HARMONY

WP2 / WP6 – Core Outcome Set Project

AML DELPHI - Core Outcome Set (COS) AML

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A. INTRODUCTION

The HARMONY Alliance is a public-private European Network established in 2017, which currently includes 53 partners and 32 associated members from 22 countries. One of HARMONY's goals is to use Big Data to improve understanding and treatment of Hematological Malignancies. In order to achieve this aim, HARMONY is structured into eight work packages of which Work Package 2 (WP2) is focused on defining outcomes that are relevant to each Hematological Malignancy. In accordance, a **pilot study will be performed to define Core Outcome Set (COS) in acute myeloid leukemia (AML),** 1 out of 7 Hematological Malignancies considered in HARMONY. Following the start of this pilot study, further disease-specific COS defining studies are planned for each of the Hematological Malignancy groups in HARMONY. Finally, a core outcome set applicable to all seven Hematological Malignancies will be defined.

Acute Myeloid Leukemia is the most common acute leukemia that affect adults. Although scientific and technical advances have resulted in a number of new treatment strategies in recent years, AML still poses a challenge to curative approaches. For decades, the basis of AML treatment has remained virtually unchanged. However, over the last few years driver mutations have been identified and molecular subgroups were defined. This has led to improved prognostic stratification and the resulting updated European LeukemiaNET guidelines published in 2017. However, despite these recent advances, cure rates remain still poor in AML compared to other Hematologic Malignancies. Currently several innovative compounds are being tested in randomized, controlled clinical trials with the objective to improve both patient outcomes and patient management in AML.

Unfortunately, these trials are not always directly comparable, as they do not always measure the same outcomes, and there are no current COS that can be utilized to guide outcome selection and harmonization in this disease area. For example, measurement of long-term side effects and their influence on the patients' quality of life has not yet been assessed in most of these clinical trials.

A COS is a minimum set of outcomes developed by consensus, usually using multi-stakeholder consensus-based Delphi methodology. The COS functions as a reference point and provides the minimum outcomes that should be collected in further clinical trials on a given condition. Use of COS can improve the comparability of clinical trials, improves the consistency of reporting, reduces selective reporting bias and ensures appropriate outcomes are measured that are valued by a range of stakeholders.

Furthermore, such a COS could be used in other clinical settings or types of research, and in follow-up in real world settings. COS can be incorporated into clinical guidelines and improve the clinical practice and patient outcomes and management.

The COS usually includes the least number of outcomes is necessary. These should always be collected and reported in future clinical trials, but of course researchers can include more outcomes of special relevance than this minimum COS, if relevant.

In this context, it is important to distinguish between outcomes and prognostic factors. An outcome is defined as an effect of treatment or intervention on the disease or well-being of patients. To define a COS “what to measure” should first be identified. After that, “how the outcome should be defined and measured” can be determined.

On the other hand, prognostic factors can be understood as a patient characteristic that identifies subgroups of untreated patients that are likely to have different outcomes. As such prognostic factors are not part of a core outcome set and will not be included within this study. Of course, some patient characteristics, just like age or cytogenetics are relevant for treatment decisions and patient prognosis, therefore these factors should be still collected in every future trial.

Not all measured outcomes are objective and standardized, as they are influenced by individual interpretation. Measurement across larger patient numbers, by multiple healthcare providers and across a number of studies will increase the confidence in the outcome reporting, resulting in a more objective result. By increasing the frequency of new surrogate or potentially subjective patient reported outcome measurement and by their inclusion within COS could help in their validation, evaluation and wider acceptance.

Within this study, key stakeholders that provide their expert feedback are selected based on their skills and experience relevant to the disease or project. By participating in the Delphi survey, they vote on which outcome should be included within the COS. The stakeholders include health service users, health service practitioners, researchers, drug developer and patient advocates. Participants of all stakeholder groups were in particular recruited from members of the HARMONY work packages 2 and 6, but also participants outside the HARMONY Alliance are welcome to take part of the Delphi survey within their stakeholder group.

It is particularly important that we have involvement of patients and patient advocates within the development of the COS to ensure that the COS includes outcomes that are important not only for health care professionals but also for patients. To show the improved meaning of patient involvement in the Delphi an additional category is included in the analysis, called patient important. While this category will not be used in the final analysis to determine whether a specific outcome measure will be included or excluded, patient important outcomes will be presented to participants as part of the summary after the survey.

