DELIVERABLE 1.4

Standard and report for the collection and analytics for QoL data

WP1 – Guidelines, standards, and SOPs for RWD collection based on fully structured data

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Authors

Name: Samu Eränen (HUS), Sami Pakarinen (HUS)

Lead contributor	1. HUS
Other contributors	-

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Executive summary

The main objective of work package (WP) 1 is to develop guidelines and standard operating procedures for the collection of fully structured data, including clinical outcome measures, as part of routine clinical work in cancer hospitals. The outcome measurements also contain Heath related Quality of life (HR-QoL, later referred to QoL in this report) questionnaires that fully integrate to the electronic medical records system and are collected with patient portals/applications.

This deliverable report describes the documentation and collection of QoL data in completely electronic documentation environment. During the first 18 months of the ONCOVALUE project, Helsinki University Hospital (HUS) has been the only cancer center in WP1 with technical capabilities and established procedures to automatically collect QoL data and this report concentrates on the experiences in HUS. Rigshospitalet (RHP) and HUS have similar EMR in use and thus the same technical ability to exploit its patient portal in the future.

In Finland, the prevailing generic QoL questionnaire is 15-dimensional (15D) which has been developed domestically. The questionnaire is widely used by Finnish hospitals and HUS. The electronic medical record (EMR) of HUS includes a patient portal module, which is fully integrated into the medical records and enables efficient collection of QoL data from patients. Using this patient portal HUS has been capable of setting up different time points for automatic QoL collection. HUS's Datalake data repository enables versatile QoL data analytics.

Evaluation of the comparability of different QoL questionnaires requires still progress in other ongoing tasks of WP1 and it is not widely covered in this report. The complete version of standard and report for the collection and analytics for QoL data will be finalized once related tasks are completed.

1. List of abbreviations and definitions

Abbreviation	Definition
RWD	Real-world data
RWE	Real-world evidence
RCT	Randomized controlled trial
HUS	Helsinki University Hospital (Finland)
RHP	Rigshospitalet (Denmark)
NSCLC	Non-small cell lung cancer
AI	Artificial Intelligence
HTA	Health technology assessment
WP	Work package
QoL	Quality of life
HR-QoL	Heath related Quality of life
EMR	Electronic medical record
15D	15-dimensional
Apotti	EPIC based EMR in use in HUS
PROM	Patient-reported outcome measure
MyChart	Patient portal module in EPIC

2. Background

Real-world evidence (RWE) has become an important component in evaluating healthcare outcomes. Although randomized controlled trials (RCTs) are the primary method for assessing effects of new therapies, RWE can offer important benefits. The results of RCTs have external validity only in similar patient populations that have been studied, and the strict eligibility criteria of RCTs may significantly differ from real-world population and their outcomes. Real-world data (RWD) studies typically require less time and expense, allowing for larger sample size and longer-term follow-up. Furthermore, RWD studies can be more accessible in a regulatory and ethical manner. (Hall 2017, Slattery et al. 2020, Silverman 2009, Yang et al. 2010)

Due to the continual increase in the global cancer prevalence and rising prices of novel cancer therapies, combined with the increase of the overall aging population and the rise in people diagnosed with cancer, the global healthcare system for the treatment of cancer is at risk of becoming unaffordable. One of the present challenges in effectively utilizing RWD is the absence of a standardized data model for clinical cancer treatment information, which constrains data sharing across various registries (Kent et al. 2021). Additionally, regulatory and technical obstacles can create further complexities in integrating data from multiple sources. (Boyle et al. 2021)

For easing these burdens, Horizon Europe has funded the ONCOVALUE project. In this project coordinated by HUS, a consortium of leading European cancer hospitals in collaboration with private companies will build data collection and processing capabilities to create a high-quality clinical data source for assessing RWE. Besides structured data, unstructured data originating from medical notes and medical images will be transformed into structured data with the use of artificial intelligence (AI) technologies to enable analytics and RWE creation. For that, the primary goal of the project is to provide an end-to-end infrastructure for RWD reporting in health regulatory and health technology assessment (HTA) decision-making and to address the legal constraints in the cancer hospitals to ensure secure and legal access to RWD. Furthermore, ONCOVALUE will ensure the implementation of the developed guidelines and methodologies by providing trainings for the collection and management of high-quality RWD in European cancer centers and for the use of this data by HTA and regulatory bodies. As such, ONCOVALUE is positioned to contribute to increased cost-effectiveness and subsequent sustainability of cancer care.

