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STUDY PROTOCOL

REVISED Towards an ontology of mental health: Protocol for developing an ontology to structure and integrate evidence regarding anxiety, depression and psychosis

[version 3; peer review: 2 approved, 2 approved with reservations]

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Abstract

Background

Research about anxiety, depression and psychosis and their treatments is often reported using inconsistent language, and different aspects of the overall research may be conducted in separate silos. This leads to challenges in evidence synthesis and slows down the development of more effective interventions to prevent and treat these conditions. To address these challenges, the Global Alliance for Living Evidence on aNxiety, depressiOn and pSychosis (GALENOS) Project is conducting a series of living systematic reviews about anxiety, depression and psychosis. An ontology (a classification and specification framework) for the domain of mental health is being created to organise and synthesise evidence within these reviews and present them in a structured online data repository.

Aim

This study aims to develop an ontology of mental health that includes entities with clear labels and definitions to describe and synthesise

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evidence about mental health, focusing on anxiety, depression and psychosis.

Methods

We will develop and apply the GALENOS Mental Health Ontology through eight steps: (1) defining the ontology's scope; (2) identifying, labelling and defining the ontology's entities for the GALENOS living systematic reviews; (3) structuring the ontology's upper level (4) refining the upper level's clarity and scope via a stakeholder consultation; (5) formally specifying the relationships between entities in the Mental Health Ontology; (6) making the ontology machine-readable and available online; (7) integrating the ontology into the data repository; and (8) exploring the ontology-structured repository's usability.

Conclusion and discussion

The Mental Health Ontology supports the formal representation of complex upper-level entities within mental health and their relationships. It will enable more explicit and precise communication and evidence synthesis about anxiety, depression and psychosis across the GALENOS Project's living systematic reviews. By being computer readable, the ontology can also be harnessed within algorithms that support automated categorising, linking, retrieving and synthesising evidence.

Plain language summary

While anxiety, depression and psychosis impact millions of people globally, our current interventions (strategies) to support people with these conditions vary in their effectiveness. We need a shared knowledge base to identify which interventions have worked in the past, and how we can develop better interventions moving forward. The Global Alliance for Living Evidence on aNxiety, depressiOn and pSychosis (GALENOS) aims to address these challenges by conducting systematic reviews relating to anxiety, depression and psychosis. To support these systematic reviews, an ontology (classification framework) of mental health will be developed. This ontology will include concepts (formally called entities) to specify aspects of mental health, along with labels and definitions for these concepts and relationships between them. An ontology of mental health can serve as a shared language and framework to communicate and organise evidence about aspects of mental health, such as mental health symptoms (*e.g.*, insomnia) or different treatments (*e.g.*, exercise interventions). The ontology will be developed by: (1) identifying concepts that are needed in systematic reviews of the GALENOS Project, (2) identifying and refining concepts based on existing classification frameworks, (3) refining the ontology based on feedback from relevant experts, (4) specifying the relationship between concepts, and (5) making it computer-readable and available online.

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Any reports and responses or comments on the article can be found at the end of the article.

This ontology could support clearer communication and understanding of evidence about mental health, thereby contributing to building a shared knowledge base about mental health.

Keywords

ontology, framework, classification system, evidence synthesis, living systematic review, GALENOS, mental health, anxiety, depression, psychosis

This article is included in the The Global Alliance for Living Evidence on aNxiety, depressiOn and pSychosis (GALENOS) gateway.

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REVISED **Amendments from Version 2**

The revisions to the manuscript are based on peer reviewers' feedback on the second version of the article, as well as adjustments to the methods in response to the needs of the Global Alliance for Living Evidence on Anxiety, Depression, and Psychosis (GALENOS) Project. In the Methods section, we report changes to the project plan to improve its feasibility and focus more on the usability of the ontology within the GALENOS repository. The changes include: (1) further updates to the stakeholder consultations and (2) additional details exploring the usability the repository and the ontology's application. Updates have been made throughout the Introduction and Methods to further clarify the rationale and ontology's development steps. A key revision was specifying more clearly where GALENOS team members and stakeholders will contribute to the ontology's development. This included adding an overview at the beginning of the Methods to describe contributors from the GALENOS Project and updating Figure 2 to show the involvement of the different contributors. Additional updates describe the advisory board's expertise and the status of ontology development and application.

Any further responses from the reviewers can be found at the end of the article

Background

Mental health conditions (e.g., anxiety, depression and psychosis) affect the well-being of millions of people across the world (GBD 2019 Mental Disorders Collaborators, 2022). However, current strategies to prevent and treat these conditions vary in their effectiveness (Leichsenring et al., 2022; Patel et al., 2016). An up-to-date and cumulative knowledge base could support identifying, adapting or developing more effective approaches for prevention and treatment (Cipriani et al., 2023). To develop such a knowledge base, several challenges in mental health research need to be addressed, including:

1. **Silos in mental health research** (Gardner & Kleinman, 2019): Mental health research and treatments often develop in silos, separated by researchers' education background, disciplines, perspectives and sometimes even ideologies rather than evidence.

2. **Increase in number of publications in mental health** (Elliott et al., 2021): Efforts to synthesise the literature can quickly become out-of-date, as new evidence is produced at a high speed.

3. **Inconsistent use of language to communicate about specific aspects of mental health** (e.g., Smoktunowicz et al., 2020): Many constructs in mental health have the same label but different definitions, or vice versa, have the same definition but different labels, creating challenges for communicating about these constructs and synthesising evidence across different studies.

4. **Lack of focus on studying the mechanisms and biomarkers within mental health interventions** (Domhardt et al., 2021; Insel & Gogtay, 2014): Studying the causes of mental health issues and the mechanisms through

which interventions work can provide evidence for biomarkers for pharmacological, and targets for psychological and social interventions and more broadly 'why' the interventions work, thereby supporting the translatability of findings across different populations and settings. However, interventions are often evaluated solely in terms of their influence on outcomes rather than their mechanisms.

5. **Lack of focus on studying mental health outcomes that are important to those most affected** (Nature Editorial, 2018; White et al., 2023): People with lived experience of mental health issues are often not consulted when designing research and studying these issues, leading to their needs being insufficiently addressed in research projects and their outputs.