B PROJECT GOALS

Based on this background, this project aims to define a COS for AML agreed by consensus by all stakeholder groups and to define a standardized core set of outcomes to be measured in future trials. The definition of a COS may also be used to improve future clinical management strategies, and influence the collection of registry data, treatment decisions and finally handling of real-world data.

This kind of pilot study aims to establish the Delphi method in a three-step approach to achieve a consensus of a standardized COS applicable for AML. The protocol has been written following the COS-STAP recommendations.

C. METHODS

The development of the COS will follow COMET recommendations from the international COS-STAD study.

The COS is intended as the international standard for 'clinical trials' and 'real-world evidence practice' to ascertain the efficacy and effectiveness of treatments and treatment strategies in AML patients. The COS is defined for effectiveness trials to measure the degree of beneficial effect under real-world clinical settings, but the COS might also be used for other applications.

C.1. Participants

Concerning the patients' participation in this Delphi survey the target population for the COS includes adult patients (18 years or older) with AML. Different subtypes of AML are equally included, regardless of previous treatments including stem cell transplantation. Patients treated as outpatients were included as well as patients treated in hospital settings. Due to the English language used for this Delphi, the participation is limited to English speaking stakeholders.

Participants have been recruited from stakeholder organizations that are members of HARMONY, including clinicians, European Federation of Pharmaceutical Industries and Associations (EFPIA) member companies, regulators and health technology assessment (HTA) agencies, patients and patient advocates as well as all other members of the HARMONY consortium and they all have confirmed participation in the project. These individual participants have been identified in the run-up to the Delphi survey (see below).

C.2. Study management

A study management group has been assembled as recommended by COMET to oversee the project. Members include a study coordinator, a hematologist with leading roles in AML treatment and clinical trials, researcher/drug developer with experience in past and current trials, patient advocates, and methodological experts with experiences of systematic reviews and Delphi studies.

C.3. Selection of the outcome list for AML

The empirical basis for identifying a long list of preliminary set of AML outcomes for the Delphi study so far has been threefold:

First – A literature research was conducted in the COMET database to get an overview of the outcomes already used in existing clinical trials. The primary AML outcomes list was generated by extracting outcomes from the published literature and the views of clinicians and trialists.

Second – several semi-structured interviews of clinical public and private key opinion leaders were conducted to assess the initial selection of the particular outcome parameters and additional outcomes were supplemented. This was followed up by several face to face meetings to further expand and discuss the potential outcome list, including a multi-stakeholder group meeting including clinicians, EFPIA company members, regulators, HTA agencies and patient advocates, and a further meeting consisting of top European AML key opinion leaders.

Third – in order to include the patients' perspective, we consulted with patient representatives, people who have or have had AML, to complement the preliminary list of outcomes by including additional outcomes and revise the list in accordance with their comments.

D. DELPHI PROCESS

The preliminary AML outcome list (ANNEX 1), which was created in this threefold process mentioned above, will be used to create a Delphi survey in a representative pool of stakeholders to agree in a pre-defined and iterative process on a COS for AML.

Participants will be recruited out of all key stakeholder groups, including clinicians, EFPIA members, regulators/HTA agencies, patients and patient advocates as well as all other members of the HARMONY consortium. Potential participants will be contacted by an invitation email in which the aim of the Delphi will be explained, as well as their role, expected input and timeline of the Delphi.

To date, there is no recommendation found in literature regarding the number of participants to include in a Delphi survey. However, we aim to recruit stakeholder groups in equal participant numbers wherever possible. For certain stakeholder groups, for example for regulators and HTA bodies, we are aware that it may be hard to recruit a large number of participants, which may lead to an imbalance of group size. We will reflect on outcomes selected by these groups to ascertain if this impacts on the COS. With providing summarized results for each stakeholder group separately, the effect of inequitable distribution of group size is minimized. No new participants will be invited after the completion of the first round of the Delphi survey.

The Delphi survey aims to generate a comprehensive empirical basis concerning the judgment of outcomes by the stakeholders.

The Delphi instrument used is an online tool, DelphiManager, provided by the COMET Initiative.