3. Introduction

The main objective of WP 1 is to develop guidelines and standard operating procedures for the collection of fully structured data, including clinical outcome measures, as part of routine clinical work in cancer hospitals. The outcome measurements also contain QoL questionnaires that fully integrate to the electronic medical records system and are collected with patient portals/applications.

HUS and RHP have been collaborating on developing and testing a structured real-time data collection pathway for breast cancer and non-small cell lung cancer (NSCLC). HUS has led the design, construction, and testing of the breast cancer pathway while RHP has focused on NSCLC. HUS and RHP will later cross-validate their respective cases. As the ONCOVALUE project progresses, HUS and RHP will expand their structured data entry system to encompass additional cancer types. The selection of additional cancer types has been discussed in the ONCOVALUE Scientific and Clinical Coordination group meetings during 2023 and 2024. HUS and RHP will be testing and validating data collection for colon cancer. Also melanoma vill be validated if it is feasible during project timeline.

This deliverable report describes the documentation and collection of QoL data in completely electronic documentation environment. This means that the related questionnaires are sent, filled, and collected digitally and the results stored automatically in data repository. During the first 18 months of the ONCOVALUE project, HUS has been the only cancer center in WP1 with established procedures to automatically collect QoL data. In HUS, the patient portal of electronic medical record (EMR) is efficiently utilized for QoL data collection, and it is also widely adapted by the patients. HUS and RHP use the same EMR system, and in the future, RHP will also utilize its patient portal for data collection.

Different QoL questionnaires

Heath related Quality of life questionnaires are comprehensive tools designed to assess patients' overall well-being, including physical, psychological, and social aspects of health. QoL questionnaires are essential in understanding the patient's perspective, guiding clinical decisions, evaluating treatment outcomes, and improving the overall quality of care. There are multiple widely-used QoL questionnaires in the healthcare domain. Different questionnaires are tailored to different aspects of health and diseases, providing valuable data for clinicians, researchers, and policymakers.

In ONCOVALUE consortium clinics several most common QoL questionnaires are used. They include for example generic 5-level EQ-5D version (EQ-5D-5L) and cancer specific EORTC QLQ Core Questionnaire (EORTC QLQ-C30) and its cancer type extensions. In Finland, the prevailing generic QoL questionnaire is 15-dimensional (15D) which has been developed domestically. The 15D questionnaire is presented in Appendix I. The questionnaire is widely used by Finnish hospitals and HUS. In this report QoL questionnaire refers consistently to 15D as the report describes the experiences of HUS. The methods and procedures used in HUS are completely independent of the questionnaire in use. The QoL data collection using other questionnaires could be accomplished with the same practices.

4. Collecting QoL data

This chapter concentrates on the practices and results HUS has experienced with the collection of QoL data in completely electronic documentation environment. Naturally, QoL data can also be collected using separate applications integrated into the EMR or with paper forms, in which case the data must be entered into the EMR manually.

EMR environment in HUS

The primary Electronical Medical Record (EMR) in HUS is EPIC based Apotti, which was implemented gradually in different hospitals from 2018 to 2020. For clarity, the HUS EMR is referred to in this document as 'EPIC'. HUS Comprehensive Cancer Center started using EPIC in October 2020.

EPIC includes a patient portal module, which is fully integrated into the medical records. This module called MyChart ('*Maisa*' in Finland) can be utilized for versatile and secure bidirectional communication between patient and healthcare professionals. It can be used for example for scheduling appointments and messaging and delivering health information. From the perspective of collecting QoL data, the advantage of MyChart is the possibility to send electronic patient-reported outcome measure (PROM) questionnaires to patients. When a patient fills in the questionnaire, the documentation is automatically available for healthcare professionals. HUS has put a lot of emphasis on developing and deploying MyChart as an essential communication channel between clinics and patients and its utilization rate has been growing steadily since EPIC implementation. Currently, 75% of HUS's patients use MyChart.