The Global Alliance for Living Evidence on aNxiety, depressiOn and pSychosis (GALENOS) aims to address these challenges by synthesising and maintaining up-to-date knowledge relating to anxiety, depression and psychosis through a range of living systematic reviews (Cipriani et al., 2023). GALENOS is a global project, funded by the Wellcome Trust, that aims to identify promising routes of new treatments, novel diagnostic tools and more accurate predictions within anxiety, depression and psychosis, by evaluating existing evidence across animal and human data. The three broad mental health conditions (anxiety, depression and psychosis) have been prioritised by the Wellcome Trust, as they are among the top contributors to the global burden of disease (GBD 2019 Mental Disorders Collaborators, 2022; https://wellcome.org/what-we-do/mental-health).

This project has global reach, with a Leadership Team of members from Australia, Europe, Japan and South Africa, and Global Lived Experience Advisory Board with members from Canada, India, Nigeria, Philippines and Zimbabwe. These contributors include clinicians, researchers and lived experience advisors (mental health activists, campaigners and advocates), with expertise across data science, psychology and psychiatry. Detailed information about the GALENOS Project and its contributors can be found on the project website (https://www.galenos.org.uk/about), as well as in the protocol for the overarching project (https://mentalhealth.bmj.com/content/ebmental/26/1/e300759.full.pdf).

A key outcome of the project will be an online repository to present and maintain the data and findings of all living systematic reviews and each of their updates, allowing people to review and reuse this data in the future. To help structure the GALENOS Project's repository, we will develop an **ontology** for the domain of mental health, with specific focus on anxiety, depression and psychosis (see glossary of bold, italicised terms in Table 1). An ontology is a classification system including representations of **entities** (anything that exists in the universe, such as objects and processes) with clear labels and definitions, interconnected by **relationships** (Arp et al., 2015). Ontologies are being increasingly recognised

Table 1. Glossary of terms. (Marques *et al.*, 2024; Michie *et al.*, 2017; Schenk *et al.*, 2024).

Term	Definition	Source
Basic Formal Ontology (BFO)	An upper-level ontology specifying foundational distinctions between different types of entity, such as between continuants and occurrents, developed to support integration, especially of data obtained through scientific research.	Arp *et al.* (2015)
Entity	Anything that exists, including objects, processes, and their attributes. According to Basic Formal Ontology, entities can be broadly divided into continuants and occurrents. The terms 'entity' and 'class' can be used interchangeably to refer to the entities represented in an ontology. Classes can be arranged hierarchically by the specification of parent and child classes; see definition of parent class in the glossary	Arp *et al.* (2015)
Issue tracker	An online log for problems identified by users accessing and using an ontology.	https://docs.github.com/en/issues/tracking-your-work-with-issues/about-issues
Ontology	A standardised representational framework providing a set of entities for the consistent description (or 'annotation' or 'tagging') of data and information across disciplinary and research community boundaries.	Arp *et al.* (2015)
Parent class	An entity within an ontology that is hierarchically related to one or more child classes (subclasses) such that all members of the child class are also members of the parent class, and all properties of the parent class are also properties of the child class.	Arp *et al.* (2015)
Relationship	The manner in which two entities are connected or linked.	Arp *et al.* (2015)
ROBOT	An automated command line tool for ontology workflows.	Jackson *et al.* (2019); http://robot.obolibrary.org
Uniform Resource Identifiers (URI)	A string of characters that unambiguously identifies an ontology or an individual entity within an ontology. Having URI identifiers is one of the OBO Foundry principles.	http://www.obofoundry.org/principles/fp-003-uris.html
Versioning	Ontologies that have been released are expected to change over time as they are developed and refined, leading to a series of different files. Consumers of ontologies must be able to specify exactly which ontology files they used to encode their data or build their applications and be able to retrieve unaltered copies of those files in perpetuity. Versioning is one of the OBO Foundry principles.	http://www.obofoundry.org/principles/fp-004-versioning.html
Web Ontology Language (OWL)	A formal language for describing ontologies. It provides methods to model classes of 'things', how they relate to each other and the properties they have. OWL is designed to be interpreted by computer programs and is extensively used in the Semantic Web where rich knowledge about web documents and the relationships between them are represented using OWL syntax.	https://www.w3.org/TR/owl2-quick-reference/

as tools that can facilitate a shared language to communicate about and help integrate evidence across behavioural and social sciences (National Academies of Sciences, 2022; Sharp *et al.*, 2023). In the GALENOS Project, the ontological entities are developed or reused from other ontologies, where relevant, to organise constructs for which data are extracted in the systematic reviews. Constructs that overlap across systematic reviews can be identified and linked by mapping these to the Mental Health Ontology and organising them in the online repository structured by the ontology. The ontology serves as a framework to consistently label and define constructs, link relevant constructs and synthesise findings across systematic reviews. Figure 1 presents a workflow of the GALENOS Project, indicating where the ontology fits in.

In the context of this work, mental health has been defined as "*a state of mental well-being that enables people to cope with the stresses of life, realize their abilities, learn well and work*
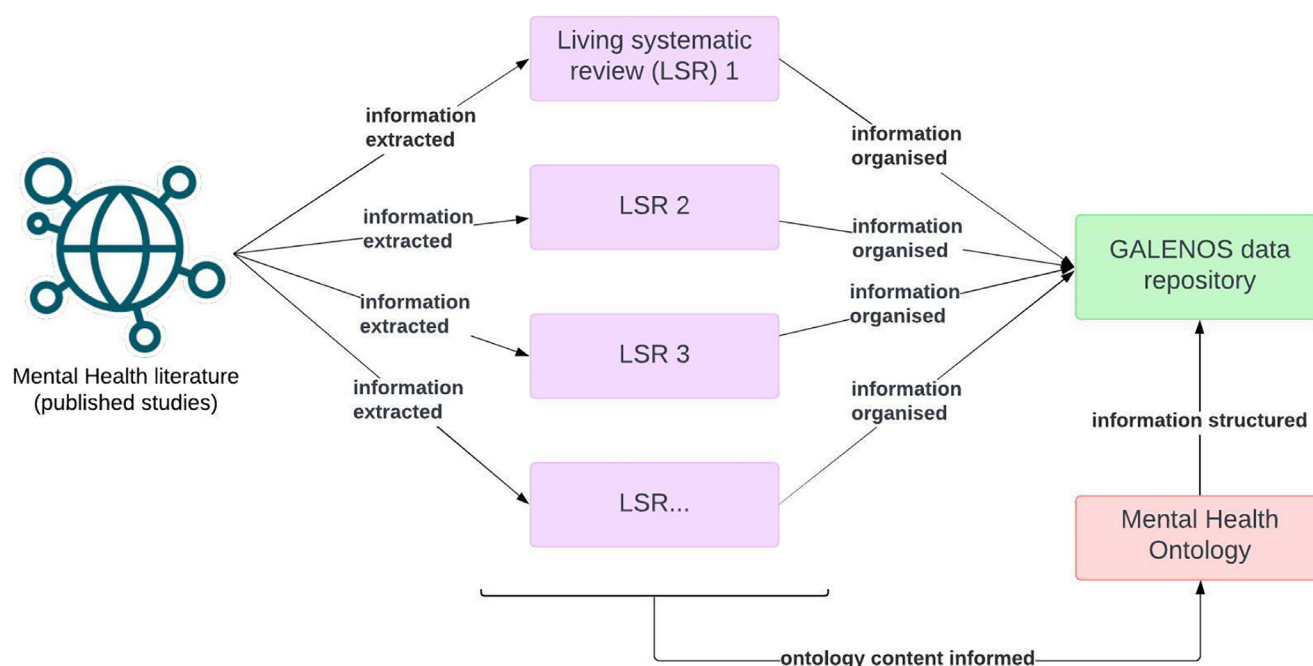
Figure 1. Overview of the GALENOS Project's workflow.

