.6.5/284/2023).

VI.2.1 Study design and patients

This study analyzed baseline data from a single-center longitudinal study conducted in Indonesia from September 2023 to March 2024.[30-31] The data were collected at the Hasan Sadikin General Hospital Bandung, a primary public referral hospital in West

Java. The inclusion criteria for patients were: i) female, ii) at least 18 years of age, iii) diagnosed with breast cancer of any type and stage, iv) undergoing any treatment, v) possessed the cognitive ability to complete the survey, v) fluent in Indonesian language, and vi) provided written informed consent. Patients in the initial round of therapy (e.g., chemotherapy and immunotherapy) were excluded. The recruitment of the patients was performed by research assistants and overseen by the chief oncologist and team of nurses. Patients were approached for survey participation prior to their consultation or treatment session in the waiting area of the hospital's oncology department. Two separate paper-and-pencil questionnaires were prepared: one for the patients and the other for the nurses.

The patients' questionnaire included standardized measures in the official Indonesian language version, presented in a fixed order: EQ-HWB, EQ-5D-5L, and FACIT-COST. Patients were also asked to report their socio-demographic background (age, marital status, education, employment status, ethnicity, residential setting, number of children living in the same household, net monthly household income, and health insurance status), symptoms experienced over the past week, and respond to a question on OFT. Three trained research assistants, present in the waiting area, explained the study to the patients, obtained their informed consent, and assisted them when they had difficulties in completing the questionnaires. Pilot testing involving five patients was conducted to assess the feasibility of the survey instrument, and no subsequent modifications were made. All participating patients received a compensation of IDR 100,000 (≈USD 6.30) after completing the questionnaire, which they were not informed about beforehand.

The oncology nurses' questionnaire was prepared to gather clinical data on patients based on the hospital's computerized medical records: stage and type of breast cancer, disease duration, metastasis status, comorbidities, and previous and current treatment(s) (e.g., chemotherapy, immunotherapy, and surgery).

VI.2.2 EQ-5D-5L

The EQ-5D-5L is a generic preference-accompanied measure of HRQoL consisting of two parts.[32] The first part is a descriptive system comprising five single-item dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each item has five levels of responses: no problems (1), slight problems (2), moderate problems (3), severe problems (4), and extreme problems/unable to (5). An EQ-5D-5L health state profile may be described by a five-digit string. For

example, ‘11111’ indicates no problems in all dimensions, and ‘22133’ indicates slight problems in the mobility and self-care dimensions, no problems in the usual activities dimension, and moderate problems in the pain/discomfort and anxiety/dimension dimensions. The descriptive system was scored by assigning an index value to each health state profile using the Indonesian EQ-5D-5L value set, with higher values indicating better HRQoL.[33] The second part of the EQ-5D-5L is the EQ visual analogue scale (EQ VAS). In this part, the patients were asked to indicate their health using a vertical visual analogue scale which has a value of between 0 (‘the worst health you can imagine’) and 100 (‘the best health you can imagine’). The EQ-5D-5L descriptive system as well as EQ VAS have been widely validated in cancer populations.[34-37]

VI.2.3 EQ Health and Wellbeing (EQ-HWB)

The EQ-HWB is a newly developed measure that goes beyond conventional measures of HRQoL to include carer- and social care-related quality of life.[38] Development of the measure drew on different theories of well-being including objective lists, preference satisfaction, and capabilities under the extra-welfarist paradigm of measuring social welfare.[39] There are two versions of the measure: a long 25-item form, and a short 9-item form (EQ-HWB-S), which is a subset of the long version.[38] The long form serves a profile measure, while the short form functions a self-classifier for economic evaluations. The items are answered using three different five-level response scales: difficulty, frequency, and severity. The EQ-HWB has earlier been used in cancer populations,[40-43] and was shown to perform well in item response theory and classical psychometric testing.[38,40] In this study, the patients completed the 25-item EQ-HWB, from which the responses for the EQ-HWB-S were derived. For the EQ-HWB, a level summary score (LSS) was calculated by summing the responses from the 25 items, with higher scores indicating worse health and well-being. The theoretical LSS range of 25-125 was transformed to a scale of 0-100 for analysis. For the EQ-HWB-S, the index value was derived using the UK pilot value set, as no Indonesian value set was available. Higher index values indicating better health and well-being.[44]

VI.2.4 COST: A FACIT Measure of Financial Toxicity (FACIT-COST)

The FACIT-COST is the most widely validated and used cancer-specific measure of SFT.[13,18,45] The latest version (v2) has 12 items with 0-4 response scale, from ‘not at

all' (=0) to 'very much' (=4). The items relate to financial adequacy, psychosocial reaction, anticipating future financial problems, and financial hardship on family, among others. The FACIT-COST total score was computed by summing items 1 through 11, with items 2, 3, 4, 5, 8, 9, and 10 scored in reverse. The theoretical score ranges between 0 and 44, with lower scores indicating worse SFT. Following a receiver operating characteristic analysis, a cut-off score of ≤17.5 was proposed to indicate high SFT.[46]

VI.2.5 Questions on objective financial toxicity (OFT)

To assess OFT, the patients were asked if they experienced one or more of the following financial coping strategies in treating breast cancer: i) withdrawing savings or pension fund, ii) selling assets such as vehicle, land, and gold/jewelry, iii) incurring debt from a relative or financial institution, and iv) closing business. These items were selected based on previous studies,[47,48] while also giving the option to respondents to specify other financial coping strategies using an open-ended 'other' response option.

VI.2.6 Statistical analysis

All variables were descriptively summarized using frequencies and percentages, means and standard deviations, depending on the type of data. Four subgroups were defined by the combination of SFT and OFT experiences: i) low SFT and no OFT, ii) low SFT and at least one OFT, iii) high SFT but no OFT, and iv) high SFT and at least one OFT.[12] The twelfth item of FACIT-COST ('financial hardship to my family and me'), which was not included in the calculation of the FACIT-COST total score, was also used to define three subgroups derived from the five-level response scale of the instrument: i) 'not at all', ii) 'a little bit' or 'somewhat', and iii) 'quite a bit' or 'very much'. The mean EQ-5D-5L, EQ-HWB-S index values, EQ-HWB LSS, and EQ VAS were compared among patient subgroups using the Mann-Whitney or Kruskal-Wallis test.

Spearman's rho was used to examine the correlations between FACIT-COST total score and selected individual items of EQ-5D-5L and EQ-HWB where associations were hypothesized: EQ-5D-5L pain/discomfort, anxiety/depression, EQ-HWB-S exhaustion, anxiety, sadness/depression, no control over daily life, pain (severity), and EQ-HWB frustration, coping, and discomfort (severity).[49-52] The EQ-5D-5L pain/discomfort and EQ-HWB discomfort items were predicted because the literature suggests that they may also capture psychological forms of discomfort despite primarily targeting physical

discomfort.[53] The EQ-HWB pain (severity) item was mainly selected as a control because it specifically asks about pain, while the EQ-5D-5L combines pain and discomfort in a single item. Additionally, Pearson's coefficient was used for the correlations between FACIT-COST total score and: EQ-5D-5L and EQ-HWB-S index values, EQ-HWB LSS, an EQ VAS. The strength of correlations was interpreted as: strong (≥0.50), moderate (0.30-0.49), weak (0.10-0.29), and very weak (<0.10).[54]

To further evaluate the associations between FT (both SFT and OFT), HRQoL, and well-being, regression models were used. For this purpose, the total score of FACIT-COST was recoded to align higher scores with increased SFT. OFT was operationalized as an ordinal variable indicating the number of financial coping strategies employed by the patients. To adjust for covariates in the regressions, a subset of key socio-demographic and clinical characteristics was selected by applying a forward stepwise regression procedure. Variables which exhibited a $p \geq 0.05$ in bivariate analyses with the outcome variables were excluded: marital status, education, employment status, residential setting, insurance coverage, breast cancer type, cancer stage at diagnosis, and treatments other than chemotherapy. The retained socio-demographic covariates were age, household income, and number of children, while the clinical covariates were cancer diagnosis of one year or less, metastasis status, undergoing chemotherapy, number of comorbidities, and number of symptoms (reported in the past week). Ordinal logistic models were also developed to examine the associations between FT and EQ-5D-5L and EQ-HWB items, adjusted for the selected socio-demographic and clinical covariates, with odds ratios and their respective 95% confidence intervals calculated. The ordinal regressions were only performed for items with sufficient variability in responses, thereby excluding EQ-HWB-S no control over daily life and EQ-HWB coping items.

Multivariable ordinary least squares (OLS) models were used for FT predicting EQ-5D-5L and EQ-HWB-S index values, EQ-HWB LSS, and EQ VAS. In the OLS, three models were gradually developed with FT (SFT and OFT) as predictors: i) no covariates, ii) adjusted for socio-demographic covariates, and iii) adjusted for both socio-demographic and clinical covariates. Robust standard errors were used to address heteroskedasticity, which was verified using the Breusch-Pagan test. No instances of multicollinearity among the independent variables were detected in any of the models (variance inflation factor >5). The R-squared values were compared to assess which outcome variable was better predicted by the FT variables. All statistical analyses were

performed using Stata 18 (StataCorp LLC) and a significance level of $p<0.05$ was deemed statistically significant.

VI.3 RESULTS

VI.3.1 Patient characteristics

Overall, 300 female patients with breast cancer completed the survey. The mean age was 51.26±10.29 years (range 23-84). Most patients were married (77.7%), homemakers (73.7%), resided in a rural area (59.7%), had children aged <17 living in the same household (52.0%), and completed secondary education (52.3%) (Table VI.1).

Table VII.1. Characteristics of the patients

Characteristic	N or Mean	% or SD
Socio-demographic characteristics		
Age	51.26	10.29
< 50 years	132	44.0%
50 years and above	168	56.0%
Marital status	-	-
Married	233	77.7%
Single/divorced/widower	67	22.3%
Education	-	-
Primary or less	92	30.7%
Secondary	157	52.3%
Tertiary	51	17.0%
Employment status	-	-
Employed	55	18.3%
Homemaker	221	73.7%
Unemployed (seeking for work)	4	1.3%
Retired	20	6.7%
Residential setting		
Rural	179	59.7%
Urban	121	40.3%
Number of children (aged <17) living in the same household	-	-
0	144	48.0%
1	80	26.7%
2+	76	20.7%
Net monthly household income[b]	-	-
5 million IDR and less	270	90.0%
> 5 million IDR	30	10.0%
Health insurance coverage	299	99.7%
Clinical characteristics		
Breast cancer type	-	-
Invasive lobular carcinoma	140	46.7%
Invasive ductal carcinoma[d]	117	39.0%
Ductal carcinoma in situ	37	12.3%
Lobular carcinoma in situ	3	1.0%
Inflammatory breast cancer	2	0.7%
Mucinous carcinoma	1	0.3%
Cancer stage at diagnosis[c]		
1	26	8.7%
2	186	62.0%
3	81	27.0%
4	5	1.7%
Unknown	2	0.7%
Disease duration (in years)	2.45	3.18

Characteristic	N or Mean	% or SD
Metastasis	24	8.0%
Current treatment[a]	-	-
Immunotherapy	253	84.3%
Chemotherapy	37	12.3%
Radiation therapy	11	3.7%
Stem cell or bone marrow	2	0.7%
Unknown	2	0.7%
Palliative care	23	7.7%
Surgery history[f]	243	81.0%
Number of comorbidities[g]		
0	78	26.0%
1	123	41.0%
2+	99	33.0%
Number of symptoms in the past week[h]		
0	17	5.7%
1-3	71	23.7%
4-6	68	22.7%
7-9	60	20.0%
10+	84	28.0%

[a]May belong in more than one category
[b]IDR= Indonesian Rupiah, 324.34 USD = 5 million IDR (based on the closing 2023 middle exchange rate from Bank Indonesia)
[c]Based on the American Joint Committee on Cancer Staging (0: non-invasive, pre-cancerous, 1: early stage, spread to other tissue in small area, 2: localized, tumor between 20-50mm and lymph nodes involved or tumor larger than 50 mm with no lymph nodes involved), 3: regional spread, tumor larger than 50mm with lymph nodes involved in larger region, may have spread to skin or chest wall, 4: metastatic, distant spread beyond the breast and nearby lymph nodes)
[d]Included subtypes: triple negative breast cancer, luminal A, luminal B HER-2 negative, luminal B HER-2 positive, and HER-2 positive
[e]Most common sites were bone (n=7), lung (n=5), and liver (n=3)
[f]Surgeries included single/double mastectomy and lumpectomy
[g]Most common comorbidities: chronic gastritis (n=172), hypertension (n=72), and obesity (n=39)
[h]Most reported symptoms: fatigue (n=175), dizziness (n=143), muscle pain (n=133), sleep problem (123), anxiety (n=122), and hair loss (n=120)

The net monthly household income of the patients was <5 million IDR (≈USD 324) for 90% of the patients. All except one patient (99.7%) had insurance coverage for their treatment. The two most common breast cancer types were invasive lobular carcinoma (46.7%) and invasive ductal carcinoma (39.0%). Most patients were diagnosed at stage 2 (62.0%) and 8.0% had metastasis. The most common types of treatment at the time of the survey were immunotherapy (84.3%) and chemotherapy (11.33%). Overall, 81% of the patients underwent surgeries, such as mastectomy or lumpectomy.

VI.3.2 Financial toxicity, health, and well-being

The majority of patients reported overall good health status with mean EQ-5D-5L index value of 0.85±0.21, mean EQ VAS of 81.18±15.63, and mean EQ-HWB-S index value of 0.84±0.17 (Table VI.2). The mean FACIT-COST total score was 24.24±8.65. High SFT as measured by the FACIT-COST (≤17.5), was experienced by 21% patients (Table VI.3). Meanwhile, OFT was experienced by 51% patients who reported at least one financial strategy used to cope with their breast cancer treatment. The two most common

strategies used by the patients were borrowing from relatives or financial institution (30.0%) and withdrawing from savings/pension (25.7%).

Table VII.2. Descriptive statistics of the outcome measures

Measure	Theoretical range	Observed range	Mean	Standard deviation	Q1	Median	Q3
FACIT-COST total score[a,e]	0 - 44	2 - 42	24.24	8.65	19	25	30
EQ-5D-5L index value[a,b]	-0.865 to 1	-0.31 to 1	0.85	0.21	0.80	0.91	1
EQ VAS[a]	0 - 100	10 - 100	81.18	15.63	75	80	90
EQ-HWB-S index value[a,d]	-0.384 to 1	-0.245 to 1	0.84	0.17	0.79	0.89	0.95
EQ-HWB LSS[c]	0 - 100	0 - 65	16.48	11.76	8	13	23

Abbreviations. EQ-HWB= EQ Health and Wellbeing, EQ-HWB-S= EQ-HWB short form, EQ VAS= EQ Visual analogue scale, FACIT-COST= COST - A FACIT Measure of Financial Toxicity, LSS= level summary scores
[a]Higher scores indicate better health-related quality of life, better wellbeing, or lower financial toxicity
[b]Computed using the Indonesian value set (Purba et al., 2017)
[c]LSS recoded into a 0-100 scale
[d]Computed using the pilot UK value set (Mukuria et al., 2023)
[e]Following the scoring guidelines, the 12th item of FACIT-COST was not included in the overall score computation

Among the four coping strategies, patients who sold their assets had the lowest mean EQ-5D-5L and EQ-HWB-S index values of 0.76±0.25 and 0.75±0.26, respectively. Overall, 42.3% experienced low SFT and no OFT, 36.7% experienced low SFT but at least one OFT, 6.7% experienced high SFT and no OFT, and 14.3% experienced both high SFT and at least one OFT. The mean EQ-5D-5L index values for these four subgroups were 0.88±0.17, 0.86±0.21, 0.81±0.17, 0.73±0.25, while the mean EQ-HWB-S index values were 0.88±0.13, 0.86±0.14, 0.77±0.22, and 0.71±0.25 respectively ($p<0.001$ for both instruments) (Figure VI.1). The EQ-5D-5L and EQ-HWB-S index values had statistically significant differences for the FACIT-COST item 'financial hardship to my family and me': not at all (0.90±0.12, 0.91±0.09), a little bit/somewhat (0.84±0.24, 0.84±0.16), and quite a bit/very much (0.79±0.21, 0.76±0.22) ($p<0.001$). Comparisons of EQ-5D-5L and EQ-HWB index values or scores among subgroups as defined by socio-demographic and clinical characteristics are presented in Appendix VI.1.