Common QoL data collection in HUS

During the last years, HUS has built technical capabilities and practices for documenting and collecting of QoL data. The goal has been to systematically collect QoL data from all HUS's adult patients, at the baseline and during follow-up. Separate data collection procedures have been developed and built in the EMR for both urgent and elective settings. This data collection applies to all patients, not only cancer patients.

- For emergency patients who are transferred from the emergency department to the ward, a QoL questionnaire is automatically sent three months and one year after admission.
- For patients arriving with a referral, a QoL questionnaire is automatically sent upon acceptance of the referral. These patients are automatically sent a second questionnaire seven months after referral.

The automatic sending times for the questionnaires have been standardized across all disease groups at HUS to obtain comparable QoL data at the hospital-wide level. However, the quality of life experienced and reported by the patient can vary significantly depending on the stage of the treatment pathway, and for example, in cancer treatment, the phase of the medication cycle affects the questionnaire results.

QoL data collection intervals for breast cancer patients

One of the objectives of WP1 has been to evaluate and determine the timing of sending quality of life questionnaires to breast cancer patients. At HUS, the timing of sending additional QoL questionnaires to breast cancer patients was discussed and assessed among clinicians. The assessment concluded that in addition to HUS's general QoL sending times, few other time intervals are needed.

In HUS EMR it is possible to build automatic sending procedures which is attached certain activities in treatment pathways. However, this requires significant development work from the system provider, and building the solution will take up to 1-2 years to complete. Therefore, the sending of additional QoL questionnaires was resolved with a temporary semi-automatic solution where all additional questionnaires are sent to the patient during the processing of referral. In practice, this means that after the referral is accepted, it is forwarded to a referral secretary who does, for example, appointments, additional diagnostics orders etc. The secretary then sends several delayed patient messages including QoL questionnaires to patients and they appear to patient's portal in specific point of time. QoL time intervals which have been implemented in HUS are:

- In accordance with HUS's general practice, breast cancer patients are automatically sent a QoL questionnaire upon acceptance of the referral in cancer center. This point of time sets the **baseline** for later evaluation of QoL change.
- The referral secretary sends a QoL questionnaire to the patient 90 days after referral processing.
- In accordance with HUS's general practice, breast cancer patients are automatically sent a QoL questionnaire seven months after acceptance of the referral in the cancer center.
- The referral secretary sends a QoL questionnaire to the patient one year (exactly 335 days) after referral processing. This time point refers to first annual follow-up visit and ideally, patient fills in the questionnaire before the visit.
- The referral secretary sends a QoL questionnaire to patient two years (exactly 700 days) after referral processing. This time point refers to second annual follow-up visit and ideally patient fills in the questionnaire before the visit.

The time points for sending QoL questionnaires detailed in this report are primarily specified for HUS's use case in WP1, i.e. neoadjuvant treatment setting for breast cancer. RWD collection for adjuvant or metastatic treatment setting may require different or additional QoL sending intervals and they will be assessed later in ONCOVALUE project. It is noteworthy that previous semiautomatic QoL sending procedure is very flexible and can be easily applied to other treatment settings or cancer types as delay times can be changed easily. The procedure is also very efficient, and it takes only few seconds per patient to execute from the referral secretary.

Matching structured 15D and EQ-5D

HUS team has evaluated research concentrating on 15D and EQ-5D questionnaire comparison and discussed with the main developer of 15D questionnaire about the matching of different questionnaires. In general, using bot questionnaires parallelly for example in HTA work can be inaccurate. The correspondence of questionnaires needs to be primarily evaluated by cancer type and treatment setting.

As HUS has been the only WP1 participant capable of collecting and processing QoL documentation to the desired extent, it has not yet been feasible to evaluate the match between these questionnaires in cancer treatment pathways within the project. This comparison issue is still assessed in TASK 1.3 – Validating the structured data entry for selected cancer types as RHP has conducted trial-based collection of QoL data. The comparison can be conducted by focusing on treatment settings of chosen WP1 use cases of breast cancer and NSCLC.

Basic analytics and reports for 15D QoL data

General reports have been built in HUS EMR which include the data from HUS's general QoL questionnaire sending intervals (baseline and seven months after). Report includes measures from both QoL sending intervals:

- The number of patients to whom a 15D questionnaire has been sent
- The number of patients who have filled in the 15D questionnaire
- Response rate
- QoL index values

The report enables the user to drill in more to the detailed organizational level, for example, in the breast cancer polyclinic level in HUS comprehensive cancer center. Currently, the response rate at the hospital level for general QoL questionnaires is approximately 30% for both baseline and 7 months collection points. The response rate of HUS cancer center is equivalent.