well, and contribute to their community" (WHO, 2022). By defining and categorising a broad range of aspects of mental health and the experiences associated with the conditions in which mental health (e.g., anxiety, depression and psychosis) is impacted, the ontology can encompass broad psychological and experiential views of mental health (*e.g.*, Johnstone & Boyle, 2018), as well as more traditional diagnostic models of mental health conditions (Larsen & Hastings, 2018). An ontology can help organise and synthesise data from various sources (e.g., findings from studies informed by different views of mental health). This aspect of ontological frameworks can be particularly useful for the mental health domain, considering ongoing debates about the best way of classifying mental health conditions. For example, key debates have centred around people with the same diagnoses experiencing very different symptoms, while people with different diagnoses experiencing the same or very similar symptoms (Clark *et al.*, 2017; Conway *et al.*, 2021; Feczko *et al.*, 2019; Robinaugh *et al.*, 2020). Given these debates, the ontology aims to provide a strategy for representing experienced symptoms as entities in addition to representing diagnoses and the potential interrelationships between these. In the future, the ontology can be linked to existing mental health classification systems such as DSM-5, ICD and RDoC (Clark *et al.*, 2017) by associating ontological entities with cross-references to relevant DSM/ICD/RDoC concepts or categories (e.g., diagnosis).

As the current ontology is developed to organise data relevant to systematic reviews about anxiety, depression and psychosis in the GALENOS Project's data repository, this ontology will focus on these three mental health conditions. However, the upper-level structure will be broad enough to be relevant to any mental health condition (as well as to allow the inclusion of a wide range of populations or interventions in the future). Therefore, the upper-level entities and structure can serve as a foundation for developing an ontology of mental health beyond the current scope. A key advantage of ontologies is that they can be continually updated based on evidence and feedback (Arp *et al.*, 2015; He *et al.*, 2018), allowing entities and their relationships to evolve in response to broadening consensus within the mental health field.

Ontologies are 'readable' by both humans and computers and therefore can be used to generate computer algorithms to categorise, retrieve and synthesise evidence (Hastings, 2017; Seppälä *et al.*, 2014). Within the GALENOS repository, the ontology will enable linking and synthesising data across reviews. As more research enters the system and is classified according to concepts in the ontology, machine learning will become more attuned to the precise research relevant to each living systematic review. We will use the ontology to populate a comprehensive online living evidence summary (see AD-SOLES, for example) (Hair, 2022).

The GALENOS Mental Health Ontology will:

- provide a shared framework to communicate, organise and analyse evidence about aspects of anxiety, depression and psychosis across research teams in GALENOS Project;

- support the online data repository by informing how research is browsed, categorised, indexed and summarised;

- facilitate the use of machine learning algorithms as a step towards enabling more efficient processes to categorise, retrieve and synthesise evidence as it is published in the future;

- provide upper-level entities and structure to serve as a foundation for expanding this ontology into an extensive ontology of mental health.

Methods

Developers and contributors to the ontology and its application in the GALENOS Project

The ontology's development is being led by two researchers with post-graduate degrees in psychology and experience in mental health research (MS & PS). Two senior researchers, both with experience in ontologies and clinical psychology (JH & SM), supervise and regularly provide feedback on the ontology's development and application. The project manager of GALENOS (JP) and two researchers leading systematic reviews within the project (CF & JK) also continuously support the work to refine the ontology and its application. Additional members across the GALENOS Project, such as from the data repository team (DB) and other systematic review team members (SS & SW), also regularly provide feedback to improve this work.

Set up the Mental Health Ontology Advisory Board
Terms of reference of Advisory Board

Members of the advisory board will bring their perspectives to the work, recognising that ontologies seek to reflect many perspectives, and that consensus is aimed for but not always immediately achieved (Open Biological and Biomedical Ontology [OBO] Foundry, 2019). They will be invited to attend online meetings once or twice a year, in which they will be given an overview of the methods and progress in developing the ontology. In these meetings, they will be prompted to provide feedback about the methodology, emerging ontology content and organisation, and ontology-structured evidence. They will also be invited to submit feedback to written documents that will inform ontology development and join the formal stakeholder consultation to refine the ontology content (see Step 4) and usability evaluations of the ontology's application (see Step 8). Based on the number of participants in previous studies to provide feedback on ontologies, we aim to recruit at least 10 members for the advisory board before the initial round of feedback (Michie *et al.*, 2020; Norris *et al.*, 2020). However, this number is subject to change, with more experts being recruited when people with relevant expertise and lived experience express interest and/or specific expertise are needed or available.

Criteria for selection of members

Selection to reflect representativeness across geography and discipline include:

1. Representation from Global Experiential Advisory Board

2. Volunteers from the Galenos International Advisory Board (including experts with animal and human science content expertise)

3. Individuals who have done work in Mental Health classification or measurement

4. Mental Health organisations to be invited to send a representative

5. Ontology experts

Current members of the advisory board

At the time of submission, the Mental Health Advisory Board has 18 board members from 10 countries (Australia, Belgium, Canada, Germany, India, Israel, Portugal, UK, USA and Zimbabwe), with expertise in various domains, including psychiatry, clinical psychology, neuroscience and health psychology, as well as lived experience. Many advisory board members have expertise in more than one discipline (e.g., clinical experience and health psychology research experience), with some focusing on specialised topics such as paediatric traumatic stress, pain and chronic illness, physical activity, mood disorders and various others. The members include 14 with professor, associate or assistant professor roles at universities (with some also working as clinicians), a research fellow (JK), a psychiatrist and two lived experience advisors with undergraduate or post-graduate degrees related to psychology.