The AML Delphi will be conducted in at least three sequential rounds. In every round, the stakeholders will be asked to rate the importance of each outcome based on their personal experiences. Each outcome will be ranked into three categories (1-3 “not important”, 4-6 “important but not critical” and 7-9 “critical”) using a Likert scale of 1 to 9.

Within the questionnaire, outcomes will be grouped into domains so that similar or related outcomes can be viewed and rated together. Each outcome will be described both in medical terms and in plain language. Plain language descriptions are used from lists provided by COMET and also from native-speakers with medical background.

The language used in the Delphi survey will be English. Before the first iteration, each participant is asked to which stakeholder group, he/she belongs. Once the individual participant has completed the first ranking round, he/she will also be able to provide feedback, and there will be also the opportunity to suggest additional outcome parameters, which have not yet been included and which might be added within the subsequent Delphi rounds. An additional outcome will be included in the following Delphi rounds when two or more participants proposed this outcome to be included.

After each round, all participants will be provided with their own answers and an anonymized, graphical summary of the other participants’ answers across all different stakeholder groups, in terms of the percentage scoring each of 1 to 9 on a particular outcome. Thereby feedback is provided from all stakeholder groups separately.

This allows the participants to revise their answers during the next round of the Delphi survey by taking the previous round’s results into account. No outcome will be dropped out between the rounds, so the participants can revise their initial ranking. The range of answers should decrease from round to round and a consensus opinion result. The process is stopped after pre-defined consensus criteria as described below.

If consensus is reached, the range of scores for each outcome parameter should be reduced, and a core outcome set is defined.

It will be important that as many participants as possible complete every round of the Delphi survey to ensure robust results.

The rate of non-response after the Delphi rounds, so called attrition is often highly variable. The attrition rate described over different Delphi studies varies from 0% to 20%. There is no recommendation regarding attrition rates, however an acceptable response rate would be 80%.

To increase the response rates personalized email reminders will be sent out.

Attrition bias may occur if participants give no response to subsequent rounds of survey. Little evidence is available regarding the extent to which attrition bias influences the Delphi result. To examine the attrition bias the average scores after round 2 will be compared for those completing the next round and those dropping out after round 2.

E. RESULTS AND ANALYSIS

To reduce potential bias in the interpretation of the results a clear definition of consensus is important. Consensus can be considered to have been reached if the majority of participants rank an outcome in a similar way. There are three categories of consensus defined in previous works (e.g. Fish R et al 2017), that will be modified used after the final Delphi round to assign each outcome to a category for each stakeholder group:

1. Consensus in
   70 % or more respondents over all the respondents (clinicians, EFPIA members, regulators/HTA, patients and patient advocates) scored the outcome as critically important (7-9) AND 15% or fewer rate the outcome as limited important (1-3)

2. Consensus out
   70 % or more of all the respondents (clinicians, EFPIA members, regulators/HTA, patients and patient advocates) scored the outcome as limited important (1-3)
   AND 15 % or fewer rate the outcome as critically important (7-9)

3. No consensus

Outcomes that do not achieve a consensus through the several rounds in the Delphi survey will be discussed at a consensus meeting to finally ratify the AML core outcome set. This applies especially for outcomes that are necessary for special stakeholder groups and have not reached consensus in accordance with the consensus criteria.

After completing the last Delphi round, each participant will be asked about willingness to participate in a face-to-face consensus meeting. The participants to this meeting will be randomly selected from this Delphi's participants, who completed the whole Delphi process. In addition, representatives from all stakeholder groups will be part of this meeting.

A detailed description of the statistical methods used for this AML pilot Delphi survey is provided in ANNEX 2.

F. STRENGTH & LIMITATIONS

As mentioned above different stakeholder groups take part in the Delphi survey. To ensure the impact of the highly important patient involvement in this process, a further specific category was added, called patient important. Thereby outcomes with a special interest for patients can be marked and emphasized in analysis.

The language used in the Delphi survey is English. This limits the group of people to participate in the Delphi to persons who do speak English. This might introduce a bias, especially for the patients advocate group, as fewer patients might speak English than physician and EFPIA members participating in the project.

This might also introduce a bias with regard to the countries participating in the Delphi, with e.g. a potential overrepresentation of English speaking countries and/or Nordic countries, where almost all inhabitants do speak English. While it was considered to translate the questionnaires into other European languages, this could pose additional problems and might introduce a different bias, e.g. depending on quality of the translations or depending on the number of participants per language, to name only few.