Cancer type or treatment setting level report is conducted in the HUS Datalake data repository. In the HUS Datalake repository, it is possible to analyze QoL index values and their change over time points.

5. Conclusions

HUS has the advantage of having a versatile EMR patient portal which enables the efficient sending of QoL questionnaires or other PROM documents to patients and process the data electronically. The portal is a natural delivery channel for questionnaires as the patients are using it for many other health related communication. RHP and HUS have similar EMR in use and thus the same technical ability to exploit its patient portal. With a reasonable usage rate, the portal is very usable for data collection.

As HUS is dependent on its system provider in patient portal development, the desirable changes and related building work are achieved with some delay. It would be beneficial, for example, to automatize the sending of QoL questionnaires in such a way that the time intervals are attached to some unambiguous procedures or activities in treatment pathway. This kind of building work will need very exact specification.

Another efficient way of collecting QoL data is to use an external application which is integrated into the hospital EMR. Naturally, using external applications cause costs, the integration work can be time consuming and achieving reasonable usage rate takes time.

Concerning the patient perspective, it is very important to motivate patients to fill in QoL or any other PROM questionnaires. When the responsibility of documentation is completely on patient's side, the response rates tend to be low. This is true especially when they receive different but similar questionnaires frequently. Communication with patients should emphasize the benefits and reasoning of documentation and the importance of their replies. This also requires a common agreement among healthcare professionals about the benefits and their involvement in promoting the patient-centered documentation.

6. References

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APPENDIX I: 15D questionnaire

QUALITY OF LIFE QUESTIONNAIRE (15D©/Harri Sintonen)

Please read through all the alternative responses to each question before placing a cross (x) against the alternative which best describes your present health status. Continue through all 15 questions in this manner, giving only one answer to each.

QUESTION 1. MOBILITY

1 ( ) I am able to walk normally (without difficulty) indoors, outdoors and on stairs.

2 ( ) I am able to walk without difficulty indoors, but outdoors and/or on stairs I have slight difficulties.

3 ( ) I am able to walk without help indoors (with or without an appliance), but outdoors and/or on stairs only with considerable difficulty or with help from others.

4 ( ) I am able to walk indoors only with help from others.

5 ( ) I am completely bed-ridden and unable to move about.

QUESTION 2. VISION

1 ( ) I see normally, i.e. I can read newspapers and TV text without difficulty (with or without glasses).

2 ( ) I can read papers and/or TV text with slight difficulty (with or without glasses).

3 ( ) I can read papers and/or TV text with considerable difficulty (with or without glasses).

4 ( ) I cannot read papers or TV text either with glasses or without, but I can see enough to walk about without guidance.

5 ( ) I cannot see enough to walk about without a guide, i.e. I am almost or completely blind.

QUESTION 3. HEARING

1 ( ) I can hear normally, i.e. normal speech (with or without a hearing aid).

2 ( ) I hear normal speech with a little difficulty.

3 ( ) I hear normal speech with considerable difficulty; in conversation I need voices to be louder than normal.

4 ( ) I hear even loud voices poorly; I am almost deaf.

5 ( ) I am completely deaf.

QUESTION 4. BREATHING

1 ( ) I am able to breathe normally, i.e. with no shortness of breath or other breathing difficulty.

2 ( ) I have shortness of breath during heavy work or sports, or when walking briskly on flat ground or slightly uphill.

3 ( ) I have shortness of breath when walking on flat ground at the same speed as others my age.

4 ( ) I get shortness of breath even after light activity, e.g. washing or dressing myself.

5 ( ) I have breathing difficulties almost all the time, even when resting.

QUESTION 5. SLEEPING

1 ( ) I am able to sleep normally, i.e. I have no problems with sleeping.

2 ( ) I have slight problems with sleeping, e.g. difficulty in falling asleep, or sometimes waking at night.

3 ( ) I have moderate problems with sleeping, e.g. disturbed sleep, or feeling I have not slept enough.

4 ( ) I have great problems with sleeping, e.g. having to use sleeping pills often or routinely, or usually waking at night and/or too early in the morning.