VI.3.3 Correlations between FACIT-COST, EQ-5D-5L, and EQ-HWB

The FACIT-COST total score demonstrated correlations that were borderline moderate with EQ-HWB coping (-0.34), EQ-HWB-S no control over daily life (-0.33), exhaustion (-0.31), and weakly correlated with the following items: EQ-HWB frustration (-0.29), EQ-HWB-S sadness/depression (-0.28), EQ-5D-5L pain/discomfort (-0.28),

Table VII.3. EQ-5D-5L, EQ VAS, and EQ-HWB scores across financial toxicity categories

Financial toxicity	n	%	Mean EQ-5D-5L index value	p-value	Mean EQ VAS	p-value	Mean EQ-HWB-S index value	p-value	Mean EQ-HWB LSS[a]	p-value
Subjective financial toxicity (SFT)[b,c]										
High SFT	63	21.0%	0.75 ± 0.23	<0.001	72.94 ± 17.75	<0.001	0.73 ± 0.24	<0.001	24.44 ± 14.65	<0.001
Low SFT	237	79.0%	0.87 ± 0.19		83.38 ± 14.28		0.87 ± 0.13		14.36 ± 9.87	
Objective financial toxicity (OFT)[d]										
At least one OFT	153	51.0%	0.82 ± 0.23	0.027	79.74 ± 17.03	0.103	0.82 ± 0.19	0.030	17.61 ± 11.95	0.089
No OFT	147	49.0%	0.87 ± 0.17		82.69 ± 13.93		0.86 ± 0.14		15.30 ± 11.48	
Borrowing from relatives or financial institution										
-Yes	90	30.0%	0.81 ± 0.21	0.061	78.39 ± 16.62	0.042	0.79 ± 0.21	0.002	19.30 ± 13.15	0.006
-No	210	70.0%	0.86 ± 0.20		82.38 ± 15.07		0.86 ± 0.15		15.27 ± 10.92	
Withdrawing savings or pension										
-Yes	77	25.7%	0.82 ± 0.26	0.185	79.94 ± 15.95	0.417	0.82 ± 0.20	0.320	17.13 ± 12.43	0.573
-No	223	74.3%	0.85 ± 0.19		81.61 ± 15.53		0.85 ± 0.16		16.25 ± 11.54	
Selling assets (e.g., vehicle, land)										
-Yes	33	11.0%	0.76 ± 0.25	0.010	75.76 ± 18.38	0.034	0.75 ± 0.26	<0.001	22.70 ± 14.85	0.001
-No	267	89.0%	0.86 ± 0.20		81.85 ± 15.16		0.85 ± 0.15		15.71 ± 11.12	
Closing business										
-Yes	10	3.3%	0.78 ± 0.25	0.270	78.50 ± 12.92	0.582	0.76 ± 0.13	0.142	22.40 ± 12.12	0.105
-No	290	96.7%	0.85 ± 0.20		81.28 ± 15.73		0.84 ± 0.17		16.27 ± 11.72	
SFT and OFT										
High SFT and at least one OFT	43	14.3%	0.73 ± 0.25	<0.001	69.30 ± 17.48	<0.001	0.71 ± 0.25	<0.001	24.60 ± 14.18	<0.001
High SFT and no OFT	20	6.7%	0.81 ± 0.17		80.75 ± 16.08		0.77 ± 0.22		24.10 ± 15.99	
Low SFT and at least one OFT	110	36.7%	0.86 ± 0.21		83.82 ± 15.07		0.86 ± 0.14		14.87 ± 9.74	
Low SFT and no OFT	127	42.3%	0.88 ± 0.17		82.99 ± 13.60		0.88 ± 0.13		13.91 ± 10.00	
FACIT-COST item 12[e]										
Quite a bit/very much	85	28.3%	0.79 ± 0.21	<0.001	74.82 ± 17.12	<0.001	0.76 ± 0.22	<0.001	22.93 ± 13.77	<0.001
A little bit/somewhat	114	38.0%	0.84 ± 0.24		81.93 ± 15.66		0.84 ± 0.16		17.07 ± 10.77	
Not at all	101	33.7%	0.90 ± 0.12		85.69 ± 12.31		0.91 ± 0.09		10.38 ± 7.04	

Abbreviations. EQ-HWB= EQ Health and Wellbeing, EQ-HWB-S= EQ-HWB short form, FACIT-COST=COST - A FACIT Measure of Financial Toxicity, LSS= level summary scores

[a]LSS recoded to a 0-100 scale

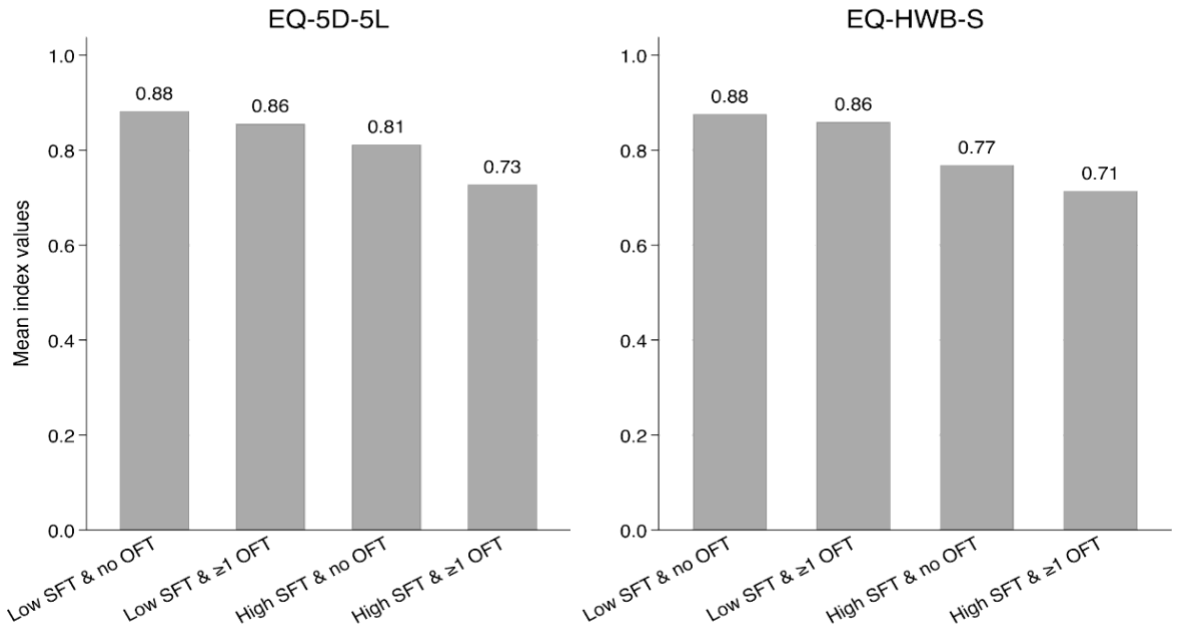
[b]High subjective financial toxicity: FACIT-COST score of ≤ 17.5 (Ng et al., 2021)

[c]Following the scoring guidelines, item 12 of the FACIT-COST was not included in the overall score computation

[d]Each patient may have incurred more than one financial coping strategy

[e] '*Financial hardship to my family and me*' item (responses recoded from five to three levels)

Figure VII.1. Mean EQ-5D-5L and EQ-HWB-S index values across financial toxicity subgroups



Abbreviations
EQ-5D-5L= EQ Five-level EQ-5D Version, EQ-HWB-S= EQ-HWB short form (9 items), OFT = objective financial toxicity, SFT = subjective financial toxicity

and anxiety/depression (-0.27), among others (Table VI.4).

Table VII.4. Correlations between the EQ-5D-5L, EQ-HWB, and FACIT-COST

Pearson's correlations

	FACIT-COST total score*
EQ-5D-5L index value	0.30
EQ VAS	0.35
EQ-HWB-S index value	0.44
EQ-HWB LSS	-0.48

Spearman's correlations

	FACIT-COST total score*
EQ-5D-5L pain/discomfort	-0.28
EQ-5D-5L anxiety/depression	-0.27
EQ-HWB-S exhaustion	-0.31
EQ-HWB-S anxiety	-0.22
EQ-HWB-S sadness/depression	-0.28
EQ-HWB-S pain (severity)	-0.23
EQ-HWB-S no control over daily life	-0.33
EQ-HWB frustration	-0.29
EQ-HWB coping	-0.34
EQ-HWB discomfort (severity)	-0.19

Abbreviations. EQ-HWB= EQ Health and Wellbeing, EQ-HWB-S= EQ-HWB short form, FACIT-COST= COST - A FACIT Measure of Financial Toxicity, LSS= level summary scores
*Following the scoring guidelines, the 12th item of FACIT-COST was not included in the overall score computation
All correlation coefficients were p<0.001

At instrument level, FACIT-COST total score exhibited moderate correlations with EQ-HWB LSS (-0.48), EQ-HWB-S index values (0.44), EQ VAS (0.44), EQ-5D-5L LSS (-0.32), and EQ-5D-5L index values (0.30).

VI.3.4 Associations between financial toxicity and EQ-5D-5L and EQ-HWB items

After adjusting for socio-demographic and clinical covariates, reporting higher SFT was associated with more problems in the EQ-5D-5L pain/discomfort (OR=1.07), anxiety/depression (OR=1.06), EQ-HWB-S exhaustion (OR=1.06), anxiety (OR=1.04), sadness/depression (OR=1.06), pain (OR=1.06), EQ-HWB frustration (OR=1.10), and discomfort (OR=1.04) items (Table VI.5). Meanwhile, higher OFT was only significantly associated with more problems in the EQ-HWB-S exhaustion item (OR=1.40).

VI.3.5 Associations between financial toxicity and EQ-5D-5L and EQ-HWB level sum scores and index values

In the unadjusted OLS models, higher SFT was significantly associated with lower EQ-5D-5L index values (‘Model 1’), EQ VAS (‘Model 4’), EQ-HWB-S index values (‘Model 7’), and higher EQ-HWB LSS (‘Model 10’) (p<0.001 each) (Table VI.6).

Table VII.5. Ordinal logistic regression results

Variables	EQ-5D-5L pain/discomfort		EQ-5D-5L anxiety/depression		EQ-HWB-S exhaustion		EQ-HWB-S anxiety	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Subjective financial toxicity[a]	1.07***	(1.04, 1.1)	1.06**	(1.02, 1.10)	1.06***	(1.03, 1.10)	1.04**	(1.01, 1.08)
Objective financial toxicity	1.16	(0.87, 1.56)	1.23	(0.88, 1.71)	1.40*	(1.06, 1.87)	1.12	(0.84, 1.51)
Pseudo R-squared	12.63%		14.40%		15.14%		9.68%	
Variables	**EQ-HWB-S sadness/depression**		**EQ-HWB-S pain (severity)**		**EQ-HWB frustration**		**EQ-HWB discomfort (severity)**	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Subjective financial toxicity[a]	1.06**	(1.02, 1.09)	1.06***	(1.03, 1.10)	1.10**	(1.05, 1.15)	1.04*	(1.01, 1.07)
Objective financial toxicity	1.18	(0.87, 1.59)	0.94	(0.71, 1.24)	0.90	(0.61, 1.34)	1.03	(0.77, 1.36)
Pseudo R-squared	6.68%		9.20%		17.34%		10.34%	

***$p<0.001$, **$p<0.01$, *$p<0.05$

Abbreviations. CI= confidence interval, EQ-HWB= EQ Health and Wellbeing, EQ-HWB-S= EQ-HWB short form, OR= odds ratio

All regression models were controlled for age, income, number of children, diagnosis duration, metastasis status, current chemotherapy, number of comorbidities and symptoms in the past week

[a]Measured using COST - A FACIT Measure of Financial Toxicity

Table VII.6. Multivariable linear regression results

Variables	Outcome: EQ-5D-5L index value						Outcome: EQ VAS					
	Model 1		**Model 2**		**Model 3**		**Model 4**		**Model 5**		**Model 6**	
	B	***SE***	***B***	***SE***	***B***	***SE***	***B***	***SE***	***B***	***SE***	***B***	***SE***
Intercept	*1.00*	*0.00*	0.98	0.05	1.13	0.03	95.15	1.98	98.08	2.65	99.94	3.75
Subjective financial toxicity[a]	-0.01***	0.01	-0.01***	0.00	-0.01***	0.00	-0.63***	0.11	-0.66***	0.11	-0.56***	0.11
Objective financial toxicity	-0.02	0.03	-0.03	0.01	-0.02	0.01	-0.49	0.97	-0.87	0.96	-0.22	0.94
Aged 50 years and above	-	-	-0.06**	0.02	-0.03	0.02	-	-	-5.26**	1.67	-3.53*	1.69
Income > 5 million IDR[b]	-	-	-0.08	0.05	-0.01*	0.05	-	-	1.64	1.96	0.57	1.88
Number of children	-	-	0.02*	0.01	0.03**	0.01	-	-	1.11	0.77	1.25	0.79
Diagnosed 1 year or less	-	-	-	-	-0.04	0.02	-	-	-	-	-0.29	1.68
Metastasis	-	-	-	-	-0.11*	0.05	-	-	-	-	1.74	3.08
Undergoing chemotherapy	-	-	-	-	-0.10**	0.04	-	-	-	-	-5.12	2.94
Comorbidities *(ref: none)*												
1	-	-	-	-	-0.01	0.03	-	-	-	-	-1.77	1.82
2+	-	-	-	-	-0.03	0.03	-	-	-	-	-3.89	2.31
Symptoms in the past week *(ref: none)*												
1-3	-	-	-	-	-0.02	0.03	-	-	-	-	2.49	3.22
4-6	-	-	-	-	-0.07*	0.03	-	-	-	-	-2.36	3.36
7-9	-	-	-	-	-0.09**	0.03	-	-	-	-	-2.32	3.53
10+	-	-	-	-	-0.18***	0.04	-	-	-	-	-8.77*	3.55
Model fit	F(2,297)= 16.01 (p<0.001) R^2 = 9.12%		F(5,294)= 8.11 (p<0.001) R^2 = 14.88%		F(14,285)= 7.50 (p<0.001) R^2 = 31.23%		F(2,297)= 21.37 (p<0.001) R^2 = 12.63%		F(5,294)= 11.50 (p<0.001) R^2 = 16.36%		F(14,285)= 6.27 (p<0.001) R^2 = 25.60%	

Table VII.6. Multivariable linear regression results (cont.)

Variables	Outcome: EQ-HWB-S index value						Outcome: EQ-HWB LSS[c]					
	Model 7		Model 8		Model 9		Model 10		Model 11		Model 12	
	B	***SE***	***B***	***SE***	***B***	***SE***	***B***	***SE***	***B***	***SE***	***B***	***SE***
Intercept	1.02	0.03	1.07	0.04	1.11	0.04	2.39	1.53	-0.84	2.04	-3.82	2.54
Subjective financial toxicity[a]	-0.01*	0.00	-0.01***	0.00	-0.01***	0.00	0.63***	0.08	0.69***	0.08	0.54***	0.07
Objective financial toxicity	-0.02	0.01	-0.02	0.01	-0.01	0.01	0.61	0.84	1.00	0.82	-0.03	0.73
Aged 50 years and above	-	-	-0.06**	0.02	-0.03	0.02	-	-	3.81**	1.28	1.88	1.16
Income > 5 million IDR[b]	-	-	-0.05*	0.03	-0.07**	0.02	-	-	2.50	1.69	3.27*	1.45
Number of children	-	-	0.02**	0.01	0.02**	0.01	-	-	-0.98	0.58	-0.68	0.56
Diagnosed 1 year or less	-	-	-	-	0.00	0.02	-	-	-	-	-1.58	1.06
Metastasis	-	-	-	-	-0.09*	0.04	-	-	-	-	4.83	2.76
Undergoing chemotherapy	-	-	-	-	-0.06*	0.03	-	-	-	-	1.62	1.65
Comorbidities *(ref: none)*												
1	-	-	-	-	-0.01	0.02	-	-	-	-	1.96	1.23
2+	-	-	-	-	-0.03	0.02	-	-	-	-	2.13	1.40
Symptoms in the past week *(ref: none)*												
1-3	-	-	-	-	-0.01	0.02	-	-	-	-	1.28	2.13
4-6	-	-	-	-	-0.05*	0.02	-	-	-	-	4.26*	2.12
7-9	-	-	-	-	-0.05	0.03	-	-	-	-	5.98**	2.28
10+	-	-	-	-	-0.18***	0.03	-	-	-	-	14.06***	2.25
Model fit	F(2,297)=19.94 (p<0.001) R^2 = 19.60%		F(5,294)= 9.71 (p<0.001) R^2 = 25.98%		F(14,285)=8.82 (p<0.001) R^2 = 46.39%		F(2,297)=34.21 (p<0.001) R^2 = 22.74%		F(5,294)=16.58 (p<0.001) R^2 = 26.94%		F(14,285)=15.31 (p<0.001) R^2 = 46.15%	

***p<0.001, **p<0.01, *p<0.05

Abbreviations. B= unstandardized beta coefficient, EQ HWB: EQ Health and Wellbeing, EQ-HWB-S: EQ-HWB short form, LSS= level summary scores, SE= robust standard error of the regression

[a]Measured using COST - A FACIT Measure of Financial Toxicity

[b]Net monthly household income. IDR= Indonesian Rupiah, 324.34 USD = 5 million IDR (based on the closing 2023 middle exchange rate from Bank Indonesia)

[c]LSS recoded to a 0-100 scale, where higher score indicates worse health and wellbeing

After controlling for the socio-demographic and clinical covariates, the significant associations between SFT and the outcomes persisted ($p<0.001$ each): EQ-5D-5L index values (beta=-0.01, 'Model 3'), EQ VAS (beta=-0.56, 'Model 6'), EQ-HWB-S index values (beta=-0.01, 'Model 9'), and EQ-HWB LSS (beta=0.54, 'Model 12'). After covariate adjustment, FT explained more variance in EQ-HWB-S index value (R^2=46.39%) and EQ-HWB LSS (R^2=46.15%) than in EQ-5D-5L index values (R^2=31.23%) and EQ VAS (R^2=25.60%).