Finally, a potential unequal distribution in group size as discussed above is likely, but by presenting summarized results for each stakeholder group separately, this potential source of bias can be addressed, as described by COMET.

G. OUTLOOK

The anticipated way of developing the COS ensures that clinicians, industry, health authorities, as well as patients are involved in each stage of the development. In addition, the Delphi survey helps to make sure, that the COS represents the priorities of all stakeholders. Ultimately, utilization of the COS will improve the relevance of trial endpoints to all stakeholders. Furthermore, it will increase the capacity for data synthesis between different trials.

With the completion of the pilot Delphi in AML, it is intended to do Delphi surveys to define a COS for the remaining Hematological Malignancies included in HARMONY.

After defining a COS, an additional challenge is the implementation of these outcomes in clinical guidelines and at last in clinical practice. Finally, patient treatment and patient satisfaction during and after treatment might be improved.

ANNEX 1 | PRELIMINARY AML OUTCOME LIST

Name	HelpText	Domain Name
Response - CR (complete remission)	Leukemia gets better, resulting in no evidence of abnormally high levels of "blast cells" in the bone marrow. Also no signs of leukemia detectable outside the bone marrow, and levels of other blood cells return to normal.	Clinical outcome - Event type
Response - CRi (complete remission with incomplete Hematologic recovery)	All criteria of CR are met other than return of levels of certain white blood cells (neutrophils and platelets) to normal range.	Clinical outcome - Event type
Response - CR and MRD negative (complete remission and MRD negative)	All criteria of CR are met, plus "residual disease" that can only be detected by very sensitive measures (PCR or flow cytometry) is undetectable within a specific range.	Clinical outcome - Event type
Response - PR (partial remission)	Leukemia gets better, with a substantial reduction of "blast cells" compared to levels before treatment, but not enough to qualify as CR. Also, levels of other blood cells return to normal.	Clinical outcome - Event type
Response - SD (stable disease)	Leukemia stays the same after treatment.	Clinical outcome - Event type
Morphologic leukemia-free state (MLFS)	All criteria of CR related to reduction of "blast cells" in the bone marrow are met and no leukemia is detectable outside the bone marrow. Recovery of bone marrow function or blood cell counts are not considered for this outcome measure.	Clinical outcome - Event type
Relapse - Clinical relapse	Symptomatic return of leukemia after a patient initially responds well to treatment.	Clinical outcome - Event type
Relapse - Biochemical relapse	When a patient has had a positive response to treatment, and despite not having any symptoms has a result on a blood test that suggests that leukemia may be recurring.	Clinical outcome - Event type

Relapse - Molecular relapse	When a patient has had a positive response to treatment, and despite not having any symptoms has a result on a "minimal residual leukemia" test that suggests that leukemia may be recurring.	Clinical outcome - Event type
Cause of death	Death for any reason, whether related to leukemia or not. This records the specific reason for death, not the time until death.	Clinical outcome - Event type
PD (progressive disease)	Worsening of a patient's leukemia defined by a set of specific criteria for their leukemia.	Clinical outcome - Event type
OS (overall survival)	Length of time that a patient remains alive from either the date of diagnosis or the start of treatment for the leukemia.	Clinical outcome - Time to event
PFS (progression free survival)	Time until someone's leukemia either gets worse or they die from any cause.	Clinical outcome - Time to event
EFS (event free survival)	Time until someone's leukemia either gets worse, they die from any cause or they stop their treatment because of side-effects.	Clinical outcome - Time to event
DOR (duration of response)	Length of time from responding positively to a treatment to the leukemia starting to recur / to get worse.	Clinical outcome - Time to event
TTP (time to progression)	Time until someone's leukemia recurs / gets worse (excluding death).	Clinical outcome - Time to event
TTR (time to response)	Time from starting a treatment until a positive response to treatment is documented.	Clinical outcome - Time to event
LFS (leukemia free survival)	Time from receiving a transplant to evidence of leukemia getting worse.	Clinical outcome - Time to event
DSS (disease specific survival)	Time until someone dies from leukemia, but not from other causes.	Clinical outcome - Time to event
RFS (relapse free survival)	Time from achieving a leukemia-free state, to treatment until leukemia recurs.	Clinical outcome -