Ontology development and integration into the GALENOS Project repository

The Mental Health Ontology will be developed and integrated into the GALENOS Project's repository in eight iterative steps, broadly drawing on the methods applied for developing the Behaviour Change Intervention Ontology (BCIO; Wright *et al.*, 2020). Figure 2 presents an overview of these steps.

Step 1: Specifying the scope of the Mental Health Ontology within the GALENOS Project

The preliminary scope of the Mental Health Ontology will cover: (1) human mental health conceptualisations, including constructs representing symptoms, conditions (*i.e.*, diagnoses) and wellbeing and promoting mental health rather than merely treating dysfunction, (2) mental health interventions (*i.e.*, coordinated sets of activities designed to change specified aspects of mental health) and their delivery, (3) settings in which interventions are delivered, (4) populations to whom interventions are delivered, (5) intervention mechanisms and biomarkers for mental health outcomes, (6) intervention outcomes (including risk prediction) and spillover effects related to mental health and (7) research methods. The ontology's level of detail for entities will be informed by its use case in the GALENOS Project, namely integrating evidence across systematic reviews. Therefore, we will only include detailed entities where required for the associated data extraction of these reviews, focusing on research questions related to anxiety, depression and psychosis. This scope will be refined during later steps.

Step 2: Identifying, labelling and defining entities needed for living systematic reviews

To ensure the ontology is fit for structuring the GALENOS online repository, ontological entities will be identified to capture the data extracted in the GALENOS Project's living systematic reviews. The project's ontology development and
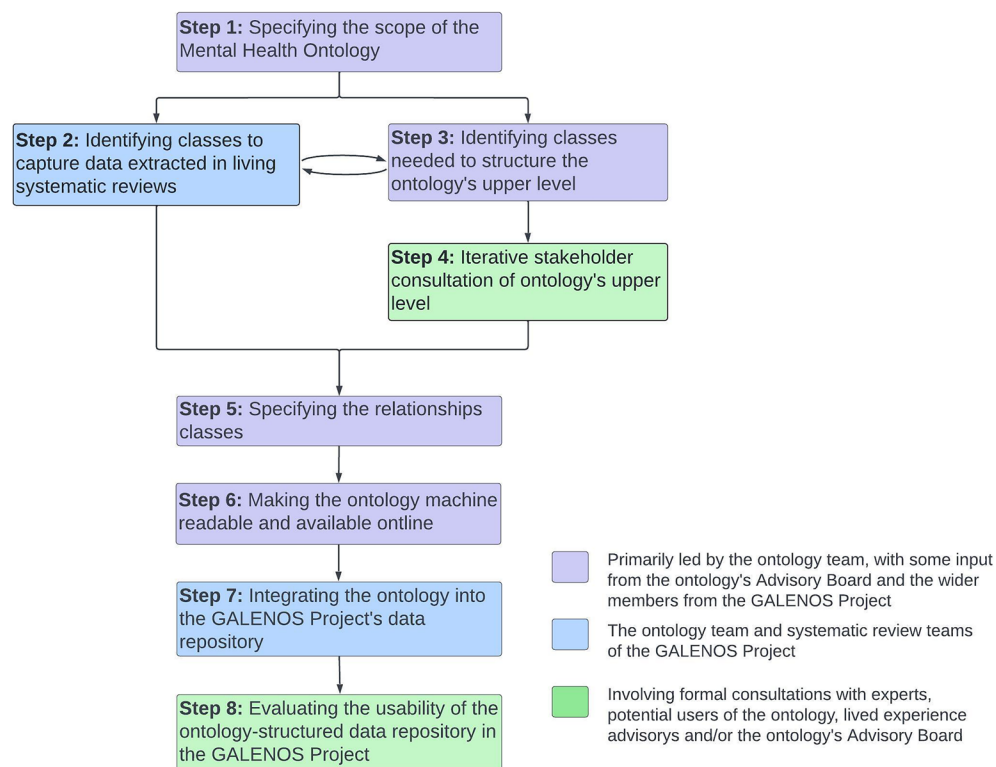
Figure 2. **Overview of steps to develop the Mental Health Ontology within the GALENOS Project.**

systematic review teams will work together to identify and refine these ontological entities.

Approximately three systematic reviews on human studies will be conducted per year, completing in January 2026. Each is led by two or three researchers with an MSc or PhD in an area related to mental health. Table 2 presents the topics that the 10 planned systematic reviews will cover, with references to their protocols and final papers where available.

The review teams will share an initial extraction template with the ontology team, who will review these sheets and provide feedback about their clarity and propose potential ontological entities for defining constructs. Following the first three systematic reviews, it became clear that stronger data governance was needed during the preparation and data extraction phases of the reviews. Therefore, members of the ontology development team (MS & JH), the living systematic review teams (CF, JK & SS) and the data repository team (DB) are meeting regularly to formulate rules for more consistent data extraction across different reviews.

Once each review is completed, the ontology development team will review the data extracted within the systematic reviews from published papers (e.g., mean age and mental health outcomes) in an Excel spreadsheet. The team will focus on formally capturing **the categories for which data is extracted**

(e.g., mean age) in the ontology, rather than capturing the entire extracted dataset (e.g., a study's mean age being 45) in an ontological format. These categories (e.g., mean age) are captured through a mapping exercise, in which one or two researchers (MS & PS) map ontology entities onto these categories, developing new entities where needed (see example in Figure 3).

For the mapping exercise, the ontology development team will first check if a relevant entity is already included in the Mental Health Ontology. If not, the team will identify relevant entities from existing ontologies or develop new entities. Entities from other ontologies will be identified by using specialist ontology databases, *e.g.*, the Ontology Lookup Service (European Bioinformatics Institute, 2019), and where appropriate, these entities will be reused or cross-referenced in the Mental Health Ontology. For example, we will reuse relevant parts from the Behaviour Change Intervention Ontology (BCIO; Michie *et al.*, 2020), the Mental Functioning Ontology (MFO; Hastings *et al.*, 2012), Emotion Ontology (MFOEM; Hastings *et al.*, 2011) and Information Artifact Ontology (IAO; Ceusters & Smith, 2015). Where we identify that changes are needed to an external ontology, we will log the relevant change on the ontology's GitHub repository for the external developers' consideration. New entities will be developed, labelled and defined by drawing on mental health classification systems or dictionaries, and assigned unique alphanumeric identifiers.