VI.4 DISCUSSION

This study aimed to examine the associations between FT, HRQoL, and well-being outcomes in patients with breast cancer. We demonstrated higher SFT to be associated with more problems in EQ-5D-5L pain/discomfort, anxiety/depression, EQ-HWB-S exhaustion, anxiety, sadness/depression, pain, EQ-HWB frustration, discomfort items, lower EQ-5D-5L index values, EQ VAS, EQ-HWB-S index values, and higher EQ-HWB LSS. Higher OFT was also related to more problems in the EQ-HWB-S exhaustion item.

The distress brought about by the financial challenges arising from cancer care was, to some extent, captured by the EQ-5D-5L, EQ VAS, and EQ-HWB. This could be attributed to increased negative emotions related to financial difficulties. Insufficient financial resources may hinder access to optimal healthcare, potentially leading to a diminished HRQoL and well-being.[55,56] Alternatively, it is also possible that the association is bi-directional as shown by studies using HRQoL to predict SFT.[15] It can be argued that patients with worse HRQoL or well-being subjectively report higher FT due to their condition and possible productivity loss. Hence, complementing the measurement of SFT with OFT seems important for a more comprehensive description of FT by identifying financial metrics or activities of patients.

Our findings suggest that FT accounted for a greater proportion of the variances in well-being, compared to HRQoL. Higher FT could mean that patients may have to make sacrifices in terms of necessities and wants, which may be related to feelings of isolation and frustration. Well-being may better capture the dynamics of FT, as it may include domains broader than HRQoL, such as pursuits that individuals desire or find meaningful, and sense of connection with one's environment.

Overall, our results align with the existing literature from other countries and neighboring regions. Previous studies conducted in the United States, Australia, and

China, focusing on various cancer types such as gastrointestinal, gynecological, and lung, have investigated associations between the SFT (FACIT-COST) and HRQoL as measured by the EQ-5D; employing other diverse methods such as generalized linear model, latent class analysis, and correlations.[52,57-60] All the studies demonstrated SFT to be significantly related to lower HRQoL. Additionally, two studies, found SFT to be moderately correlated with well-being.[25,61] Recent studies have also demonstrated significant associations between FT and EQ-5D-5L pain/discomfort and anxiety/depression domains with comparable association strengths,[50-52] suggesting that FT captures or represents a form of psychological distress, a burden commonly experienced by patients with cancer. Patients with higher symptom burden may experience greater financial strain due to non-medical costs related to symptom management and hospital visits, intensifying their psychological distress.

Our analysis did not reveal a statistically significant association between OFT and the outcome variable across most regression models, despite showing significance in the subgroup comparisons. This suggests that the OFT measurement may have benefitted from a more comprehensive approach, such as the currency amount of out-of-pocket health expenditure, as well as more detailed exploration of the financial coping strategies (e.g., loan amount or receipt from sale of assets). For example, two investigations from China and Malaysia found negative associations between both SFT and OFT with HRQoL.[48,62,63] Notably, these two studies consistently measured OFT using the healthcare cost-to-income ratio, while HRQoL was assessed using various instruments: EORTC QLQ-C30, EQ-5D-5L, and FACT-Lung. However, obtaining precise data on actual healthcare costs may present challenges, such as the patient not being completely in charge of their own finances. Recalling the accurate cost amount would also be challenging, particularly in the case of our sample, whose average disease duration since diagnosis was 2.45 years and nearly 100% had insurance coverage that mitigated direct medical expenses, including diagnostic tests, medications, surgeries, and physician fees.

Reflecting on our findings, some policy implications may be considered. While causality has not been established, our findings indicate a significant correlation between higher FT and diminished HRQoL and well-being. Health and social policymakers may consider interventions aimed at alleviating FT. Firstly, it may be important to screen for FT in patients and their families. Through proper identification of those at risk, necessary mitigation strategies can be implemented. One of the most adopted FT interventions involves financial navigation programs aimed at supporting patients and families with

managing the financial hardships of their treatment.[64-66] In the most extreme cases of poverty, extending coverage to include non-medical, cancer-related costs (e.g., transportation and accommodation for outpatients residing at a distance from healthcare facilities) may be an approach. The income-earning capacities of patients should also be protected from disruptions due to cancer,[67] such as through employment reintegration programs to facilitate their return to work.[68]

This study has some limitations. First, the data were collected from a single center within one country with a focus on females with breast cancer. There are also less developed areas in Indonesia with higher poverty rate and lower access to healthcare. Therefore, the results may not be generalized to other types of cancer, male patients, or more resource-poor settings. Second, we solely focused on patients and did not include their caregivers or core family members in our study. In the Indonesian context, men are still predominantly perceived as providers. Our sample primarily consisted of female homemakers and thus, FT may not have been comprehensively captured without the perspectives of the income provider. Third, nearly all patients had insurance coverage that may have led to some socio-demographic covariates not being significantly associated with the outcome variables and thus excluded from the regressions. However, this could also be attributed to limited response variability. Fourth, our measurement of SFT had its drawbacks. The FACIT-COST was developed in the United States and another measure may be more suited to capture financial well-being in the Indonesian context. However, it is the most widely used cancer-specific measure for SFT, which allows for comparability with previous studies. Fifth, the pilot UK value set was used for calculating the EQ-HWB-S index values, which does not fully reflect the preferences of the Indonesian population. Sixth, our study design did not allow exploring causality, while also incorporating broader measures of well-being and identifying potential mediating factors for future studies, such as social support.

VI.5 CONCLUSIONS

This is the first study to identify associations between FT, HRQoL, and well-being outcomes in patients with breast cancer, and the first in the FT literature to use the recently developed EQ-HWB instrument to measure health and well-being. Our findings provide additional insight into the burden of cancer and its link to the HRQoL and well-being of patients in a middle-income country context; further highlighting the importance of establishing health and social policies aimed at measuring and alleviating FT.

References

1. Kocarnik, J.M., et al., *Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis for the global burden of disease study 2019.* JAMA oncology, 2022. 8(3): p. 420-444.
2. Brüggen, E.C., et al., *Financial well-being: A conceptualization and research agenda.* Journal of business research, 2017. 79: p. 228-237.
3. Witte, J., et al., *Methods for measuring financial toxicity after cancer diagnosis and treatment: a systematic review and its implications.* Ann Oncol, 2019. 30(7): p. 1061-1070.
4. Fitch, M.I., et al., *Experiencing financial toxicity associated with cancer in publicly funded healthcare systems: a systematic review of qualitative studies.* J Cancer Surviv, 2022. 16(2): p. 314-328.
5. Udayakumar, S., et al., *Cancer treatment-related financial toxicity experienced by patients in low- and middle-income countries: a scoping review.* Support Care Cancer, 2022. 30(8): p. 6463-6471.
6. Pangestu, S. and F. Rencz, *Comprehensive Score for Financial Toxicity and Health-Related Quality of Life in Patients With Cancer and Survivors: A Systematic Review and Meta-Analysis.* Value Health, 2023. 26(2): p. 300-316.
7. Bhanvadia, S.K., et al., *Financial Toxicity Among Patients with Prostate, Bladder, and Kidney Cancer: A Systematic Review and Call to Action.* Eur Urol Oncol, 2021. 4(3): p. 396-404.
8. Ritter, J., et al., *Financial hardship in families of children or adolescents with cancer: a systematic literature review.* Lancet Oncol, 2023. 24(9): p. e364-e375.
9. Sitlinger, A. and S.Y. Zafar, *Health-Related Quality of Life: The Impact on Morbidity and Mortality.* Surg Oncol Clin N Am, 2018. 27(4): p. 675-684.
10. Azzani, M., et al., *Subjective and objective financial toxicity among colorectal cancer patients: a systematic review.* BMC Cancer, 2024. 24(1): p. 40.
11. Lueckmann, S.L., et al., *Identifying missing links in the conceptualization of financial toxicity: a qualitative study.* Supportive Care in Cancer, 2022. 30(3): p. 2273-2282.
12. Kang, D., et al., *Impact of objective financial burden and subjective financial distress on spiritual well-being and quality of life among working-age cancer survivors.* Support Care Cancer, 2022. 30(6): p. 4917-4926.
13. de Souza, J.A., et al., *Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the COmprehensive Score for financial Toxicity (COST).* Cancer, 2017. 123(3): p. 476-484.
14. Head, B.A. and A.C. Faul, *Development and validation of a scale to measure socioeconomic well-being in persons with cancer.* J Support Oncol, 2008. 6(4): p. 183-92.
15. Pangestu, S., et al., *Financial Toxicity Experiences of Patients With Cancer in Indonesia: An Interpretive Phenomenological Analysis.* Value Health Reg Issues, 2023. 41: p. 25-31.
16. Jiang, H., et al., *Association between financial toxicity and health-related quality of life in cancer survivors: A systematic review.* Asia Pac J Clin Oncol, 2023. 19(4): p. 439-457.
17. Zhu, Z., et al., *Cancer survivors' experiences with financial toxicity: A systematic review and meta-synthesis of qualitative studies.* Psychooncology, 2020. 29(6): p. 945-959.
18. Zhu, Z., et al., *Psychometric properties of self-reported financial toxicity measures in cancer survivors: a systematic review.* BMJ Open, 2022. 12(6): p. e057215.
19. Donkor, A., et al., *Financial toxicity of cancer care in low- and middle-income countries: a systematic review and meta-analysis.* Support Care Cancer, 2022. 30(9): p. 7159-7190.
20. Ehsan, A.N., et al., *Financial Toxicity Among Patients With Breast Cancer Worldwide: A Systematic Review and Meta-analysis.* JAMA Netw Open, 2023. 6(2): p. e2255388.
21. Romero, M., D. Vivas-Consuelo, and N. Alvis-Guzman, *Is Health Related Quality of Life (HRQoL) a valid indicator for health systems evaluation?* Springerplus, 2013. 2(1): p. 664.
22. Yin, S., et al., *Summarizing health-related quality of life (HRQOL): development and testing of a one-factor model.* Popul Health Metr, 2016. 14: p. 22.
23. Nutbeam, D. and D.M. Muscat, *Health Promotion Glossary 2021.* Health Promot Int, 2021. 36(6): p. 1578-1598.
24. Linton, M.J., P. Dieppe, and A. Medina-Lara, *Review of 99 self-report measures for assessing well-being in adults: exploring dimensions of well-being and developments over time.* BMJ Open, 2016. 6(7): p. e010641.
25. Yu, H.H., et al., *The COmprehensive Score for financial Toxicity in China: Validation and Responsiveness.* J Pain Symptom Manage, 2021. 61(6): p. 1297-1304.e1.
26. Cotlear, D., et al., *Going universal: how 24 developing countries are implementing universal health coverage from the bottom up*. 2015: World Bank Publications.

27. Bray, F., et al., *Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries.* CA Cancer J Clin, 2018. 68(6): p. 394-424.
28. Kosen, S., *Coverage and implementation of healthcare delivery for cancer under national health insurance, experience of Indonesia.* Lancet Reg Health Southeast Asia, 2022. 6: p. 100065.
29. Ministry of Health of Republic of Indonesia. *Health Research and Development Ethical Guidelines and Standards (In Indonesian)*. 2021 [cited 2024 January 18]; Available from: https://repository.badankebijakan.kemkes.go.id/id/eprint/4214/1/Pedoman%20dan%20Standar%20Etik%20Penelitian%20dan%20Pengembangan%20Kesehatan%20Nasional.pdf.
30. Pangestu S., et al., *Validity, test-retest reliability, and responsiveness of the Indonesian version of FACIT-COST measure for subjective financial toxicity*. Health Qual Life Outcomes, 2024. 22(1):89.
31. Pangestu S., et al., *The Psychometric Properties of the EQ-HWB and EQ-HWB-S in Patients With Breast Cancer: A Comparative Analysis With EQ-5D-5L, FACT-8D, and SWEMWBS*. Value Health, 2024. Online ahead of print.
32. Herdman, M., et al., *Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L).* Qual Life Res, 2011. 20(10): p. 1727-36.
33. Purba, F.D., et al., *The Indonesian EQ-5D-5L Value Set.* Pharmacoeconomics, 2017. 35(11): p. 1153-1165.
34. Shim, S., et al., *Validation of Korean Version of the COmprehensive Score for financial Toxicity (COST) Among Breast Cancer Survivors.* Cancer Res Treat, 2022. 54(3): p. 834-841.
35. Sagberg, L.M., A.S. Jakola, and O. Solheim, *Quality of life assessed with EQ-5D in patients undergoing glioma surgery: what is the responsiveness and minimal clinically important difference?* Qual Life Res, 2014. 23(5): p. 1427-34.
36. Zeng, X., et al., *Measurement Properties of the EQ-5D-5L and EQ-5D-3L in Six Commonly Diagnosed Cancers.* Patient, 2021. 14(2): p. 209-222.
37. Zhu, J., et al., *Comparing EQ-5D-3L and EQ-5D-5L performance in common cancers: suggestions for instrument choosing.* Qual Life Res, 2021. 30(3): p. 841-854.
38. Brazier, J., et al., *The EQ-HWB: Overview of the Development of a Measure of Health and Wellbeing and Key Results.* Value Health, 2022. 25(4): p. 482-491.
39. Peasgood, T., et al., *What is the best approach to adopt for identifying the domains for a new measure of health, social care and carer-related quality of life to measure quality-adjusted life years? Application to the development of the EQ-HWB?* Eur J Health Econ, 2021. 22(7): p. 1067-1081.
40. Peasgood, T., et al., *Developing a New Generic Health and Wellbeing Measure: Psychometric Survey Results for the EQ-HWB.* Value Health, 2022. 25(4): p. 525-533.
41. Augustovski, F., et al., *The Development of a New International Generic Measure (EQ-HWB): Face Validity and Psychometric Stages in Argentina.* Value Health, 2022. 25(4): p. 544-557.
42. Monteiro, A.L., M. Kuharic, and A.S. Pickard, *A Comparison of a Preliminary Version of the EQ-HWB Short and the 5-Level Version EQ-5D.* Value Health, 2022. 25(4): p. 534-543.
43. Kuharić, M., et al., *The Measurement Properties of the EQ Health and Well-being and EQ Health and Well-Being Short Form in Italian Population: A Comparative Study With EQ-5D-5L.* Value Health, 2024.
44. Mukuria, C., et al., *Valuing the EQ Health and Wellbeing Short Using Time Trade-Off and a Discrete Choice Experiment: A Feasibility Study.* Value Health, 2023. 26(7): p. 1073-1084.
45. de Souza, J.A., et al., *The development of a financial toxicity patient-reported outcome in cancer: The COST measure.* Cancer, 2014. 120(20): p. 3245-53.
46. Ng, M.S.N., et al., *Identifying a cut-off score for the COST measure to indicate high financial toxicity and low quality of life among cancer patients.* Support Care Cancer, 2021. 29(10): p. 6109-6117.
47. Gordon, L.G., et al., *A Systematic Review of Financial Toxicity Among Cancer Survivors: We Can't Pay the Co-Pay.* Patient, 2017. 10(3): p. 295-309.
48. Ting, C.Y., et al., *Financial toxicity and its associations with health-related quality of life among urologic cancer patients in an upper middle-income country.* Support Care Cancer, 2020. 28(4): p. 1703-1715.
49. Chan, R.J., et al., *Relationships Between Financial Toxicity and Symptom Burden in Cancer Survivors: A Systematic Review.* J Pain Symptom Manage, 2019. 57(3): p. 646-660.e1.
50. Thaduri, A., et al., *Financial toxicity and mental well-being of the oral cancer survivors residing in a developing country in the era of COVID 19 pandemic - A cross-sectional study.* Psychooncology, 2023. 32(1): p. 58-67.
51. Murphy, P.B., et al., *Financial toxicity is associated with worse physical and emotional long-term outcomes after traumatic injury.* J Trauma Acute Care Surg, 2019. 87(5): p. 1189-1196.