		Time to event
WBC (white blood cells)	Number of cells of the immune system that are involved in fighting leukemia but may also grow out of control, causing leukemia at diagnosis.	Clinical outcome - clinical parameter
Infections	How often and how bad a patient gets sick or picks up a bacterial, viral or fungal infection, that needs antibacterial or antifungal treatment. Number of bacterial, viral or fungal infections, that needs antibacterial or antifungal treatment.	Clinical outcome - clinical parameter
Use of G-CSF	Treatment given to help a patient to make a certain type of white blood cell called a neutrophil that is sometimes reduced in number because of treatment given or the patient's leukemia.	Clinical outcome - clinical parameter
Bleeding	Number of events recorded when a patient has an unexpected bleeding event, which may indicate a deficiency or issue with a certain type of blood cell, and may require transfusions or other interventions.	Clinical outcome - clinical parameter
Marrow MRD negativity	No detection of leukemia using very sensitive techniques to analyze bone marrow blood samples.	Clinical outcome - MRD
MRD cytogenetic	The level of leukemia that can be detected as measured by looking at how many cells there are with certain changes in the chromsomes.	Clinical outcome - MRD
MRD molecular	The level of leukemia that can be detected as measured by using a DNA sequencing technique.	Clinical outcome - MRD
MRD negativity post consolidation therapy	No detection of leukemia using specific techniques after the end of "consolidation" therapy, ie the completion of standard leukemia therapy with subsequent bone marrow transplantation.	Clinical outcome - MRD
AEs (adverse events) according to CTCAE v 4.0	A negative event or side-effect that happens during or after treatment, classified according to the latest "Common Terminology Criteria for Adverse Events", a descriptive terminology of adverse events. For each adverse event there is a grading for severity.	Safety outcome - AE / Toxicity

SAEs (serious adverse event)	A negative event that happens during or after treatment that is life-threatening or results in death, that requires hospitalisation or an extension of hospitalisation, that causes a birth defect or that needs treatment to prevent permanent damage.	Safety outcome - AE / Toxicity
Discontinuation of treatment	Patient decides to stop treatment themselves or under the direction of his/her doctor for any reason other than finishing a course of treatment.	Safety outcome - AE / Toxicity
Hematological toxicity	Side-effects that cause changes in the blood or number of blood cells.	Safety outcome - AE / Toxicity
Non-Hematological toxicity	Side-effects that cause changes anywhere other than in the blood, e.g. nausea, neuropathy, mucositis, renal or liver failure, infections.	Safety outcome - AE / Toxicity
SPM (second primary malignancies)	A new cancer occurring in someone who has had a cancer in the past. It is different to recurrence, which is where the original cancer has returned.	Safety outcome - AE / Toxicity
GVHD (graft versus host disease)	Side-effect that can happen after somebody gets a bone marrow or stem cell transplant from somebody else, when the immune cells from the donor attack the body of the person given the transplant.	Safety outcome - AE / Toxicity
Tolerability related outcomes	Measurement of how well patients are able to manage side-effects and whether they need to reduce dose or stop treatment as a result.	Safety outcome - AE / Toxicity
Fatigue	Feeling more lethargic and tired than normal.	PRO / HR-QoL - general - non-clinical
Insomnia	Finding it difficult to get to sleep or to stay asleep.	PRO / HR-QoL - general - non-clinical
Pain	Unpleasant physical sensation, which may vary in intensity from mild discomfort to pain that limits activities of daily life, limits self care and/or requires medication or hospitalisation. Medication may be necessary.	PRO / HR-QoL - general - non-clinical