Table 2. Overview of topics covered in the living systematic reviews of the GALENOS Project.

No	Topic of living systematic review	References (if available)
1	Pro-dopaminergic pharmacological interventions for anhedonia in depression	Ostinelli *et al.* (2023)
2	The therapeutic potential of exercise in post-traumatic stress disorder and its underlying mechanisms	Wright *et al.* (2025a); Wright *et al.* (2025b)
3	Trace amine-associated receptor 1 (TAAR1) agonists for psychosis	Siafis *et al.* (2023); Siafis *et al.* (2024)
4	Circadian disruption in mood disorders	Kurtulmus *et al.* (in prep)
5	Association between cardiovascular and metabolic factors and cognitive functioning in psychosis	Friedrich *et al.* (in prep)
6	Cognitive bias modification for social anxiety	Kennett *et al.* (2025)
7	Relationship between type/duration of internet use and mental health symptoms in young people	
8	Heat and mental health	
9	Efficacy, safety, and mechanisms of estrogenic compounds in the treatment of schizophrenia spectrum disorders	
10	Association between gut microbiome and mood disorders	
11	Efficacy and safety for cardiometabolic interventions for cognition in psychosis	

Dimension	Extraction category	Categories	Class label	Class definition	Parent class
Study identification	Author	Free text	author identification	A textual entity intended to identify a particular author.	textual entity
	Year	Numerical	publication year textual entity	A textual entity documenting the year in which some study was published.	textual entity
	Country	Free text	country of intervention	A geographical location of a country where the intervention takes place.	geographical location
	Email	Free text	author email address textual entity	A textual entity documenting the email address of an author of a publication.	textual entity
	Sponsorship source	Free text	funding source declaration textual	A textual entity documenting the source of funding that supported some study.	textual entity

Figure 3. Example of mapping ontology entities onto extraction sheet used in a systematic review.

To avoid introducing too much detail into the ontology, detailed categories will be mapped using multiple entities to capture all aspects of these categories. For example, the category 'mean anhedonia after intervention' could be captured with the entities 'average value', 'anhedonia symptom severity' and 'measurement datum post-intervention'.

Once ontology entities have been mapped to categories in the data extraction sheets, the ontology development team will share these entities, their labels and definitions with the systematic review teams. These teams will provide feedback on whether each entity appropriately captures the category of interest (see example mapping presented to review teams in Figure 3). Where teams suggest changes to entities, updates will be made to the ontology and mapping record where

necessary. This mapping record will be used to inform the structure of the data repository (see Step 7). If the entities have previously been applied by other systematic review teams, these teams will be informed of the changes and given the opportunity to raise issues with these changes.

Step 3: Identifying and refining entities needed to structure the upper level of the ontology
Parallel to developing entities used to map the living systematic reviews, we will identify upper-level entities (e.g., 'mental health intervention') to provide the Mental Health Ontology an overarching structure. Such a structure can help organise the entities in the ontology, as well as serve as a scaffold to build a more comprehensive ontology for the mental health field in the future.

To identify the upper-level entities, we will first review the upper-level entities in the BCIO (Michie *et al.,* 2020) and note down entities (e.g., 'intervention population') that are relevant to mental health and mental health interventions. The BCIO was selected as starting point, as the mental health ontology will need to synthesise data from interventions. Relevant BCIO entities (e.g., 'behaviour change intervention') can be used as examples to inform the development of corresponding entities needed for the current scope, namely mental health (e.g., 'mental health intervention'). Some GALENOS systematic reviews will have research questions about human populations beyond interventions (e.g., the effect of childhood experiences). Therefore, the structure of the Mental Health Ontology upper-level entities will be specified to represent knowledge about interventions, but also human populations more generally (e.g., representing that human populations may or may not participate in interventions). After the core ontology team has drafted these entities, they will be presented to the wider GALENOS team and ontology advisory board for feedback and updates will be made accordingly.

Step 4: Iterative stakeholder consultation of the Mental Health Ontology's upper level
A stakeholder consultation will be conducted to refine the ontology's upper-level entities. This consultation on the upper-level entities aims to ensure that the ontology's broader structure: (1) clearly reflects broad entities important to specify people having positive or negative experiences related to their mental health, (2) captures a broader scientific consensus in the mental health field, and (3) meets the needs of potential ontology users (OBO Foundry, 2019; Wright *et al.,* 2020). This consultation will primarily be conducted through a Qualtrics survey, followed by a second round of feedback from advisory board members, involving an online meeting and then written input over email (see details in 'Analysis of stakeholder consultations').

We aim to recruit at least 10 participants, with broad theoretical knowledge and expertise relating the mental health field, lived experience of mental health conditions or ontologies. The number of participants is considered appropriate based on the development of ontologies part of the BCIO, which included 3–29 participants in their stakeholder consultations (Michie *et al.,* 2020; Norris *et al.,* 2020). Participants will be recruited by (1) inviting members of the Mental Health Ontology Advisory Board (2) asking these members to suggest individuals or groups with relevant expertise, with the two lived experience advisors being asked separately to share the invitation with their networks and (3) advertising the study through the UCL Centre of Behaviour Change and GALENOS Project's official social media accounts (LinkedIn and X). The inclusion criteria will be having professional or volunteering experience on mental health project, being able to read and write in English and having access to an electronic device.

When developing the materials for the stakeholder consultations, we will ask for feedback from the Mental Health Ontology Advisory Board and at least one lived experience advisor in order to enable the participation of people less familiar with

ontologies in the stakeholder consultation process (National Institute for Health Research [NIHR], 2019).

Before being invited to complete the survey, participants will be provided with online training videos that cover: (1) what an ontology is and (2) an overview of the Mental Health Ontology. In the Qualtrics survey, they will then be presented with: (1) the Mental Health Ontology's upper-level entities and relationships as a diagram, (2) a list of the relationships between entities, which are informally described to help participants better understand these relationships and (3) the labels and definitions of the upper-level entities. Participants will be invited to provide feedback on the upper-level entities and relationships in the ontology in terms of:

1). The clarity of the upper level: Whether any entity, label or definition is unclear and needs changing

2). The comprehensiveness of the upper level: Whether any entities are missing from the upper level of the ontology

3) Accuracy of relationships: Whether any relationships between entities need to be changed to better capture aspects of mental health

Participants will be able to indicate which entities need changing by clicking options 'Change label' or 'Change definition' for the respective entities and providing open-ended feedback on how these should be changed. They will also be able to indicate that entities are missing or that relationships need changing in an open-ended response format. Finally, participants will be asked if they have any additional feedback which was not prompted by other survey questions.