52. Xu, R.H., et al., *Urban-rural differences in financial toxicity and its effect on cancer survivors' health-related quality of life and emotional status: a latent class analysis.* Support Care Cancer, 2022. 30(5): p. 4219-4229.
53. Rencz, F. and M.F. Janssen, *Analyzing the Pain/Discomfort and Anxiety/Depression Composite Domains and the Meaning of Discomfort in the EQ-5D: A Mixed-Methods Study.* Value Health, 2022. 25(12): p. 2003-2016.
54. Cohen, J., *Quantitative methods in psychology: A power primer.* Psychol. Bull., 1992. 112: p. 1155-1159.
55. Chino, F. and S.Y. Zafar, *Financial Toxicity and Equitable Access to Clinical Trials.* Am Soc Clin Oncol Educ Book, 2019. 39: p. 11-18.
56. Tucker-Seeley, R.D., *Financial Toxicity: A Barrier to Achieving Health Equity in Cancer Care.* J Am Coll Radiol, 2023. 20(1): p. 37-39.
57. Ehlers, M., et al., *A national cross-sectional survey of financial toxicity among bladder cancer patients.* Urol Oncol, 2021. 39(1): p. 76.e1-76.e7.
58. Gordon, L.G., et al., *The Economic Impact on Australian Patients with Neuroendocrine Tumours.* Patient, 2020. 13(3): p. 363-373.
59. Bouberhan, S., et al., *Financial toxicity in gynecologic oncology.* Gynecol Oncol, 2019. 154(1): p. 8-12.
60. Esselen, K.M., et al., *Crowdsourcing to measure financial toxicity in gynecologic oncology.* Gynecol Oncol, 2021. 161(2): p. 595-600.
61. Chen, G., et al., *Measuring the Wellbeing of Cancer Patients with Generic and Disease-Specific Instruments.* Cancers (Basel), 2023. 15(4).
62. Xu, R.H., et al., *Quantifying the Effect of Financial Burden on Health-Related Quality of Life among Patients with Non-Hodgkin's Lymphomas.* Cancers (Basel), 2020. 12(11).
63. Chen, J.E., et al., *Objective and subjective financial burden and its associations with health-related quality of life among lung cancer patients.* Supportive Care in Cancer, 2018. 26(4): p. 1265-1272.
64. Smith, G.L., et al., *Navigating financial toxicity in patients with cancer: A multidisciplinary management approach.* CA Cancer J Clin, 2022. 72(5): p. 437-453.
65. Edward, J., et al., *Interventions to address cancer-related financial toxicity: Recommendations from the field.* J Rural Health, 2022. 38(4): p. 817-826.
66. Knight, T.G., et al., *Financial Toxicity Intervention Improves Outcomes in Patients With Hematologic Malignancy.* JCO Oncol Pract, 2022. 18(9): p. e1494-e1504.
67. Mols, F., et al., *Financial toxicity and employment status in cancer survivors. A systematic literature review.* Supportive Care in Cancer, 2020. 28(12): p. 5693-5708.
68. Pearce, A., et al., *Financial toxicity is more than costs of care: the relationship between employment and financial toxicity in long-term cancer survivors.* J Cancer Surviv, 2019. 13(1): p. 10-20.

CHAPTER VII

General Discussion and Conclusions

Achieving universal health coverage means providing health care access to every person without financial hardship. Countless individuals with cancer worldwide are experiencing financial toxicity, an issue exacerbated by increasing prevalence of cancer and rising costs of healthcare. Financial toxicity may be causing, *inter alia*, individuals unable to follow their necessary treatment, thereby adversely impacting their survivorship. These trends are confirmed by the growing literature of financial toxicity in recent years, including the development of instruments for financial toxicity measurement, impact of financial toxicity on health outcomes, and ways to mitigate financial toxicity.

Indonesia is the world's largest archipelago, fourth most populous country, and third largest democracy. It is a middle-income country with systemic and structural challenges regarding quality and equitable access to healthcare across the nation. Indonesia has made significant progress toward universal health coverage since the beginning of the healthcare system reform in 2014. However, financial toxicity is profoundly understudied in the country.

This dissertation sought to investigate financial toxicity, HRQoL, and well-being, and their associations in patients with cancer in Indonesia. To fulfill this aim, five distinct chapters have been presented to provide a cohesive research narrative. Chapter II provided a systematic literature review and meta-analyis on the association between subjective financial toxicity and HRQoL. Chapter III empirically explored the experience of financial toxicity in Indonesia using a qualitative study design in patients with different types of cancer. The remaining chapters employed quantitative longitudinal study designs and focused on breast cancer, the most prevalent cancer worldwide, including in Indonesia. Chapters 4 and 5 psychometrically validated the instruments which measured financial toxicity, HRQoL, and well-being, and Chapter VI reported on the associations among the key constructs.

Finally, this concluding chapter (Chapter VII) provides a summary of the main findings of the studies presented in this dissertation, followed by methodological considerations, recommendations for future research, and theoretical and health and social policy implications.

VII.1 Summary of findings

The first aim of the dissertation was to perform a systematic literature review and meta-analysis on studies investigating the association of financial toxicity and HRQoL in

patients with cancer. Chapter II presents the results of systematic review and meta-analysis on studies reporting the associations of HRQoL and financial toxicity measured with the FACIT-COST. Overall, 31 studies from 9 countries were included in the systematic review, of which almost all studies used cross-sectional design. HRQoL was measured using 19 different HRQoL measures. All studies but one reported that higher financial toxicity was linked to worse HRQoL. In total, there were ten HRQoL domains that were correlated with financial toxicity, including physical, social, mental health, and daily functioning. Afterward, a meta-analysis was performed between financial toxicity and overall HRQoL as measured by the FACT-G, which showed a statistically significant moderate correlation. In summary, this chapter substantiates financial toxicity to be a relevant adverse outcome of cancer which is related to reduced HRQoL.

The second aim of the dissertation was to explore how patients with cancer experience financial toxicity in Indonesia using interpretive phenomenological analysis. Chapter III reports the results of interpretive phenomenological analysis of in-depth qualitative interviews with patients with various types of cancer in Indonesia. The analysis identified two main themes. The first main theme was "experienced financial burden." Three subthemes were identified which elaborates the contributing factors to the subjective lived experience of financial toxicity: underinsurance, out-of-pocket non-healthcare cancer-related costs, and negative income effect from employment disruption. The other main theme was "financial coping strategies". Four subthemes which discussed the strategies implemented by the patients to cope with financial toxicity were: reallocating household budget, seeking family support, rationalizing treatment decisions, and topping up insurance for family members. This study confirms the possible wider presence of financial toxicity issue in patients with cancer in Indonesia, which was further investigated in the subsequent quantitative chapters.

The third dissertation aim was to validate the Indonesian version of the subjective financial toxicity measure, FACIT-COST in a population of breast cancer in Indonesia. Chapter IV reports the measurement properties of the official Indonesian version of FACIT-COST. The results showed that the Indonesian FACIT-COST is a psychometrically valid and reliable measure, evidenced by its distributional characteristics, discriminatory power across multiple relevant known-groups, excellent scale-level test-retest reliability, and adequate responsiveness to change. Furthermore, structural validity analysis suggested that the Indonesian FACIT-COST has a good-fitting

two-factor structure. Overall, this chapter indicates that the Indonesian FACIT-COST can be applied in the Indonesian context as a measure of subjective financial toxicity.

The fourth aim of the dissertation was to validate the EQ-HWB and EQ-HWB-S and compare it to other preference-accompanied instruments in a breast cancer population in Indonesia. Chapter V details the psychometric validation of the EQ-HWB and EQ-HWB-S, including a comparative analysis with three other preference-accompanied measures: EQ-5D-5L, FACT-8D, and SWEMWBS. The findings showed that the EQ-HWB, along with its short form EQ-HWB-S, has robust psychometric performance that is comparable to, and in some measurement properties, better than the generic EQ-5D-5L (in terms of ceiling effect) and cancer-specific FACT-8D (in terms of test-retest reliability). Therefore, the EQ-HWB can be recommended as an outcome measure, with the EQ-HWB-S potentially useful in cost-utility analysis of breast cancer interventions.

The fifth and final aim of the dissertation was to investigate the associations between financial toxicity, well-being, and HRQoL in patients with breast cancer in Indonesia. Chapter VI highlights the results of the examination of associations between objective and subjective financial toxicity, EQ-5D-5L, and EQ-HWB outcomes in patients with breast cancer. The Indonesian FACIT-COST was used to measure subjective financial toxicity, whereas a question about the patients' financial coping strategies against cancer-related costs was used to evaluate the objective form of financial toxicity. Multivariate logistic regression analyses showed that higher subjective financial toxicity is significantly associated with more problems in the EQ-5D-5L pain/discomfort, anxiety/depression, EQ-HWB frustration, discomfort, and EQ-HWB-S exhaustion, anxiety, sadness/depression, and pain. Meanwhile, higher objective financial toxicity is associated with more problems in EQ-HWB-S exhaustion. Multivariate linear regression analyses showed that higher subjective financial toxicity is significantly associated with lower EQ-5D-5L, EQ-HWB-S index values, and EQ VAS. Furthermore, the findings also indicated that financial toxicity explains greater variances in well-being than in HRQoL.

VII.2 Methodological considerations and future research

Due to limitations of the studies presented in this dissertation, it is important to contextualize the results when interpreting them. Some key methodological considerations are highlighted below, along with the potential avenues for future research based on these limitations.

The relationships among constructs investigated in this dissertation have been correlational in nature, i.e., no causal effects were established. However, we provide a possible foundation for establishing causality between financial toxicity and HRQoL and well-being outcomes. Considering our findings, future research should strongly consider exploring these associations through designs such as randomized controlled trials (RCTs). The added value of an RCT is the possibility of simultaneously testing an intervention aimed at mitigating financial toxicity, e.g., financial navigation programs or direct financial assistance with non-healthcare expenditures.[1,2] Alternatively, an observational prospective cohort design can be employed, utilizing the causal inference tool "directed acyclic graphs" (DAGs) to address endogeneity problems.[3] Some important factors to be considered in determining the suitable follow-up period include the disease prognosis, treatment complexity, and socioeconomic background of the patients.

The primary data for the quantitative empirical chapters in this dissertation were gathered through a survey which relied on a single-center collection with small sample size, focusing on one type of cancer and female patients, of whom more than 99% were covered by public health insurance. These constraints potentially limit the generalizability of the findings in this dissertation and raise further research questions, particularly related to financial toxicity in male patients, other types of cancer, private hospital context or other medical settings where high out-of-pocket costs are incurred. Furthermore, the longitudinal design had its limitations. Despite an extremely low dropout rate (<1%) and no missing data reported due to rigorous data-checking procedures by the research assistants, the follow-up period was relatively short, lasting only up to 26 weeks. While different follow-up time points were initially designed to assess test-retest reliability and responsiveness, they were ultimately combined due to minimal differences between subsamples.[4] Future research could address these limitations by incorporating longer follow-ups, particularly for constructs related to financial well-being that may require more time to observe significant changes, and by increasing sample sizes to improve statistical power.

Another important aspect that was not explored in depth in this dissertation is the role of caregivers or family members. There are a few considerations to be made. First, measuring financial toxicity in patients who are (still) dependent on their family members for complete financial support may not precisely capture the construct. In instances such as children, adolescents, and young adults with cancer, it would be more appropriate to obtain data from the parents. Other examples include unemployed homemakers and

seniors who are dependent on their children. Second, providing informal care to patients may have financial implications due to reduced labor engagement, such as direct loss of income or opportunity loss. This indicates the possibility that caregivers may experience a "secondhand" financial toxicity by association, despite not being individuals with cancer or other chronic diseases themselves.

The measurement of subjective financial toxicity in this dissertation used the official Indonesian language version of FACIT-COST, which was developed initially in the United States. Although the instrument shows good psychometric performance and can be fitted in the context, it does not fully capture the unique aspects of Indonesia's health system and culture. Therefore, it is recommended to develop a localized instrument that better reflects the ethnic and geographic diversity, as well as the distinct characteristics of the Indonesian healthcare system. The development of a new instrument can employ mixed-methods design, involving multiple stakeholders (e.g., patients, academics, social and health policy experts, healthcare providers, general population) and should adhere to established methodological standards.[5] In addition, benchmarking with other internationally developed financial toxicity measures may be warranted. For instance, at the time of writing this dissertation, the European Organisation for Research and Treatment of Cancer (EORTC) has an ongoing study to develop a new measure of financial toxicity.[6]

Developing a validated, standardized, and contextually relevant measure of financial toxicity with strong measurement properties is essential for supporting evidence-based mitigation strategies. However, literature on the mitigation of financial toxicity remains scarce. So far, the effectiveness of interventions has been poorly designed, and the results have been controversial.[7] Future research should prioritize rigorous evaluation of mitigation strategies at both the patient and healthcare provider levels. These strategies should focus on equity and address specific aspects of financial toxicity requiring support. For instance, individuals with sufficient financial resources may benefit most from financial navigation or counseling programs, while those at the highest risk of treatment non-adherence due to non-treatment-related expenditures may require direct financial assistance.

Currently, the EQ-HWB and EQ-HWB-S are experimental instruments undergoing modifications and testing. Nevertheless, both instruments demonstrate favorable performance compared to other commonly used generic and disease-specific measures in cancer. The EQ-5D, which is recommended for pharmacoeconomic

evaluations in over 20 countries,[8] has been noted in previous studies to exhibit lower sensitivity when compared to cancer-specific preference-accompanied measures like FACT-G, a widely employed measure in cancer trials.[9] In this context, the EQ-HWB and EQ-HWB-S hold promise as outcome measures in economic evaluations, potentially due to their inclusion of broader and more diverse dimensions. Further validation studies across diverse cancer populations are necessary to substantiate their applicability.

Although multiple preference-accompanied instruments were used in this dissertation, only one— the EQ-5D-5L—measured health utility using the Indonesian value set. In contrast, due to their novelty, the utility values of the EQ-HWB-S, FACT-8D, and SWEMWBS were derived from value sets developed in other countries. Health Technology Assessment (HTA) evaluates the costs and benefits of interventions to guide resource allocation decisions in healthcare. Measuring intervention outcomes in QALYs requires instruments that assess health states using societal preferences. Future studies can consider developing an Indonesian value set for the EQ-HWB-S to ensure decisions are informed by local societal preferences. Additionally, this could also address a gap in the Indonesian HTA Guidelines, which currently do not recommend any well-being measure for health interventions that may have both health and social care impacts.[10] While the EQ-5D is already recommended for HRQoL assessments, incorporating a well-being instrument, such as the EQ-HWB, would provide a more comprehensive framework for evaluating the broader impacts of health interventions on health and well-being.

VII.3 Implications

VII.3.1 Theoretical contributions

This dissertation offers some novel contributions to the financial toxicity literature. Firstly, we conducted the first-ever systematic review and meta-analysis to summarize the published research on the association of subjective financial toxicity, as measured by FACIT-COST, and HRQoL in patients and survivors of cancer. Secondly, we carried out the first qualitative study on financial toxicity in Indonesia, employing interpretive phenomenological analysis. Thirdly, we performed the first psychometric validation of FACIT-COST in breast cancer and validated the official Indonesian version of FACIT-COST in any cancer population for the first time.