Diarrhea / constipation	Passing looser stools (poo) or passing stools more often than is normal for you / Having difficulty passing stools (poo), which may be small and hard.	PRO / HR-QoL - general - non-clinical
Nausea	Feeling or being sick, which may lead to impact on intake of food and/or fluids and/or normal activities.	PRO / HR-QoL - general - non-clinical
Anxiety	Feelings of constant worry, or deep concern or uneasy about uncertainties.	PRO / HR-QoL - general - non-clinical
Dyspnoea	Shortness of breath, which may happen at rest and may limit activities of daily living or self care, and may require treatment.	PRO / HR-QoL - general - non-clinical
Anorexia	Loss of appetite, which may lead to weight loss and malnutrition.	PRO / HR-QoL - general - non-clinical
Cognitive problems	Problems with mental processes of perception, memory, judgment and reasoning.	PRO / HR-QoL - general - non-clinical
Depression	Feelings of severe sadness and unhappiness, often with decreased energy, constant feelings of guilt, doubt or self-blame, worthlessness and hopelessness.	PRO / HR-QoL - general - non-clinical
Sensory neuropathy	Problems involving damage to the peripheral nerves (those that connect the limbs and organs to the central nervous system and control sensation, movement and coordination) or symptoms caused by those issues, including numbness, tingling or burning sensations, increased sensitivity to touch, weakness or dysfunction especially of extremities.	PRO / HR-QoL - general - non-clinical
Psychological function	The effect of leukemia or its treatment on psychological function; for example thinking and feeling.	PRO / HR-QoL - PRO domains
Physical function	The effect of leukemia or its treatment on day to day physical activities; for example, walking, climbing stairs, driving.	PRO / HR-QoL - PRO domains
Social function	The effect of leukemia or its treatment on relationships with partner, family and friends including ability to join in with social activities.	PRO / HR-QoL - PRO domains

Role function	The effect of leukemia or its treatment on your role; for example, ability to look after children or to work or earn money.	PRO / HR-QoL - PRO domains
Finances	Financial losses because of co-payment for medical treatment, and if a patient was working before disease diagnosis or progression, loss of salary during sick leave, which may include leave taken by a carer.	PRO / HR-QoL - PRO domains
Eating and drinking	The effect of leukemia or its treatment on eating and drinking.	PRO / HR-QoL - PRO domains
Hospitalization days	Total days you are in hospital specifically because of leukemia or side effects in addition to planed days in hospital for treatment.	Health resource utilization - resource use
cost of leukemia treatment	Money which must be spend on leukemia treatment.	Health resource utilization - resource use
Emergency Unit admissions	Emergency or unplanned hospital treatment is necessary.	Health resource utilization - resource use
Intensive care admissions	Requirement for treatment on an intensive care ward due to serious or life threatening disease progression or side-effects.	Health resource utilization - resource use
Outpatient visits	Treatment or diagnostic visits in hospital without spending a night there.	Health resource utilization - resource use
Need of care giver assistance	Requirement for assistance given by caregiver (who could be a family member, friend or a professional care giver) in or outside the hospital.	Health resource utilization - resource use

ANNEX 2 | DETAILED DESCRIPTION OF STATISTICAL METHODS

ANALYSIS OF DELPHI SURVEY DATA

The analysis of the Delphi study described in this protocol will use descriptive statistics. The results for each of the Delphi rounds, for each outcome and for each stakeholder group, will be presented in frequency tables. As the 9-point Likert scale that was used from stakeholders to express their opinion can be assumed to be an interval scale, descriptive statistics such as the mean, median and standard deviation can be calculated for each outcome at each round. Quantitative analysis of the Delphi survey include calculations of i) percentage of panel's response rates and ii) percentages of responses in each of the three importance categories (1-3: "not important", 4-6: "important but not critical" and 7-9: "critical" based on 9-point Likert scale) for each outcome.

The mean is a measure to express the average opinion of the panel and the standard deviation (SD) represents the variability of answers around the mean answer. If the standard deviation is low then the panel is in strong agreement about the importance of outcome, whilst if the standard deviation is high then there is disagreement within the panel. Therefore, means and SD will be reported for assessing any tendency for disagreement (i.e. opinion stability) for each stakeholder group across the Delphi rounds. The interquartile range (IQR), calculated as the difference between the third and the first quartile, for each outcome will be reported to assess the extent of agreement between the participants. The data will be also displayed graphically, e.g. using histograms, for each stakeholder group and for each outcome. The plots will be reproduced for each round to further visualize the stability of panel's opinion.

The analysis of the Delphi study will be performed using the R statistical software version 3.5.2. As an exploratory analysis we identify outcomes considered as important for patients. The median Likert score for the patient group at the end of each round will be calculated and those outcomes achieving a median of greater or equal to 7 (≥7) will be considered as important to patients.

ANNEX 3 | REFERENCES

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Working dictionary of outcome definitions:

- CORMAC outcomes clinical and plain language description (R. Fish, et al, BMJ Open, 2017)
- Dictionary of outcome definitions – kindly provided by S. R. Dodd

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