5 ( ) I suffer severe sleeplessness, e.g. sleep is almost impossible even with full use of sleeping pills, or staying awake most of the night.

QUESTION 6. EATING

1 ( ) I am able to eat normally, i.e. with no help from others.

2 ( ) I am able to eat by myself with minor difficulty (e.g. slowly, clumsily, shakily, or with special appliances).

3 ( ) I need some help from another person in eating.

4 ( ) I am unable to eat by myself at all, so I must be fed by another person.

5 ( ) I am unable to eat at all, so I am fed either by tube or intravenously.

QUESTION 7. SPEECH

1 ( ) I am able to speak normally, i.e. clearly, audibly and fluently.

2 ( ) I have slight speech difficulties, e.g. occasional fumbling for words, mumbling, or changes of pitch.

3 ( ) I can make myself understood, but my speech is e.g. disjointed, faltering, stuttering or stammering.

4 ( ) Most people have great difficulty understanding my speech.

5 ( ) I can only make myself understood by gestures.

QUESTION 8. ELIMINATION

1 ( ) My bladder and bowel work normally and without problems.

2 ( ) I have slight problems with my bladder and/or bowel function, e.g. difficulties with urination, or loose or hard bowels.

3 ( ) I have marked problems with my bladder and/or bowel function, e.g. occasional 'accidents', or severe constipation or diarrhea.

4 ( ) I have serious problems with my bladder and/or bowel function, e.g. routine 'accidents', or need of catheterization or enemas.

5 ( ) I have no control over my bladder and/or bowel function.

QUESTION 9. USUAL ACTIVITIES

1 ( ) I am able to perform my usual activities (e.g. employment, studying, housework, free-time activities) without difficulty.

2 ( ) I am able to perform my usual activities slightly less effectively or with minor difficulty.

3 ( ) I am able to perform my usual activities much less effectively, with considerable difficulty, or not completely.

4 ( ) I can only manage a small proportion of my previously usual activities.

5 ( ) I am unable to manage any of my previously usual activities.

QUESTION 10. MENTAL FUNCTION

1 ( ) I am able to think clearly and logically, and my memory functions well

2 ( ) I have slight difficulties in thinking clearly and logically, or my memory sometimes fails me.

3 ( ) I have marked difficulties in thinking clearly and logically, or my memory is somewhat impaired.

4 ( ) I have great difficulties in thinking clearly and logically, or my memory is seriously impaired.

5 ( ) I am permanently confused and disoriented in place and time.

QUESTION 11. DISCOMFORT AND SYMPTOMS

1 ( ) I have no physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.

2 ( ) I have mild physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.

3 ( ) I have marked physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.

4 ( ) I have severe physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.

5 ( ) I have unbearable physical discomfort or symptoms, e.g. pain, ache, nausea, itching etc.

QUESTION 12. DEPRESSION

1 ( ) I do not feel at all sad, melancholic or depressed.

2 ( ) I feel slightly sad, melancholic or depressed.

3 ( ) I feel moderately sad, melancholic or depressed.

4 ( ) I feel very sad, melancholic or depressed.

5 ( ) I feel extremely sad, melancholic or depressed.

QUESTION 13. DISTRESS

1 ( ) I do not feel at all anxious, stressed or nervous.

2 ( ) I feel slightly anxious, stressed or nervous.

3 ( ) I feel moderately anxious, stressed or nervous.

4 ( ) I feel very anxious, stressed or nervous.

5 ( ) I feel extremely anxious, stressed or nervous.

QUESTION 14. VITALITY

1 ( ) I feel healthy and energetic.

2 ( ) I feel slightly weary, tired or feeble.

3 ( ) I feel moderately weary, tired or feeble.

4 ( ) I feel very weary, tired or feeble, almost exhausted.

5 ( ) I feel extremely weary, tired or feeble, totally exhausted.

QUESTION 15. SEXUAL ACTIVITY

1 ( ) My state of health has no adverse effect on my sexual activity.

2 ( ) My state of health has a slight effect on my sexual activity.

3 ( ) My state of health has a considerable effect on my sexual activity.

4 ( ) My state of health makes sexual activity almost impossible.

5 ( ) My state of health makes sexual activity impossible.