With respect to the HRQoL and well-being measurement literature, we conducted the first psychometric validation of the EQ-HWB and EQ-HWB-S in a breast cancer

population and provided the initial evidence of the quantitative measurement properties of the Indonesian versions of the measures. Furthermore, we were among the first to provide evidence on the test-retest reliability and responsiveness of the EQ-HWB and EQ-HWB-S in any clinical population. Additionally, we presented comparative evidence on EQ-HWB and FACT-G, as well as EQ-HWB-S, FACT-8D, and SWEMWBS.

Finally, in exploring the relationships between financial toxicity, HRQoL, and well-being, we were the first to investigate these associations, while considering both objective and subjective forms of financial toxicity, specifically within a breast cancer population. This dissertation extends the understanding of the cancer burden by providing qualitative and quantitative evidence that highlights financial toxicity as an important and relevant construct and outcome of cancer. We address a significant gap in the existing literature by presenting evidence from Indonesia, a middle-income and non-English-speaking country.

VII.3.2 Health and social policy implications

The findings of this dissertation suggest several policy implications. First and foremost, within the clinical context, educating patients about the costs related to cancer treatment and openly discussing financial issues and needs can be the first step in helping them navigate financial toxicity.[11-13] As such, properly measuring financial toxicity using a valid and reliable standardized measure during the patient's treatment trajectory, such as the FACIT-COST, may also be considered. At the patient level, financial toxicity interventions have been shown to improve clinical outcomes, with financial navigation being the most tested and effective intervention to date.[7,14-18] Financial navigation programs involve the screening of financial toxicity, discussions about costs, and active guidance on financial and non-financial resources (e.g., social support) that can be used by patients to minimize burden. In settings where healthcare costs are covered by public health insurance, coverage for non-healthcare costs (e.g., transportation to medical facilities) can be considered for individuals living in poverty. While financial navigation primarily focuses on managing costs and resources, another important approach is to protect the income-earning capacity of individuals. To aid in the social reintegration of cancer survivors, job reintegration programs can be considered (e.g., return-to-workplace, skill development programs, flexible work arrangements, micro business training).

From a health economics perspective, cost-utility analysis (CUA) offers policymakers a valuable framework for evaluating interventions by balancing their costs

against the benefits they deliver in terms both quantity (life years gained) and quality of life. The application of CUA in decision-making processes can improve population health by enhancing patient access to effective treatments, and, subsequently, improve health system efficiency (i.e., reduction of broader economic burden on societies). The use of preference-accompanied measures is essential for the calculation of health utilities across different healthcare interventions, ensuring societal preferences are also reflected in health outcomes. In Indonesia, as in many other countries, the EQ-5D-5L is recommended tool for performing QALY calculations to inform health policy decisions.[10] However, the EQ-5D may not capture the broader aspects of well-being relevant to specific patient populations. Our findings suggest that the EQ-HWB and EQ-HWB-S could address these gaps and serve as valuable tools for clinical and economic evaluations in cancer care, particularly for breast cancer interventions.

The promising psychometric performance of the Indonesian versions of instruments used to measure key constructs in this dissertation underscores their potential applicability in the Indonesian context. Furthermore, the associations between high financial toxicity, lower HRQoL, and well-being can inform future policy interventions aimed at improving cancer care. These findings suggest that mitigating financial toxicity may be related to the improvement of QALY gains for patients and survivors of cancer.

We hope that the work presented in this dissertation will inspire further research into financial toxicity, increase awareness of its impact, and promote strategies for its mitigation. and mitigation. Equally, we also encourage further investigations into economic evaluations in healthcare, emphasizing their crucial role in shaping reimbursement decision-making to support Indonesia's universal healthcare goals.

References

1. Al-Abdulla O, Sonsuz AA, Alaref M, Albakor B, Kauhanen J. The impact of humanitarian aid on financial toxicity among cancer patients in Northwest Syria. *BMC Health Services Research*. 2024;24(1):641. doi:10.1186/s12913-024-11077-x
2. Ragavan MV, Mora RV, Winder K, et al. Impact of a Comprehensive Financial Resource on Financial Toxicity in a National, Multiethnic Sample of Adult, Adolescent/Young Adult, and Pediatric Patients With Cancer. *JCO Oncol Pract*. 2023;19(2):e286-e297. doi:10.1200/op.22.00350
3. Digitale JC, Martin JN, Glymour MM. Tutorial on directed acyclic graphs. *J Clin Epidemiol*. 2022;142:264-267. doi:10.1016/j.jclinepi.2021.08.001
4. Pangestu S, Purba FD, Setyowibowo H, Mukuria C, Rencz F. Validity, test-retest reliability, and responsiveness of the Indonesian version of FACIT-COST measure for subjective financial toxicity. *Health Qual Life Outcomes*. 2024;22(1):89. doi:10.1186/s12955-024-02303-5
5. U.S. Food and Drug Administration. Guidance for industry - patient-reported outcome measures: Use in medical product development to support labeling claims. 2009. Accessed 20 January 2025, https://www.fda.gov/regulatory-information/search-fda-guidance-documents/patient-reported-outcome-measures-use-medical-product-development-support-labeling-claims
6. EORTC. Financial Toxicity project. EORTC Quality of Life. Accessed 3 January 2025, https://qol.eortc.org/questionnaire/fintox/
7. Yuan X, Zhang X, He J, Xing W. Interventions for financial toxicity among cancer survivors: A scoping review. *Crit Rev Oncol Hematol*. 2023;192:104140. doi:10.1016/j.critrevonc.2023.104140
8. Kennedy-Martin M, Slaap B, Herdman M, et al. Which multi-attribute utility instruments are recommended for use in cost-utility analysis? A review of national health technology assessment (HTA) guidelines. *Eur J Health Econ*. 2020;21(8):1245-1257. doi:10.1007/s10198-020-01195-8
9. Giesinger JM, Efficace F, Aaronson N, et al. Past and Current Practice of Patient-Reported Outcome Measurement in Randomized Cancer Clinical Trials: A Systematic Review. *Value Health*. 2021;24(4):585-591. doi:10.1016/j.jval.2020.11.004
10. Indonesian Health Technology Assessment Committee. *General Guideline for Health Technology Assessment in Indonesia*. 2022. Accessed 3 January 2025, http://www.gear4health.com/uploads/files/file-30-649513d401222.pdf
11. Miller MF, Olson JS, Doughtie K, Zaleta AK, Rogers KP. The interplay of financial toxicity, health care team communication, and psychosocial well-being among rural cancer patients and survivors. *J Rural Health*. 2024;40(1):128-137. doi:10.1111/jrh.12779
12. Sadigh G, Coleman D, Switchenko JM, Hopkins JO, Carlos RC. Treatment out-of-pocket cost communication and remote financial navigation in patients with cancer: a feasibility study. *Support Care Cancer*. 2022;30(10):8173-8182. doi:10.1007/s00520-022-07270-5
13. Hamel LM, Dougherty DW, Hastert TA, et al. The DISCO App: A pilot test of a multi-level intervention to reduce the financial burden of cancer through improved cost communication. *PEC Innov*. 2022;1:100002. doi:10.1016/j.pecinn.2021.100002
14. Arastu A, Hamilton A, Chen EY-s. Interventions to alleviate financial toxicity among patients with cancer: A systematic review. Wolters Kluwer Health; 2021. doi:10.1200/JCO.2021.39.15_suppl.e18841
15. Edward J, Petermann VM, Eberth JM, et al. Interventions to address cancer-related financial toxicity: Recommendations from the field. *J Rural Health*. 2022;38(4):817-826. doi:10.1111/jrh.12637
16. Smith GL, Banegas MP, Acquati C, et al. Navigating financial toxicity in patients with cancer: A multidisciplinary management approach. *CA Cancer J Clin*. 2022;72(5):437-453. doi:10.3322/caac.21730
17. Knight TG, Aguiar M, Robinson M, et al. Financial Toxicity Intervention Improves Outcomes in Patients With Hematologic Malignancy. *JCO Oncol Pract*. 2022;18(9):e1494-e1504. doi:10.1200/op.22.00056
18. Aviki EM, Thom B, Braxton K, et al. Patient-reported benefit from proposed interventions to reduce financial toxicity during cancer treatment. *Support Care Cancer*. 2022;30(3):2713-2721. doi:10.1007/s00520-021-06697-6

Appendix

Appendix

Appendix II.1. PubMed search strategy

Search	Search terms	Note
#1	Cancer[sb][1]	PubMed cancer filter that was developed by the National Library of Medicine and the National Cancer Institute (National Library of Medicine, 2019)
#2	("financial stress"[MeSH] OR "financial toxicit*"[tw] OR "financial hardship*"[tw] OR "financial distress" [tw] OR "financial stress*"[tw] OR "out of pocket" [tw] OR "out-of-pocket expenditure*"[tw] OR "out-of-pocket payment*"[tw] OR "out-of-pocket cost*"[tw] OR "out-of-pocket spending"[tw] OR "personal financial"[tw] OR "bankruptc*"[tw] OR "debt"[tw] OR "financial challeng*"[tw] OR "financial pressure"[tw])	Based on Bhanvadia et al., 2021 and other terms that we identified during preliminary literature search
#3	("preference-based"[tw] OR "preference-accompanied" [tw] OR "preference-weighted" [tw] OR "Quality of Wellbeing scale"[tw] OR "discreet choice experiment" [tw] OR "DCE" [tw] OR "PROPr"[tw] OR "QOL"[tw] OR "Quality of Life"[tw] OR "Quality-Adjusted Life Year*"[tw] OR "Quality Adjusted Life Year*"[tw] OR "Value of Life"[tw] OR "qaly"[tw] OR "qald"[tw] OR "qale" [tw] OR "qtime" [tw] OR "quality adjusted" [tw] OR "disability adjusted life" [tw] OR "daly" [tw] OR "qwb" [tw] OR "multiattribute*"[tw] OR "multi attribute*"[tw] OR "well-being" [tw] OR "wellbeing" [tw] OR "well being" [tw] OR "utilit*"[tw] OR "disutilit*"[tw] OR "HSUV" [tw] OR "healthy-years equivalent*"[tw] OR "HYE" [tw] OR "HUI" [tw] OR "health utilit*"[tw] OR "utility index" [tw] OR "utilities index" [tw] OR "illness stat*" [tw] OR "health stat*"[tw] OR "euro qual" [tw] OR "euro qol5d" [tw] OR "eq-5d" [tw] OR "eq5-d" [tw] OR "eq5d" [tw] OR "euroqual" [tw] OR "euroqol" [tw] OR "euroqual5d" [tw] OR "eq-sdq" [tw] OR "eqsdq" [tw] OR "short for*"[tw] OR "shortfor*"[tw] OR "sf36" [tw] OR "sf 36" [tw] OR "sf-36"[tw] OR "sf6" [tw] OR "sf 6" [tw] OR "sf6d" [tw] OR "sf 6d" [tw] OR "sf12" [tw] OR "sf 12" [tw] OR "sf16" [tw] OR "sf 16" [tw] OR "sf20" [tw] OR "sf 20" [tw] OR "15D" [tw] OR "15-D" [tw] OR "15 dimension" [tw] OR "standard gamble*"[tw] OR "SG"[tw] OR "time trade off"[tw] OR "TTO" [tw] OR "time tradeoff" [tw] OR "timetradeoff" [tw] OR "time trade-off" [tw] OR "AQOL" [tw] OR "Assessment of Quality of life" [tw] OR "EORTC*" [tw] OR "European Organisation for Research and Treatment of Cancer Quality of Life" [tw] OR "European Organisation for Research and Treatment of Cancer" [tw] OR "FACT*" [tw] OR "FACIT*"[tw] OR "Functional Assessment of Cancer Therapy" [tw] OR "Functional Assessment of Chronic Illness Therapy" [tw] OR "HQLI" [tw] OR "Hospice Quality of Life Index" [tw] OR "LASA*"[tw] OR "Linear Analog Scale Assessment*" [tw] OR "MQOL*"[tw] OR "McGill Quality of Life" [tw] OR "MIDOS" [tw] OR "Minimal Documentation System" [tw] OR "MVQOLI" [tw] OR "Missoula–VITAS Quality of Life index" [tw] OR "PROMIS" [tw] OR "Patient-Reported Outcomes Measurement Information System" [tw] OR "PEPS" [tw] OR "QUAL-E" [tw] OR "Quality of life at the End of life" [tw] OR "QUAL*"[tw] OR "QLI" [tw] OR "Quality of Life Index" [tw] OR "QOLLTI*"[tw] OR "SOSG*"[tw] OR "Spine Oncology Study Group Outcomes Questionnaire" [tw] OR "World Health Organization Quality of Life"[tw] OR "WHOQOL" [tw] OR "WHO-QOL" [tw] OR "CARES" [tw] OR "Cancer Rehabilitation Evaluation System" [tw] OR "QLACS" [tw] OR "Quality of Life in Adult Cancer Survivors"[tw])	Based on the filter developed by Arber et al., 2017 supplemented by a list of names of HRQOL instruments that have been used in patients with cancer according to a systematic review by Van Roij et al., 2018.
#4	#1 AND #2 AND #3	

We performed our initial systematic search in October 2021. However, the filter was no longer operational when we updated our search in April 2022. Therefore, the search term "Neosplasms[MeSH]" was used instead.

Appendix II.2. Correlations of HRQOL domains

Author (HRQOL measure)	HRQOL domain	Raw correlation [95% CI]
Belcher et al., 2021 (SF-36 Emotional Well-Being)	Mental Health	0.39 [0.20, 0.58]
Chan et al., 2021 (FACT-G Emotional Well-Being)		0.42 [0.36, 0.48]
Coroneos et al., 2020 (BREAST-Q Psychosocial Well-Being)		0.54 [0.48, 0.60]
Coroneos et al., 2020 (SF-12 Mental Health)		0.52 [0.46, 0.58]
Durber et al., 2021 (FACT-G Emotional Well-Being)		0.43 [0.33, 0.53]
Liang et al., 2021 (FACT-G Emotional Well-Being)		0.37 [0.22, 0.52]
Pavela et al., 2021 (PROMIS-10 Mental Health)		0.45 [0.42, 0.48]
Shim et al., 2021 (EORTC QLQ-C30 Emotional Functioning)		0.37 [0.34, 0.40]
Thom et al., 2021 (EORTC QLQ-C30 Emotional Functioning)		0.45 [0.30, 0.60]
Urek and Ugurluoglu 2021 (FACT-G Emotional Well-Being)		0.34 [0.25, 0.44]
Ver Hoeve et al., 2021 (PROMIS-29 Anxiety)		0.34 [0.17, 0.51]
Ver Hoeve et al., 2021 (PROMIS-29 Depression)		0.21 [0.02, 0.40]
Belcher et al., 2021 (SF-36 Role Limitations-Emotional)	Daily Functioning	0.27 [0.07, 0.48]
Belcher et al., 2021 (SF-36 Role Limitations-Physical)		0.28 [0.08, 0.49]
Chan et al., 2021 (FACT-G Functional Well-Being)		0.39 [0.32, 0.46]
Durber et al., 2021 (FACT-G Functional Well-Being)		0.35 [0.24, 0.46]
Liang et al., 2021 (FACT-G Functional Well-Being)		0.42 [0.27, 0.57]
Shim et al., 2021 (EORTC QLQ-C30 Role Functioning)		0.32 [0.29, 0.35]
Thom et al., 2021 (EORTC QLQ-C30 Role Functioning)		0.52 [0.38, 0.66]
Urek and Ugurluoglu, 2021 (FACT-G Functional Well-Being)		0.23 [0.12, 0.33]
Belcher et al., 2021 (SF-36 Social Functioning)	Social Health	0.18 [-0.03, 0.40]
Chan et al., 2021 (FACT-G Social/Family Well-Being)		0.23 [0.16, 0.30]
Durber et al., 2021 (FACT-G Social/Family Well-Being)		0.18 [0.06, 0.30]
Liang et al., 2021 (FACT-G Social/Family Well-Being)		0.30 [0.14, 0.46]
Shim et al., 2021 (EORTC QLQ-C30 Social Functioning)		0.44 [0.42, 0.46]
Thom et al., 2021 (EORTC QLQ-C30 Social Functioning)		0.55 [0.42. 0.68]
Urek and Ugurluoglu, 2021 (FACT-G Social/Family Well-Being)		0.16 [0.05, 0.27]
Ver Hoeve et al., 2021 (PROMIS-29 Social Functioning)		0.31 [0.13, 0.49]
Chan et al., 2021 (FACT-G Physical Well-Being)	Physical Health	0.34 [0.27, 0.41]
Coroneos et al., 2020 (SF-12 Physical Health)		0.41 [0.34, 0.48]
Durber et al., 2021 (FACT-G Physical Well-Being)		0.40 [0.30, 0.50]
Liang et al., 2021 (FACT-G Physical Well-Being)		0.66 [0.56, 0.76]
Pavela et al., 2021 (PROMIS-10 Physical Health)		0.46 [0.43, 0.49]
Urek and Ugurluoglu, 2021 (FACT-G Physical Well-Being)		0.41 [0.31, 0.50]
Belcher et al., 2021 (SF-36 Physical Functioning)	Physical Functioning	0.06 [-0.16, 0.28]
Shim et al., 2021 (EORTC QLQ-C30 Physical Functioning)		0.30 [0.27, 0.33]
Thom et al., 2021 (EORTC QLQ-C30 Physical Functioning)		0.33 [0.16, 0.50]
Ver Hoeve et al., 2021 (PROMIS-29 Physical Functioning)		0.31 [0.13, 0.49]
Belcher et al., 2021 (SF-36 Energy/Fatigue)	Fatigue	0.01 [-0.21, 0.24]
Shim et al., 2021 (EORTC QLQ-C30 Fatigue)		0.30 [0.27, 0.33]
Ver Hoeve et al., 2021 (PROMIS-29 Fatigue)		0.41 [0.25, 0.57]
Belcher et al., 2021 (SF-36 General Health)	Global Health	0.03 [-0.20, 0.25]
Shim et al., 2021 (EORTC QLQ-C30 Global QOL)		0.36 [0.33, 0.39]
Thom et al., 2021 (EORTC QLQ-C30 Global QOL)		0.44 [0.29, 0.59]
Belcher et al., 2021 (SF-36 Pain)	Pain	0.32 [0.12, 0.52]
Shim et al., 2021 (EORTC QLQ-C30 Pain)		0.26 [0.23, 0.29]
Ver Hoeve et al., 2021 (PROMIS-29 Pain)		0.27 [0.09, 0.45]
Shim et al., 2021 (EORTC QLQ-C30 Cognitive Functioning)	Cognitive Functioning	0.30 [0.27, 0.33]
Thom et al., 2021 (EORTC QLQ-C30 Cognitive Functioning)		0.22 [0.04, 0.40]
Shim et al., 2021 (EORTC QLQ-C30 Sleeping Disorder)	Sleep	0.21 [0.18, 0.24]
Ver Hoeve et al., 2021 (PROMIS-29 Sleep)		0.25 [0.07, 0.43]