Analysis of stakeholder consultations
Each piece of feedback from the participants will be recorded and reviewed by two researchers (MS & PS) to propose changes to the ontology. To ensure that the ontology's upper level is relevant to a range of geographical and social contexts, we will update the entities and their structure to be as inclusive as possible, informed by stakeholder feedback. Examples include updating entity labels and definitions to be broader, allowing them to capture wider contexts, or adding specific entities to better represent aspects of mental health that were previously insufficiently covered. The relevant feedback and proposed changes will be discussed among the researchers leading the Mental Health Ontology's development (JH, MS, SM & PS). In these discussions, the team will consider how the feedback will be addressed and review disagreements between stakeholder comments, documenting the rationale for implementing relevant changes in a log.

The updated upper level will be presented to the ontology advisory board in a meeting to verify that the changes to the ontology are appropriate to both academic experts and lived experience advisors in mental health. Following the meeting, advisory board members will be invited to share additional comments via email to allow them more time to provide feedback on the changed entities. Drawing on these comments, any

disagreements and potential updates will be discussed by the ontology development team, with a transparent log being kept showing how each comment was addressed. These logs, recording how each piece of feedback is addressed, will be shared on Open Science Framework.

Step 5: Specifying the relationships between Mental Health Ontology entities

The ontology development team will discuss, specify and refine the relationships between entities in the Mental Health Ontology. Common relationships (*e.g.*, 'is_a' and 'has_part') will be used from the widely used upper-level ontologies ***Basic Formal Ontology*** and the Relation Ontology (Smith *et al.*, 2005). To structure the ontology, each entity will be linked to a ***parent class*** with a hierarchical 'is_a' relationship (Arp *et al.*, 2015; Smith *et al.*, 2005). For instance, the entity 'motivation' will have an 'is_a' relationship to its parent class 'mental process': motivation 'is_a' mental process. The team will also discuss whether any new relations need to be specified between entities to structure the ontology and, if so, develop such relations.

Step 6: Making the Mental Health Ontology machine-readable and available online

We will develop the Mental Health Ontology as a spreadsheet of entities: Each entity will be organised as a separate row with a primary label and definition, unique alphanumeric identifier (*i.e.*, ***Uniform Resource Identifier [URI]***; e.g., BCIO:01023), relationships, and if available, synonyms, informal definitions and examples. These fields (*e.g.*, label and definition) will be organised into separate columns. When the ontology's content is ready for its initial release, we will convert this content to ***Web Ontology Language (OWL)*** (Antoniou & van Harmelen, 2004) format. In this standard format, the ontology can be viewed and visualised within ontology software, such as Protégé (Musen, 2015), and becomes compatible with other ontologies. For the conversion to OWL, we will use the ***ROBOT*** ontology toolkit library (Jackson *et al.*, 2019), which supports creating well-formatted ontologies from spreadsheet-format templates. The ROBOT template is a comma-separated values (CSV) file that is prepared from the primary ontology spreadsheets by adding instructions to the template header about how spreadsheet columns are to be converted into OWL and metadata attributes. The GALENOS Mental Health Ontology's OWL version will be stored on the ***GitHub*** repository of the project (https://github.com/galenos-project/mental-health-ontology), as this repository supports versioning of the ontology, *i.e.*, it keeps a record of different versions of the ontology and any updates made. GitHub also has an ***issue tracker*** that enables ontology users to submit any issues with the ontology and ontology developers to respond to these issues (https://github.com/galenos-project/mental-health-ontology/issues).

Step 7: Integrating the ontology into the GALENOS Project data repository

After releasing the ontology through GitHub, we will closely collaborate with members of the GALENOS Project who are leading work on the systematic reviews (CF, JK & JP) and developing the online data repository (the data repository team, DB). We will add the mapping of the ontology onto the extracted data categories for each systematic review (see Step 2.2) as a CSV file to GitHub. This mapping, along with the ontology in its OWL format, will be shared with the data repository team. The data repository team will integrate the ontology's structure and the mapping of entities onto the relevant systematic review on the online data repository: https://galenos-data.aliveevidence.org/. In this repository, the ontology's key application will be that entity labels and definitions will appear when hovering over relevant data categories for each living systematic review. In the backend, the same entities, which have been mapped onto different systematic reviews, will be linked, allowing searchability and integration across reviews.

To ensure that the repository is presented in a usable format, the ontology's formal structure will not be shown directly in the repository. Instead, discussions between the systematic review team (CF, JK & JP) and an ontology team member (MS) will inform how the upper levels in the repository should be structured. For example, rather than using formal upper-level entities such as 'disposition' in the repository, the systematic review team may suggest presenting 'population' as the highest level in the repository. The two teams will also collaborate on generating 'understandable labels' for each category extracted. The mapped ontology entities and their definitions (which will appear when hovering over the labels) will provide additional clarity.

Step 8: Evaluating the usability of the ontology-structured data repository in the GALENOS Project

The data repository's usability, along with the clarity of the ontology mapping, will be evaluated through feedback from potential users. We will recruit participants through the GALENOS Project's contacts, including the advisory boards and official social media accounts (LinkedIn and X). In line with stakeholder consultations on ontologies (3–29 participants) as part of the BCIO (Michie *et al.*, 2020; Norris *et al.*, 2020) and relevant usability studies (Bruun & Stage, 2015), we will aim to recruit at least 10 participants. As the repository is likely to be used by people interested in data synthesis, the criteria will be for participants to have experience contributing to scoping or systematic reviews or applying review evidence in work related to mental health. To ensure that we include participants from a range of backgrounds, we will ask the lived experience advisors of the GALENOS Project to circulate invitations to their networks.