Appendix IV.1. Item response distribution for T1 and T2 follow-up groups

Code	FACIT-COST item[§]	T1 follow-up (n=148)					T2 follow-up (n=150)				
		Not at all	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**	**Not at all**	**A little bit**	**Somewhat**	**Quite a bit**	**Very much**
FT1	Have enough money to cover treatment	55 (37.2%)	40 (27.0%)	40 (27.0%)	12 (8.1%)	1 (0.7%)	62 (41.3%)	44 (29.3%)	32 (21.3%)	12 (8.0%)	0 (0.0%)
FT2	Out-of-pocket expenses are more than thought	67 (45.3%)	21 (14.2%)	25 (16.9%)	24 (16.2%)	11 (7.4%)	54 (36.0%)	33 (22.0%)	33 (22.0%)	22 (14.7%)	8 (5.3%)
FT3	Worry about future financial problems	42 (28.4%)	31 (20.9%)	30 (20.3%)	29 (19.6%)	16 (10.8%)	40 (26.7%)	33 (22.0%)	40 (26.7%)	26 (17.3%)	11 (7.3%)
FT4	No choice about money spent	64 (43.2%)	21 (14.2%)	32 (21.6%)	20 (13.5%)	11 (7.4%)	37 (24.7%)	34 (22.7%)	45 (30.0%)	25 (16.7%)	9 (6.0%)
FT5	Frustrated about inability to contribute/work as usual	84 (56.8%)	30 (20.3%)	20 (13.5%)	6 (4.1%)	8 (5.4%)	79 (52.7%)	36 (24.0%)	24 (16.0%)	7 (4.7%)	4 (2.7%)
FT6	Satisfied with current finances	33 (22.3%)	32 (21.6%)	60 (40.5%)	22 (14.9%)	1 (0.7%)	24 (16.0%)	35 (23.3%)	69 (46.0%)	18 (12.0%)	4 (2.7%)
FT7	Able to meet monthly expenses	18 (12.2%)	35 (23.6%)	69 (46.6%)	22 (14.9%)	4 (2.7%)	13 (8.7%)	35 (23.3%)	73 (48.7%)	25 (16.7%)	4 (2.7%)
FT8	Feel financially stressed	36 (24.3%)	31 (20.9%)	42 (28.4%)	24 (16.2%)	15 (10.1%)	33 (22.0%)	36 (24.0%)	43 (28.7%)	26 (17.3%)	12 (8.0%)
FT9	Concerned about keeping income	65 (43.9%)	23 (15.5%)	31 (20.9%)	15 (10.1%)	14 (9.5%)	72 (48.0%)	26 (17.3%)	31 (20.7%)	13 (8.7%)	8 (5.3%)
FT10	Reduced financial satisfaction due to treatment/disease	51 (34.5%)	28 (18.9%)	33 (22.3%)	22 (14.9%)	14 (9.5%)	39 (26.0%)	25 (16.7%)	48 (32.0%)	29 (19.3%)	9 (6.0%)
FT11	In control of finances	26 (17.6%)	33 (22.3%)	65 (43.9%)	19 (12.8%)	5 (3.4%)	19 (12.7%)	45 (30.0%)	62 (41.3%)	19 (12.7%)	5 (3.3%)
FT12	Financial hardship to my family and me	44 (29.7%)	33 (22.3%)	26 (17.6%)	26 (17.6%)	19 (12.8%)	46 (30.7%)	18 (12.0%)	35 (23.3%)	37 (24.7%)	14 (9.3%)

FACIT-COST= COST: A FACIT Measure of Financial Toxicity

[§]Labeled by the authors based on the FACIT-COST items

Note. T1 follow-up= completed during the subsequent treatment cycle, T2 follow-up= completed during the post-treatment consultation.

Appendix IV.2. Internal consistency reliability results

Factor	FACIT-COST item[§]		Cronbach's alpha (95% Cl)	McDonald's omega (95% CI)	Cronbach's alpha if item dropped[*]	McDonald's omega if item dropped[*]
Factor 1	FT2	Out-of-pocket expenses are more than thought	0.882 (0.861-0.901)	0.888 (0.868-0.907)	0.893	0.896
	FT3	Worry about future financial problems			0.853	0.859
	FT4	No choice about money spent			0.852	0.857
	FT5	Frustrated about inability to contribute/work as usual			0.871	0.877
	FT8	Feel financially stressed			0.867	0.873
	FT9	Concerned about keeping income			0.859	0.868
	FT10	Reduced financial satisfaction due to treatment/disease			0.859	0.867
Factor 2	FT1	Have enough money to cover treatment	0.774 (0.729-0.813)	0.786 (0.747-0.825)	0.795	0.800
	FT6	Satisfied with current finances			0.670	0.694
	FT7	Able to meet monthly expenses			0.659	0.679
	FT11	In control of finances			0.740	0.761

CI=confidence interval, FACIT-COST= COST: A FACIT Measure of Financial Toxicity
[§]Labeled by the authors based on the FACIT-COST items
[*]Dropped from its corresponding factor

Appendix IV.3. Test-retest reliability and responsiveness for T1 and T2 follow-up groups

Code	FACIT-COST item[§]	Gwet's AC2 coefficient	
		T1 only (n=79)	T2 only (n=108)
FT1	Have enough money to cover treatment	0.60	0.81
FT2	Out-of-pocket expenses are more than thought	0.57	0.80
FT3	Worry about future financial problems	0.60	0.79
FT4	No choice about money spent	0.59	0.80
FT5	Frustrated about inability to contribute/work as usual	0.67	0.83
FT6	Satisfied with current finances	0.51	0.81
FT7	Able to meet monthly expenses	0.53	0.72
FT8	Feel financially stressed	0.57	0.77
FT9	Concerned about keeping income	0.70	0.84
FT10	Reduced financial satisfaction due to treatment/disease	0.62	0.73
FT11	In control of finances	0.52	0.75

Patient subgroups	n	%	Mean (SD) FACIT-COST total score			ICC (95% CI)	SRM (95% CI)	SES (95% CI)
			Baseline	Follow-up	Change			
T1 follow-up group	*148*	*100%*	*23.97 (8.40)*	*24.55 (9.03)*	*0.58 (5.74)*			
Improved in FT12	24	*16%*	19.33 (6.43)	25.46 (5.82)	6.13 (6.19)	-	0.99 (0.60, 1.42)	0.95 (0.53, 1.37)
Worsened in FT12	45	*30%*	23.42 (6.81)	21.13 (7.60)	-2.29 (5.44)	-	-0.42 (-0.79, -0.11)	-0.34 (-0.58, -0.09)
Unchanged in FT12	79	*53%*	25.70 (9.20)	26.23 (10.07)	0.53 (4.47)	0.89 (0.84, 0.93)	-	-
T2 follow-up group	*150*	*100%*	*24.59 (8.93)*	*24.44 (8.33)*	*-0.15 (4.03)*			
Improved in FT12	21	14%	19.62 (7.45)	23.62 (6.73)	4.00 (4.69)	-	0.85 (0.59, 1.16)	0.54 (0.30, 0.87)
Worsened in FT12	21	14%	25.76 (5.75)	22.67 (3.81)	-3.10 (4.47)	-	-0.69 (-0.98, -0.41)	-0.54 (-0.97, -0.24)
Unchanged in FT12	108	72%	25.33 (9.42)	24.94 (9.20)	-0.39 (3.10)	0.94 (0.92, 0.96)	-	-

CI= confidence interval, FACIT-COST= COST: A FACIT Measure of Financial Toxicity, FT12=twelfth item of the FACIT-COST ('financial hardship to my family and me'), ICC= intraclass correlation coefficient, SD= standard deviation, SEM= standard error of measurement, SES= standardized effect size, SRM= standardized response mean

[§]Labeled by the authors based on the FACIT-COST items

Notes.

1. T1 follow-up= completed during the subsequent treatment cycle, T2 follow-up= completed during the post-treatment consultation.
2. Gwet's AC2 was computed for patients with unchanged FT12 response at the follow-up compared to the baseline.
3. Test-retest reliability (Gwet's AC2) for item FT12 was not computed because it was used as an anchor.
4. Improved in FT12= baseline item score greater than follow-up, worsened= follow-up item score greater than baseline, unchanged= baseline item score equaled to follow-up.

Appendix V.1. Response distribution of EQ-5D-5L, FACT-G/FACT-8D, and WEMWBS/SWEMWBS at baseline (n=300)

EQ-5D-5L dimension	**Responses, n (%)**				
	No problem	***Slight problems***	***Moderate problems***	***Severe problems***	***Unable/extreme problems***
Mobility	236 (78.7%)	52 (17.3%)	11 (3.7%)	1 (0.3%)	-
Self-care	270 (90.0%)	18 (6.0%)	6 (2.0%)	2 (0.7%)	4 (1.3%)
Usual activities	240 (80.0%)	40 (13.3%)	12 (4.0%)	2 (0.7%)	6 (2.0%)
Pain/discomfort	136 (45.3%)	125 (41.7%)	24 (8.0%)	12 (4.0%)	3 (1.0%)
Anxiety/depression	209 (69.7%)	70 (23.3%)	17 (5.7%)	4 (1.3%)	-
FACT-G/FACT-8D items	**Responses, n (%)**				
	Not at all	***A little bit***	***Somewhat***	***Quite a bit***	***Very much***
Fatigue (d)	83 (27.7%)	85 (28.3%)	97 (32.3%)	27 (9.0%)	8 (2.7%)
Nausea (d)	207 (69.0%)	37 (12.3%)	37 (12.3%)	13 (4.3%)	6 (2.0%)
Trouble meeting family needs	148 (49.3%)	49 (16.3%)	49 (16.3%)	35 (11.7%)	19 (6.3%)
Pain (d)	115 (38.3%)	88 (29.3%)	67 (22.3%)	18 (6.0%)	12 (4.0%)
Bothered by side effects	158 (52.7%)	55 (18.3%)	48 (16.0%)	27 (9.0%)	12 (4.0%)
Feel ill	126 (42.0%)	78 (26.0%)	65 (21.7%)	20 (6.7%)	11 (3.7%)
Forced to be in bed	220 (73.3%)	39 (13.0%)	18 (6.0%)	18 (6.0%)	5 (1.7%)
Close to friends	9 (3.0%)	27 (9.0%)	65 (21.7%)	111 (37.0%)	88 (29.3%)
Family support (d)*	2 (0.7%)	3 (1.0%)	10 (3.3%)	71 (23.7%)	214 (71.3%)
Friend support (d)*	2 (0.7%)	16 (5.3%)	36 (12.0%)	96 (32.0%)	150 (50.0%)
Family acceptance	5 (1.7%)	5 (1.7%)	15 (5.0%)	62 (20.7%)	213 (71.0%)
Family communication	2 (0.7%)	5 (1.7%)	16 (5.3%)	92 (30.7%)	185 (61.7%)
Feel close to partner	12 (4.0%)	6 (2.0%)	14 (4.7%)	55 (18.3%)	213 (71.0%)
Satisfied with sex life[†]	27 (9.0%)	18 (6.0%)	65 (21.7%)	69 (23.0%)	32 (10.7%)
Sad (d)	146 (48.7%)	63 (21.0%)	60 (20.0%)	18 (6.0%)	13 (4.3%)
Satisfied with coping	12 (4.0%)	25 (8.3%)	83 (27.7%)	115 (38.3%)	65 (21.7%)
Losing hope	209 (69.7%)	39 (13.0%)	32 (10.67%)	9 (3.0%)	11 (3.7%)
Nervous	158 (52.7%)	76 (25.3%)	41 (13.7%)	14 (4.7%)	11 (3.7%)
Worry about dying	172 (57.3%)	54 (18.0%)	38 (12.7%)	20 (6.7%)	16 (5.3%)
Worry about worsening condition (d)	147 (49.0%)	73 (24.3%)	42 (14.0%)	21 (7.0%)	17 (5.7%)
Work (d)	20 (6.7%)	19 *6.3%)	81 (27.0%)	107 (35.7%)	73 (24.3%)
Work is fulfilling	14 (4.7%)	22 (7.3%)	92 (30.7%)	103 (34.3%)	69 (23.0%)
Enjoy life	2 (0.7%)	10 (3.3%)	47 (15.7%)	112 (37.3%)	129 (43.0%)
Accepted illness	5 (1.7%)	11 (3.7%)	38 (12.7%)	110 (36.7%)	136 (45.3%)
Sleep (d)	24 (8.0%)	31 (10.3%)	92 (30.7%)	78 (26.0%)	75 (25.0%)
Enjoying usual things	9 (3.0%)	20 (6.7%)	69 (23.0%)	124 (41.3%)	78 (26.0%)
Content with life quality	15 (5.0%)	9 (3.0%)	62 (20.7%)	113 (37.7%)	101 (33.7%)

WEMWBS/SWEWMBS items	Responses, n (%)				
	None of the time	*Rarely*	*Some of the time*	*Often*	*All of the time*
Optimistic about future (s)	7 (2.3%)	11 (3.7%)	65 (21.7%)	59 (19.7%)	158 (52.7%)
Feeling useful (s)	4 (1.3%)	7 (2.3%)	61 (20.3%)	70 (23.3%)	158 (52.7%)
Feeling relaxed (s)	6 (2.0%)	10 (3.3%)	87 (29.0%)	57 (19.0%)	140 (46.7%)
Feeling interested in otheres	6 (2.0%)	15 (5.0%)	74 (24.7%)	77 (25.7%)	128 (42.7%)
Energy to spare	13 (4.3%)	31 (10.3%)	119 (39.7%)	69 (23.0%)	68 (22.7%)
Deal with problems well (s)	2 (0.7%)	20 (6.7%)	113 (37.7%)	66 (22.0%)	99 (33.0%)
Thinking clearly (s)	1 (0.3%)	17 (5.7%)	83 (27.7%)	75 (25.0%)	124 (41.3%)
Feeling good	4 (1.3%)	7 (2.3%)	77 (25.7%)	76 (25.3%)	136 (45.3%)
Feeling close to people (s)	4 (1.3%)	15 (5.0%)	57 (19.0%)	81 (27.0%)	143 (47.7%)
Feeling confident	3 (1.0%)	13 (4.3%)	84 (28.0%)	49 (16.3%)	151 (50.3%)
Make up own mind (s)	1 (0.3%)	7 (2.3%)	76 (25.3%)	67 (22.3%)	149 (49.7%)
Feeling loved	2 (0.7%)	8 (2.7%)	26 (8.7%)	55 (18.3%)	209 (69.7%)
Interested in new things	8 (2.7%)	25 (8.3%)	116 (38.7%)	57 (19.0%)	94 (31.3%)
Feeling cheerful	7 (2.3%)	11 (3.7%)	83 (27.7%)	66 (22.0%)	133 (44.3%)

Abbreviations. FACT-G= Functional Assessment of Cancer Therapy - General, FACT-8D= Functional Assessment of Cancer Therapy Eight Dimension, SWEMWBS= Short WEMWBS, WEMWBS= Warwick-Edinburgh Mental Wellbeing Scale, (d)= FACT-8D items, (s)= SWEMWBS items

*The higher (more favorable) score of either family or friend support was used for FACT-8D

†This item was responded by 211 patients in the baseline survey

Appendix V.2. Comparison of EQ-HWB-S, EQ-5D-5L, FACT-8D, and SWEMWBS health state profiles and index values

Characteristics	EQ-HWB-S	EQ-5D-5L	FACT-8D	SWEMWBS
Health state profiles				
Floor	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Ceiling	32 (10.7%)	105 (35.0%)	15 (5.0%)*	46 (15.3%)**
Index values				
Theoretical range	-0.384 to 1	-0.865 to 1	-0.549 to 1	-0.090 to 1.008
Observed range	-0.245 to 1	-0.310 to 1	-0.091 to 1	0.215 to 1.008
Mean (SD) index value	0.84 (0.17)	0.85 (0.21)	0.72 (0.23)	0.86 (0.15)
Median (IQR) index value	0.89 (0.79-0.95)	0.91 (0.80-1)	0.77 (0.60-0.89)	0.91 (0.77-0.98)
Proportion of negative index values	0.3%	1.0%	2.0%	0.0%

Abbreviations. EQ-HWB-S= EQ Health and Wellbeing short form (9 items), FACT-8D= Functional Assessment of Cancer Therapy Eight Dimension, IQR= interquartile range SD= standard deviation, SWEMWBS= Short Warwick-Edinburgh Mental Wellbeing Scale

*Based on the FACT-8D 00000000 profile. There were other observed profiles that generated a 1.0 index value= 00020000. 01010000, 00020010, 0100000, 00020010, 00020000. Ceiling based on an index value of 1.0= 7.67% (n=23)

**Based on the SWEMWBS 5555555 profile. There were other observed profiles that generated a >1.0 index value= 5555455 and 5545455. Ceiling based on index values of ≥1.0= 16.67% (n=50)

Notes.

1. Higher index values indicate better health-related quality of life or wellbeing
2. EQ-HWB-S index was computed using the UK pilot value set (Mukuria et al., 2023)
3. EQ-5D-5L index was computed using the Indonesian value set (Purba et al., 2017)
4. FACT-8D index was computed using the Australian value set (King et al., 2021)
5. SWEMWBS index was computed using the UK value set (Yiu et al., 2023)

Appendix V.3. Distribution of responses on FACT-8D items among patients reporting no problems in EQ-HWB-S (n=32)

FACT-8D item	***Responses* (n,%)**				
	Not at all	***A little bit***	***Somewhat***	***Quite a bit***	***Very much***
Pain	31 (97%)	1 (3%)	-	-	-
Fatigue	25 (78%)	3 (9%)	4 (13%)	-	-
Nausea	30 (94%)	2 (6%)	-	-	-
Sleep	17 (53%)	11 (34%)	2 (6%)	-	2 (6%)
Work	12 (38%)	16 (50%)	2 (6%)	-	2 (6%)
Support	25 (78%)	7 (22%)	-	-	-
Sad	32 (100%)	-	-	-	-
Worry	30 (94%)	1 (3%)	1 (3%)	-	-

Note. Scores for FACT-8D sleep, work, and support were reversed from their corresponding FACT-G items to align higher scores with more problems

Appendix V.4. Descriptive statistics of the EQ-HWB, EQ-5D-5L, EQ VAS, FACT-G and WEMWBS

Measure	Theoretical range	Observed range	Mean	Standard Deviation	Q1	Median	Q3
EQ-HWB LSS[a]	0 - 100	35 - 100	83.52	11.76	77	87	92
EQ-5D-5L LSS[a]	0 - 100	25 - 100	90.67	12.57	85	95	100
EQ VAS	0 - 100	10 - 100	81.18	15.63	75	80	90
FACT-G total score[a,b]	0 - 100	37.04 - 100	76.48	13.73	66.93	76.85	87.10
WEMWBS total score[a]	0 - 100	25 - 100	76.02	17.85	62.50	78.57	92.86

Abbreviations. EQ-HWB= EQ Health and Wellbeing long form (25 items), FACT-G= Functional Assessment of Cancer Therapy-General, LSS= level summary scores, WEMWBS= Warwick-Edinburgh Mental Wellbeing Scale

Note. Higher scores indicate better health-related quality of life or wellbeing
[a]Linearly transformed to a scale of 0-100
[b]Involved imputations due to 89 patients choosing not to respond to the 'satisfied with sex life' item

Appendix V.5. Item correlation between the EQ-HWB/EQ-HWB-S and other measures

5a. Correlations between EQ-HWB/EQ-HWB-S and EQ-5D-5L

EQ-HWB items	EQ-5D-5L				
	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression
Sight	0.02	0.02	0.08	0.03	0.07
Hearing	0.21	0.09	0.20	0.18	0.18
Getting around inside and outside (s)	0.60	0.27	0.32	0.26	0.19
Day-to-day activities (s)	0.45	0.47	0.60	0.37	0.24
Personal care	0.40	0.62	0.47	0.35	0.20
Sleep	0.34	0.19	0.25	0.28	0.30
Exhaustion (s)	0.25	0.14	0.20	0.32	0.29
Loneliness (s)	0.29	0.08	0.23	0.27	0.41
Unsupported	0.12	0.02	0.00	0.09	0.25
Memory	0.13	0.01	0.08	0.15	0.10
Cognition (s)	0.16	0.00	0.22	0.22	0.35
Anxiety (s)	0.18	0.11	0.20	0.31	0.51
Unsafe	0.33	0.10	0.30	0.27	0.31
Frustration	0.21	0.07	0.20	0.37	0.44
Sadness or depression (s)	0.11	0.05	0.11	0.30	0.40
Nothing to look forward	0.16	0.04	0.11	0.27	0.32
No control over daily life (s)	0.32	0.23	0.31	0.24	0.32
Coping	0.28	0.26	0.33	0.29	0.29
Accepted by others (r)	0.11	0.04	0.08	0.11	0.17
Feel good about self (r)	0.15	0.06	0.14	0.17	0.23
Do things one wanted to do (r)	0.20	0.20	0.23	0.18	0.15
Pain (frequency)	0.31	0.19	0.28	0.64	0.26
Pain (severity) (s)	0.31	0.22	0.30	0.60	0.28
Discomfort (frequency)	0.24	0.18	0.20	0.41	0.26
Discomfort (severity)	0.26	0.23	0.29	0.44	0.26

Abbreviations. EQ-HWB= EQ Health and Wellbeing long form (25 items), EQ-HWB-S= EQ-HWB short form (9 items), (s)= EQ-HWB-S items, (r)= reverse coded for the level summary scores
Note. Correlations are presented in absolute form

Color code	Coefficient range	Correlation strength	Color code	Coefficient range	Correlation strength
	≥ 0.50	Strong		0.10 - 0.29	Weak
	0.30 - 0.49	Moderate		0 - 0.10	None

5b. Correlations between EQ-HWB/EQ-HWB-S and FACT-G/FACT-8D

EQ-HWB items	FACT-G/FACT-8D items													
	Fatigue (d)	Nausea (d)	Trouble meeting family needs	Pain (d)	Bothered by side effects	Feel ill	Forced to be in bed	Close to friends	Family support (d)	Friend support (d)	Family acceptance	Family communication	Feel close to partner	Satisfied with sex life*
Sight	0.14	0.10	0.15	0.07	0.14	0.10	0.10	0.15	0.05	0.09	0.01	0.00	0.04	0.10
Hearing	0.14	0.11	0.13	0.16	0.16	0.16	0.20	0.16	0.03	0.02	0.08	0.04	0.00	0.03
Getting around inside and outside (s)	0.25	0.14	0.26	0.30	0.21	0.33	0.37	0.24	0.01	0.09	0.03	0.08	0.07	0.19
Day-to-day activities (s)	0.44	0.16	0.40	0.37	0.26	0.40	0.48	0.16	0.07	0.00	0.01	0.09	0.00	0.12
Personal care	0.27	0.13	0.27	0.37	0.19	0.39	0.39	0.11	0.01	0.02	0.08	0.16	0.11	0.16
Sleep	0.35	0.26	0.26	0.34	0.24	0.40	0.34	0.17	0.06	0.13	0.07	0.12	0.14	0.15
Exhaustion (s)	0.43	0.29	0.38	0.39	0.33	0.46	0.34	0.12	0.02	0.06	0.03	0.09	0.06	0.17
Loneliness (s)	0.20	0.22	0.27	0.32	0.27	0.31	0.24	0.13	0.20	0.11	0.10	0.23	0.22	0.13
Unsupported	0.06	0.04	0.16	0.10	0.21	0.14	0.09	0.20	0.30	0.25	0.11	0.25	0.22	0.12
Memory	0.13	0.10	0.10	0.21	0.30	0.16	0.17	0.12	0.11	0.09	0.02	0.13	0.15	0.11
Cognition (s)	0.25	0.15	0.22	0.32	0.35	0.27	0.31	0.27	0.10	0.22	0.11	0.19	0.16	0.15
Anxiety (s)	0.32	0.29	0.27	0.38	0.32	0.39	0.31	0.23	0.10	0.17	0.12	0.16	0.14	0.08
Unsafe	0.30	0.23	0.25	0.31	0.21	0.36	0.31	0.24	0.11	0.21	0.11	0.15	0.11	0.07
Frustration	0.23	0.18	0.28	0.30	0.23	0.35	0.30	0.27	0.17	0.22	0.08	0.19	0.21	0.08
Sadness or depression (s)	0.20	0.16	0.23	0.34	0.22	0.32	0.27	0.19	0.14	0.10	0.07	0.15	0.16	0.08
Nothing to look forward	0.16	0.15	0.25	0.37	0.21	0.36	0.17	0.30	0.19	0.22	0.14	0.19	0.20	0.14
No control over daily life (s)	0.28	0.19	0.34	0.38	0.27	0.41	0.34	0.27	0.20	0.28	0.17	0.29	0.12	0.19
Coping	0.28	0.27	0.47	0.40	0.35	0.41	0.33	0.21	0.08	0.14	0.10	0.24	0.14	0.23
Accepted by others (r)	0.10	0.03	0.15	0.16	0.10	0.16	0.19	0.22	0.29	0.15	0.24	0.28	0.16	0.12
Feel good about self (r)	0.11	0.02	0.15	0.19	0.11	0.18	0.16	0.25	0.25	0.18	0.30	0.30	0.24	0.19
Do things one wanted to do (r)	0.26	0.07	0.26	0.19	0.14	0.24	0.22	0.19	0.16	0.16	0.20	0.18	0.19	0.28
Pain (frequency)	0.30	0.20	0.32	0.56	0.27	0.51	0.30	0.15	0.02	0.05	0.05	0.13	0.11	0.09
Pain (severity) (s)	0.30	0.20	0.30	0.51	0.25	0.53	0.32	0.15	0.09	0.07	0.04	0.12	0.14	0.11
Discomfort (frequency)	0.35	0.24	0.26	0.42	0.33	0.43	0.28	0.11	0.09	0.06	0.07	0.13	0.10	0.16
Discomfort (severity)	0.42	0.20	0.28	0.42	0.32	0.45	0.30	0.10	0.08	0.05	0.01	0.09	0.07	0.12

Abbreviations. EQ Health and Wellbeing long form (25 items), EQ-HWB-S= EQ-HWB short form (9 items), FACT= Functional Assessment of Cancer Therapy, FACT-G= FACT-General, FACT-8D= FACT Eight Dimension, (d)= FACT-8D items, (s)= EQ-HWB-S items, (r)= reverse coded for the level summary scores

Note. Correlations are presented in absolute form

*Non-imputed responses (n=211 because 89 patients opted not to respond)

Color code	Coefficient range	Correlation strength	Color code	Coefficient range	Correlation strength
	≥ 0.50	Strong		0.10 - 0.29	Weak
	0.30 - 0.49	Moderate		0 - 0.10	None

5b. Correlations between EQ-HWB/EQ-HWB-S and FACT-G/FACT-8D (cont.)

EQ-HWB items	FACT-G/FACT-8D items												
	Sad (d)	Satisfied with coping	Losing hope	Nervous	Worry about dying	Worry about worsening condition (d)	Work (d)	Work is fulfilling	Enjoy life	Accepted illness	Sleep (d)	Enjoying usual things	Content with life quality
Sight	0.13	0.02	0.10	0.08	0.11	0.12	0.09	0.11	0.07	0.08	0.03	0.05	0.10
Hearing	0.13	0.03	0.13	0.12	0.15	0.15	0.15	0.13	0.10	0.07	0.15	0.15	0.14
Getting around inside and outside (s)	0.27	0.04	0.14	0.29	0.17	0.18	0.22	0.22	0.15	0.09	0.33	0.28	0.21
Day-to-day activities (s)	0.41	0.05	0.21	0.38	0.12	0.19	0.40	0.40	0.17	0.02	0.29	0.27	0.21
Personal care	0.24	0.14	0.16	0.28	0.13	0.12	0.32	0.33	0.19	0.21	0.29	0.29	0.29
Sleep	0.31	0.12	0.22	0.36	0.21	0.16	0.28	0.33	0.20	0.15	0.66	0.29	0.17
Exhaustion (s)	0.45	0.03	0.22	0.35	0.22	0.25	0.21	0.21	0.14	0.02	0.28	0.19	0.22
Loneliness (s)	0.43	0.05	0.29	0.36	0.26	0.28	0.15	0.16	0.15	0.08	0.17	0.15	0.22
Unsupported	0.25	0.07	0.07	0.18	0.03	0.13	0.02	0.03	0.10	0.04	0.05	0.10	0.14
Memory	0.15	0.05	0.09	0.11	0.10	0.19	0.09	0.13	0.09	0.07	0.09	0.14	0.08
Cognition (s)	0.35	0.16	0.24	0.34	0.23	0.27	0.29	0.30	0.25	0.10	0.21	0.24	0.22
Anxiety (s)	0.49	0.10	0.32	0.57	0.34	0.42	0.21	0.21	0.23	0.08	0.24	0.22	0.18
Unsafe	0.36	0.00	0.23	0.42	0.30	0.31	0.26	0.24	0.21	0.03	0.32	0.22	0.15
Frustration	0.37	0.11	0.33	0.41	0.34	0.33	0.16	0.19	0.28	0.12	0.21	0.23	0.27
Sadness or depression (s)	0.45	0.11	0.23	0.40	0.21	0.32	0.12	0.13	0.16	0.08	0.13	0.10	0.27
Nothing to look forward	0.34	0.10	0.22	0.32	0.16	0.28	0.14	0.14	0.22	0.07	0.11	0.13	0.26
No control over daily life (s)	0.40	0.11	0.31	0.36	0.24	0.28	0.28	0.25	0.18	0.14	0.21	0.29	0.26
Coping	0.46	0.09	0.31	0.44	0.18	0.29	0.29	0.31	0.20	0.12	0.16	0.21	0.32
Accepted by others (r)	0.16	0.32	0.20	0.17	0.12	0.20	0.25	0.22	0.20	0.19	0.14	0.24	0.30
Feel good about self (r)	0.22	0.30	0.17	0.21	0.14	0.23	0.27	0.23	0.28	0.27	0.22	0.30	0.40
Do things one wanted to do (r)	0.33	0.18	0.16	0.19	0.07	0.12	0.37	0.38	0.32	0.21	0.29	0.34	0.30
Pain (frequency)	0.31	0.08	0.25	0.35	0.17	0.30	0.20	0.23	0.15	0.15	0.26	0.14	0.22
Pain (severity) (s)	0.33	0.02	0.21	0.35	0.15	0.30	0.18	0.21	0.13	0.12	0.25	0.14	0.22
Discomfort (frequency)	0.36	0.07	0.19	0.31	0.15	0.21	0.18	0.23	0.15	0.07	0.22	0.16	0.22
Discomfort (severity)	0.39	0.01	0.20	0.32	0.16	0.21	0.19	0.26	0.15	0.06	0.24	0.20	0.26