Participants will first be given an overview of the data repository by a researcher and then will be prompted to engage with the data in the repository based on their interests (e.g., finding a living systematic review, and data on a specific category, such as mean age). After participants have explored the repository on their own, a researcher will provide them with use cases about finding specific ~5 categories within the repository, visualising the data within these categories and engaging with

the ontology classes mapped to the categories. To provide a wider range of different categories to engage with, the researchers will randomly select the ~5 categories from the full list of extracted categories for each participant. We will use think-aloud methods to explore the usability and acceptability of the repository interface (McDonald *et al.*, 2012; Peute *et al.*, 2015), including whether entity labels and definitions used for the systematic reviews are sufficiently clear. Following, the interviews, we will ask participants to fill out around 10 survey questions, adapted from the System Usability Scale (SUS) on the usability of digital systems (Brooke, 1996). The think aloud method and the survey questions are expected to take around 45–60 minutes to complete.

These sessions will be recorded and analysed using thematic analysis to identify aspects of the repository that are usable and acceptable and aspects that are not in order to inform improvements to this repository (Crane *et al.*, 2017). The SUS results will involve descriptive analysis, providing a summary of users' perceived usability of the online repository. The GALENOS teams will make updates to the repository interface (e.g., improving the clarity of understandable labels) and, where needed, the ontology.

Applying the ontology to develop tools for data searching, visualising and synthesis, and partial automation of these processes

The Mental Health Ontology will be used to organise the evidence extracted from the literature in the living systematic reviews and stored in the project's online data repository (see Steps 2, 7 and 8). The systematic review publications will be linked to this database, and will be regularly updated, allowing new data to be retrieved and displayed (e.g., as plots) as part of the living systematic review. The ontology will also be used to develop tools and algorithms to support interoperability with other knowledge resources, enhanced searching, browsing and navigating of the evidence database and ontology-based summarising and visualising the data. The algorithms developed will be informed by the evolving deliverables and needs of the GALENOS Project. Thereby, the ontology development team aims to deliver:

1. A mental health ontology that is interoperable to enable more discoverable and translatable evidence across various sources, including early phase and late phase trials

2. Ontology-based algorithms to enable evidence searching, visualisation and querying

3. An open, coded and queryable database of relevant studies, characteristics of studies, risk of bias assessments and results data, richly linked to ontologies for interoperability

Ethics

Ethical approval was granted by University College London's ethics committee (CEHP/2020/579) in 2020 and (0199 PaLS- Clinical, Educational and Health Psychology LREC) in 2025. Participant informed written consent will be sought at the beginning of each stakeholder consultation.

Study status

We have invited participants to join the Mental Health Advisory Board and organised the three advisory board meetings, specified the initial scope of the ontology (Step 1), drafted the initial entities for the first three systematic reviews as part of the GALENOS Project for the extraction sheets and revised these with input from systematic review teams (Step 2), drafted the first version of the upper-level entities and specified their relationships (Step 3), collected data for the stakeholder consultation about the ontology's upper level (Step 4), started specifying relationships between entities (Step 5), released an initial version of the ontology in an OWL format (Step 6) and started integrating the ontology into the GALENOS data repository (Step 7).

Conclusion

The Mental Health Ontology will be developed to serve as a shared framework to categorise, label and define entities relating to anxiety, depression and psychosis research within the GALENOS Project. The entities will include key constructs for diagnoses of conditions affecting mental health, experiences related to mental health, mental health interventions, their target populations and settings, intervention mechanisms and biomarkers for mental health outcomes, intervention outcomes and research methods. As these groups of constructs will each be elaborated for the domains of anxiety, depression and psychosis, and categorised in the ontology, it will enable the representation of entities relevant to different perspectives about research in these three domains and the integration of evidence from sources informed by such perspectives.

This ontology will be used to support structuring the GALENOS data repository, and thereby linking, integrating, analysing and visualising data. We will develop this ontology iteratively, updating it based on the needs of living systematic reviews and stakeholder feedback. As ontologies are computer readable, some of these processes can also be partially automated in the project lifecycle or refined to be fully automated after the project.

Further work, including wider application and feedback on the ontology, are needed to ensure that the ontology better reflects the complexity of different social and cultural perspectives of mental health and relevant interventions. The Mental Health Ontology will be developed and maintained as part of the GALENOS Project, but beyond this project, the ontology will also be maintained alongside the BCIO as part of the APRICOT (Advancing behavioural and social sciences through ontology tools) Project, a 5-year long US National Institutes of Health (NIH) grant (Michie *et al.*, 2024). During this time, any issues on the ontology that are reported on GitHub will be tracked, responded to and, where needed, addressed by updating the ontology. In addition, this project will support the dissemination

of the ontology, introducing it to ontology developers and users interested in structuring knowledge about mental health across disciplines. In the future, this ontology, especially its upper level, has the potential to be expanded to capture mental health conditions beyond anxiety, depression and psychosis. For example, the ontology's upper-level structure could be applied to broadly organise information about various mental health conditions across different categorisation systems and create new lower-level entities to capture aspects of mental health (e.g., about populations and interventions), cross-referencing the relevant categorisation systems.

References

Antoniou G, van Harmelen F: **Web ontology language: owl**. In: *Handbook on ontologies.* Springer, 2004; 67–92.
Publisher Full Text

Arp R, Smith B, Spear AD: **Building ontologies with basic formal ontology**. Mit Press, 2015.
Publisher Full Text

Brooke J: **SUS-A quick and dirty usability scale.** *Usability evaluation in industry.* 1996; **189**(194): 4–7.
Reference Source

Bruun A, Stage J: **An empirical study of the effects of three think-aloud protocols on identification of usability problems.** In: *Human-Computer Interaction – INTERACT 2015: 15th IFIP TC 13 International Conference.* 2015; 159–176.
Publisher Full Text

Ceusters W, Smith B: **Aboutness: towards foundations for the information artifact ontology**. 2015.
Reference Source

Cipriani A, Seedat S, Milligan L, *et al.*: **New living evidence resource of human and non-human studies for early intervention and research prioritisation in anxiety, depression and psychosis.** *BMJ Ment Health.* 2023; **26**(1): e300759.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Clark LA, Cuthbert B, Lewis-Fernández R, *et al.*: **Three approaches to understanding and classifying mental disorder:** *ICD-11, DSM-5*, **and the National Institute of Mental Health's Research Domain Criteria (RDoC).** *Psychol Sci Public Interest.* 2017; **18**(2): 72–145.
PubMed Abstract | **Publisher Full Text**

Conway CC, Krueger RF, Cicero DC, *et al.*: **Rethinking the diagnosis of mental disorders: data-driven psychological dimensions, not categories, as a framework for mental-health research, treatment, and training.** *Curr Dir Psychol Sci.* 2021; **30**(2): 151–158.
Publisher Full Text