Abbreviations. EQ Health and Wellbeing long form (25 items), EQ-HWB-S= EQ-HWB short form (9 items), FACT= Functional Assessment of Cancer Therapy, FACT-G= FACT-General, FACT-8D= FACT Eight Dimension, (d)= FACT-8D items, (s)= EQ-HWB-S items, (r)= reverse coded for the level summary scores

Note. Correlations are presented in absolute form

Color code	Coefficient range	Correlation strength	Color code	Coefficient range	Correlation strength
	≥ 0.50	Strong		0.10 - 0.29	Weak
	0.30 - 0.49	Moderate		0 - 0.10	None

5c. Correlations between EQ-HWB/EQ-HWB-S and (S)WEMWBS

EQ-HWB items	WEMWBS/SWEMWBS items													
	Optimistic about future (s)	Feeling useful (s)	Feeling relaxed (s)	Feeling interested in others	Energy to spare	Deal with problems well (s)	Thinking clearly (s)	Feeling good	Feeling close to people (s)	Feeling confident	Make up own mind (s)	Feeling loved	Interested in new things	Feeling cheerful
Sight	0.09	0.09	0.08	0.02	0.12	0.11	0.08	0.08	0.05	0.06	0.06	0.04	0.01	0.10
Hearing	0.12	0.21	0.22	0.12	0.15	0.23	0.20	0.16	0.11	0.19	0.10	0.07	0.10	0.18
Getting around inside and outside (s)	0.10	0.24	0.32	0.21	0.28	0.31	0.25	0.29	0.15	0.26	0.19	0.12	0.18	0.26
Day-to-day activities (s)	0.10	0.14	0.27	0.15	0.31	0.19	0.21	0.21	0.09	0.20	0.10	0.08	0.08	0.25
Personal care	0.05	0.17	0.22	0.13	0.21	0.12	0.15	0.13	0.10	0.20	0.11	0.13	0.07	0.20
Sleep	0.04	0.15	0.30	0.18	0.27	0.26	0.19	0.22	0.09	0.19	0.20	0.16	0.14	0.22
Exhaustion (s)	0.12	0.21	0.36	0.15	0.34	0.29	0.22	0.27	0.13	0.18	0.19	0.18	0.18	0.31
Loneliness (s)	0.03	0.11	0.24	0.12	0.14	0.16	0.15	0.20	0.09	0.16	0.11	0.16	0.13	0.30
Unsupported	0.11	0.13	0.19	0.15	0.15	0.11	0.09	0.17	0.19	0.14	0.18	0.25	0.14	0.19
Memory	0.09	0.16	0.17	0.07	0.11	0.21	0.21	0.20	0.12	0.17	0.14	0.13	0.14	0.17
Cognition (s)	0.18	0.24	0.32	0.23	0.18	0.28	0.35	0.30	0.21	0.23	0.25	0.21	0.19	0.32
Anxiety (s)	0.20	0.22	0.41	0.25	0.27	0.26	0.29	0.34	0.23	0.27	0.32	0.27	0.24	0.40
Unsafe	0.19	0.22	0.31	0.16	0.19	0.22	0.21	0.29	0.19	0.25	0.24	0.19	0.16	0.28
Frustration	0.26	0.17	0.40	0.20	0.20	0.28	0.27	0.26	0.23	0.24	0.24	0.25	0.16	0.34
Sadness or depression (s)	0.15	0.12	0.35	0.15	0.24	0.17	0.17	0.22	0.16	0.15	0.15	0.17	0.11	0.24
Nothing to look forward	0.24	0.13	0.30	0.25	0.20	0.14	0.20	0.23	0.26	0.18	0.17	0.26	0.13	0.29
No control over daily life (s)	0.28	0.20	0.33	0.23	0.29	0.30	0.23	0.28	0.22	0.25	0.28	0.30	0.23	0.34
Coping	0.16	0.18	0.30	0.20	0.28	0.23	0.25	0.31	0.19	0.19	0.19	0.25	0.15	0.35
Accepted by others (r)	0.32	0.29	0.28	0.35	0.18	0.28	0.24	0.26	0.33	0.22	0.25	0.28	0.19	0.18
Feel good about self (r)	0.34	0.36	0.34	0.38	0.21	0.29	0.23	0.31	0.31	0.30	0.30	0.29	0.23	0.26
Do things one wanted to do (r)	0.27	0.34	0.38	0.32	0.28	0.32	0.32	0.33	0.36	0.25	0.34	0.25	0.20	0.25
Pain (frequency)	0.08	0.09	0.19	0.05	0.15	0.10	0.14	0.15	0.09	0.14	0.11	0.14	0.07	0.20
Pain (severity) (s)	0.03	0.04	0.24	0.04	0.19	0.06	0.14	0.16	0.07	0.16	0.11	0.10	0.05	0.24
Discomfort (frequency)	0.09	0.11	0.21	0.13	0.21	0.15	0.15	0.20	0.10	0.15	0.16	0.15	0.08	0.23
Discomfort (severity)	0.05	0.05	0.24	0.05	0.23	0.12	0.16	0.23	0.05	0.18	0.14	0.09	0.06	0.29

Abbreviations. EQ Health and Wellbeing long form (25 items), EQ-HWB-S= EQ-HWB short form (9 items), SWEMWBS= Short WEMWBS, WEMWBS= Warwick-Edinburgh Mental Wellbeing Scale, (s)= EQ-HWB Short or Short WEMWBS items, (r)= reverse coded for the level summary scores

Note. Correlations are presented in absolute form

Color code	Coefficient range	Correlation strength	Color code	Coefficient range	Correlation strength
	≥ 0.50	Strong		0.10 - 0.29	Weak
	0.30 - 0.49	Moderate		0 - 0.10	None

Appendix V.6. Known-group validity results for EQ-5D-5L, FACT-G/FACT-8D, and WEMWBS/SWEMWBS

Groups	n	EQ-5D-5L index		FACT-8D index		SWEMWBS index	
		Mean (SD)	Effect size (95% CI)	Mean (SD)	Effect size (95% CI)	Mean (SD)	Effect size (95% CI)
Caregiver use							
Yes	184	0.83 (0.24)	d=0.23 (-0.01, 0.46)	0.70 (0.23)	d=0.18 (-0.05, 0.42)	0.86 (0.16)	d=0.00 (-0.23, 0.24)
No	116	0.87 (0.13)		0.75 (0.21)		0.86 (0.14)	
Cancer stage at diagnosis							
1-2	212	0.86 (0.19)	d=0.22 (-0.03, 0.47)	0.72 (0.21)	d=-0.01 (-0.25, 0.25)	0.85 (0.15)	d=-0.09 (-0.33, 0.16)
3-4	86	0.81 (0.23)		0.72 (0.24)		0.86 (0.15)	
EQ VAS score							
80 and above	219	0.90 (0.14)*	d=1.08 (0.81, 1.35)	0.79 (0.16)*	d=1.24 (0.96, 1.51)	0.88 (0.13)*	d=0.75 (0.48, 1.01)
<80	81	0.70 (0.28)*		0.54 (0.27)*		0.78 (0.17)*	
Number of comorbidities							
0	78	0.87 (0.25)		0.77 (0.20)		0.87 (0.16)	
1	123	0.86 (0.16)*	η^2=0.018 (0.00, 0.05)	0.73 (0.22)*	η^2=0.028 (0.00, 0.07)	0.86 (0.14)	η^2=0.009 (0.00, 0.04)
2+	99	0.81 (0.22)*		0.67 (0.25)*		0.84 (0.15)	
Number of symptoms							
0	17	0.95 (0.06)*		0.87 (0.09)*		0.94 (0.09)	
1-3	71	0.93 (0.10)*		0.84 (0.14)*		0.90 (0.14)	
4-6	68	0.88 (0.13)*	η^2=0.164 (0.09, 0.23)	0.80 (0.16)*	η^2=0.330 (0.24, 0.40)	0.88 (0.13)*	η^2=0.094 (0.03, 0.15)
7-9	60	0.84 (0.17)*		0.72 (0.18)*		0.83 (0.14)*	
10+	84	0.72 (0.29)*		0.52 (0.25)*		0.80 (0.17)	
General health							
Very good/excellent	53	0.91 (0.11)*		0.79 (0.21)*		0.92 (0.12)*	
Good	166	0.88 (0.15)*	η^2=0.125 (0.06, 0.20)	0.77 (0.18)*	η^2=0.176 (0.10, 0.25)	0.86 (0.14)*	η^2=0.080 (0.03, 0.14)
Poor/fair	81	0.73 (0.29)*		0.56 (0.25)*		0.79 (0.17)*	

Abbreviations. CI= confidence interval, d= Cohen's D, η^2= eta-squared, FACT= Functional Assessment of Cancer Therapy, FACT-G= FACT-General, FACT-8D= FACT Eight Dimension, LSS= level summary score (linearly transformed to 0-100 scale), SWEMWBS= Short WEMWBS, WEMWBS= Warwick-Edinburgh Mental Wellbeing Scale

*p<0.05

Appendix V.6. Known-group validity results for EQ-5D-5L, FACT-G/FACT-8D, and WEMWBS/SWEMWBS (continued)

Groups	n	EQ-5D-5L LSS		FACT-G total score		WEMWBS total score	
		Mean (SD)	Effect size (95% CI)	Mean (SD)	Effect size (95% CI)	Mean (SD)	Effect size (95% CI)
Caregiver use							
Yes	184	89.53 (14.72)	d=0.23 (0.00, 0.47)	75.75 (13.65)	d=0.14 (-0.09, 0.37)	76.32 (18.93)	d=-0.04 (-0.28, 0.19)
No	116	92.46 (7.79)		77.65 (13.82)		75.54 (17.79)	
Cancer stage at diagnosis							
1-2	212	91.49 (12.00)	d=0.21 (-0.04, 0.46)	76.15 (13.35)	d=-0.11 (-0.36, 0.14)	75.45 (18.11)	d=-0.11 (-0.36, 0.14)
3-4	86	88.90 (13.71)		77.74 (14.45)		77.47 (17.42)	
EQ VAS score							
80 and above	219	94.04 (8.27)*	d=1.11 (0.84, 1.38)	80.43 (11.58)*	d=1.21 (0.93, 1.48)	79.87 (16.28)*	d=0.85 (0.59, 1.12)
<80	81	81.54 (16.99)*		65.81 (13.46)*		65.61 (17.85)*	
Number of comorbidities							
0	78	92.37 (14.81)	η^2=0.019 (0.00, 0.06)	79.70 (13.39)	η^2=0.028 (0.00, 0.07)	78.87 (17.96)	η^2=0.022 (0.00, 0.06)
1	123	91.50 (9.62)*		76.72 (12.90)		77.13 (17.63)*	
2+	99	88.28 (13.61)*		73.66 (14.52)		72.38 (17.62)*	
Number of symptoms							
0	17	97.35 (3.59)*	η^2=0.174 (0.10, 0.25)	87.35 (8.20)*	η^2=0.252 (0.17, 0.33)	88.66 (13.55)	η^2=0.134 (0.06, 0.20)
1-3	71	95.92 (6.56)*		82.71 (11.17)*		82.95 (16.25)	
4-6	68	93.46 (7.14)*		80.22 (12.42)*		78.86 (16.00)*	
7-9	60	90.17 (10.81)*		75.85 (12.02)*		71.90 (16.95)*	
10+	84	82.98 (17.51)*		66.44 (12.74)*		68.24 (18.02)	
General health							
Very good/excellent	53	94.34 (6.80)*	η^2=0.128 (0.06, 0.20)	82.18 (12.74)*	η^2=0.179 (0.11, 0.25)	85.78 (14.14)*	η^2=0.139 (0.07, 0.21)
Good	166	93.07 (9.30)*		79.24 (12.00)*		77.68 (17.14)*	
Poor/fair	81	83.33 (17.50)*		67.10 (13.25)*		66.23 (17.00)*	

Abbreviations. CI= confidence interval, d= Cohen's D, η^2= eta-squared, FACT= Functional Assessment of Cancer Therapy, FACT-G= FACT-General, FACT-8D= FACT Eight Dimension, LSS= level summary score (linearly transformed to 0-100 scale), SWEMWBS= Short WEMWBS, WEMWBS= Warwick-Edinburgh Mental Wellbeing Scale

*p<0.05

Appendix V.7. Item-level test-retest reliability of EQ-HWB/EQ-HWB-S, EQ-5D-5L, FACT-G/FACT-8D and WEMWBS/SWEMWBS items

Item		Gwet's AC2	Item		Gwet's AC2	Item		Gwet's AC2
EQ-HWB/EQ-HWB-S			**EQ-5D-5L**			**FACT-G/FACT-8D**		
1	Sight	0.57	1	Mobility	0.90	1	Fatigue (d)	0.54
2	Hearing	0.87	2	Self-care	0.97	2	Nausea (d)	0.73
3	Getting around inside and outside (s)	0.90	3	Usual activities	0.90	3	Trouble meeting family needs	0.70
4	Day-to-day activities (s)	0.72	4	Pain/discomfort	0.64	4	Pain (d)	0.51
5	Personal care	0.90	5	Anxiety/depression	0.83	5	Bothered by side effects	0.40
6	Sleep	0.32	**WEMWBS/SWEMWBS**			6	Feel ill	0.55
7	Exhaustion (s)	0.35	1	Optimistic about future (s')	0.57	7	Forced to be in bed	0.90
8	Loneliness (s)	0.73	2	Feeling useful (s')	0.61	8	Close to friends	0.59
9	Unsupported	0.97	3	Feeling relaxed (s')	0.54	9	Family support (d)*	0.69
10	Memory	0.65	4	Feeling interested in otheres	0.29	10	Friend support (d)*	0.60
11	Cognition (s)	0.62	5	Energy to spare	0.35	11	Family acceptance	0.72
12	Anxiety (s)	0.34	6	Deal with problems well (s')	0.40	12	Family communication	0.61
13	Unsafe	0.76	7	Thinking clearly (s')	0.41	13	Feel close to partner	0.65
14	Frustration	0.90	8	Feeling good	0.53	14	Satisfied with sex life†	0.59
15	Sadness or depression (s)	0.68	9	Feeling close to people (s')	0.38	15	Sad (d)	0.67
16	Nothing to look forward	0.90	10	Feeling confident	0.54	16	Satisfied with coping	0.50
17	No control over daily life (s)	0.90	11	Make up own mind (s')	0.61	17	Losing hope	0.71
18	Coping	0.72	12	Feeling loved	0.69	18	Nervous	0.55
19	Accepted by others (r)	0.72	13	Interested in new things	0.32	19	Worry about dying	0.63
20	Feel good about self (r)	0.69	14	Feeling cheerful	0.55	20	Worry about worsening condition (d)	0.52
21	Do things one wanted to do (r)	0.45				21	Work (d)	0.44
22	Pain (frequency)	0.50				22	Work is fulfilling	0.40
23	Pain (severity) (s)	0.63				23	Enjoy life	0.53
24	Discomfort (frequency)	0.43				24	Accepted illness	0.52
25	Discomfort (severity)	0.48				25	Sleep (d)	0.24
						26	Enjoying usual things	0.40
						27	Content with life quality	0.44

Abbreviations. Gwet's AC2= Gwet's agreement coefficient 2, (d)= FACT-8D items, (r)= reverse coded for the level sum scores, (s)= EQ-HWB-S items, (s')= SWEMWBS items, FACT-G= Functional Assessment of Cancer Therapy - General, FACT-8D= Functional Assessment of Cancer Therapy Eight Dimension, SWEMWBS= Short WEMWBS, WEMWBS= Warwick-Edinburgh Mental Wellbeing Scale

Note. The test-retest reliability analysis was performed on 32 patients with unchanged health status from Group 1, i.e., patients in active treatment cycle at baseline who were invited to complete the follow-up questionnaire during their next cycle

*The higher (more favorable) score of either family or friend support was used for FACT-8D

†This item was responded by 22 patients