Crane D, Garnett C, Brown J, *et al.*: **Factors influencing usability of a smartphone app to reduce excessive alcohol consumption: think aloud and interview studies.** *Front Public Health.* 2017; **5**: 39.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Domhardt M, Engler S, Nowak H, *et al.*: **Mechanisms of change in Digital Health Interventions for mental disorders in youth: systematic review.** *J Med Internet Res.* 2021; **23**(11): e29742.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Elliott J, Lawrence R, Minx JC, *et al.*: **Decision makers need constantly updated evidence synthesis.** *Nature.* 2021; **600**(7889): 383–385.
PubMed Abstract | **Publisher Full Text**

European Bioinformatics Institute: **Ontology lookup service**. 2019.
Reference Source

Feczko E, Miranda-Dominguez O, Marr M, *et al.*: **The heterogeneity problem: approaches to identify psychiatric subtypes.** *Trends Cogn Sci.* 2019; **23**(7): 584–601.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Gardner C, Kleinman A: **Medicine and the mind - the consequences of psychiatry's identity crisis.** *N Engl J Med.* 2019; **381**(18): 1697–1699.
PubMed Abstract | **Publisher Full Text**

GBD 2019 Mental Disorders Collaborators: **Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease study 2019.** *Lancet*

Psychiatry. 2022; **9**(2): 137–150.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Hair K: **AD SOLES**. [Computer software]. 2022.
Reference Source

Hastings J: **Primer on ontologies.** *Methods Mol Biol.* In: *The gene ontology handbook.* Humana Press, New York, NY. 2017; **1446**: 3–13.
PubMed Abstract | **Publisher Full Text**

Hastings J, Ceusters W, Jensen M, *et al.*: **Representing mental functioning: ontologies for mental health and disease**. 2012.
Reference Source

Hastings J, Ceusters W, Smith B, *et al.*: **Dispositions and processes in the emotion ontology**. 2011.
Reference Source

He Y, Xiang Z, Zheng J, *et al.*: **The eXtensible Ontology Development (XOD) principles and tool implementation to support ontology interoperability.** *J Biomed Semantics.* 2018; **9**(1): 3.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Insel TR, Gogtay N: **National institute of mental health clinical trials: new opportunities, new expectations.** *JAMA Psychiatry.* 2014; **71**(7): 745–746.
PubMed Abstract | **Publisher Full Text**

Jackson RC, Balhoff JP, Douglass E, *et al.*: **ROBOT: a tool for automating ontology workflows.** *BMC Bioinformatics.* 2019; **20**(1): 407.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Johnstone L, Boyle M: **The power threat meaning framework: an alternative nondiagnostic conceptual system.** *J Humanist Psychol.* 2018; 0022167818793289.
Publisher Full Text

Kennett J, Friedrich C, Chiocchia V, *et al.* **Cognitive bias modification for social anxiety: protocol for a living systematic review of human studies and meta-analysis [version 2; peer review: 2 approved, 1 approved with reservations].** *Wellcome Open Res.* 2025; **9**: 657.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Larsen RR, Hastings J: **From affective science to psychiatric disorder: ontology as a semantic bridge.** *Front Psychiatry.* 2018; **9**: 487.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Leichsenring F, Steinert C, Rabung S, *et al.*: **The efficacy of psychotherapies and pharmacotherapies for mental disorders in adults: an umbrella review and meta-analytic evaluation of recent meta-analyses.** *World Psychiatry.* 2022; **21**(1): 133–145.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Marques MM, Wright AJ, Corker E, *et al.*: **The behaviour change technique ontology: transforming the Behaviour Change Technique Taxonomy v1 [version 2; peer review: 4 approved].** *Wellcome Open Res.* 2024; **8**: 308.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

McDonald S, Edwards HM, Zhao T: **Exploring think-alouds in usability testing: an international survey.** *IEEE Trans Prof Commun.* 2012; **55**(1): 2–19.
Publisher Full Text

Michie S, Thomas J, Johnston M, *et al.*: **The Human Behaviour-Change Project: harnessing the power of artificial intelligence and machine learning for evidence synthesis and interpretation.** *Implement Sci.* 2017; **12**(1): 121.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Michie S, West R, Finnerty AN, *et al.*: **Representation of behaviour change interventions and their evaluation: development of the upper level of the Behaviour Change Intervention Ontology [version 1; peer review:**

1 approved, 1 approved with reservations]. *Wellcome Open Res.* 2020; **5**: 123.
Publisher Full Text

Michie S, West R, Hastings J, *et al.*: **The Human Behaviour-Change Project phase 2: advancing behavioural and social sciences through ontology tools [version 1; peer review: not peer reviewed].** *Wellcome Open Res.* 2024; **9**: 730.
Publisher Full Text

Musen MA: **The Protégé project: a look back and a look forward.** *AI Matters.* 2015; **1**(4): 4–12.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

National Academies of Sciences, Engineering, and Medicine, Division of Behavioral and Social Sciences and Education, Board on Behavioral, Cognitive, and Sensory Sciences, *et al.*: **Ontologies in the behavioral sciences: accelerating research and the spread of knowledge.** The National Academies Press, 2022.
PubMed Abstract | **Publisher Full Text**

National Institute for Health Research (NIHR): **Guidance on co-producing a research project.** 2019.
Reference Source

Nature Editorial: **The best research is produced when researchers and communities work together.** *Nature.* 2018; **562**(7725): 7.
PubMed Abstract | **Publisher Full Text**

Norris E, Marques MM, Finnerty AN, *et al.*: **Development of an intervention setting ontology for behaviour change: specifying where interventions take place [version 1; peer review: 2 approved].** *Wellcome Open Res.* 2020; **5**: 124.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Open Biological and Biomedical Ontology (OBO) Foundry: **Principle: commitment to collaboration (principle 10).** 2019.
Reference Source

Ostinelli EG, Chiocchia V, Macleod M, *et al.*: **Pro-dopaminergic pharmacological interventions for anhedonia in depression: protocol for a living systematic review of human and non-human studies [version 1; peer review: 1 approved, 2 approved with reservations].** *Wellcome Open Res.* 2023; **8**: 425.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Patel V, Chisholm D, Parikh R, *et al.*: **Addressing the burden of Mental, Neurological, and Substance use disorders: key messages from *Disease Control Priorities, 3rd edition*.** *Lancet.* 2016; **387**(10028): 1672–1685.
PubMed Abstract | **Publisher Full Text**

Peute LW, de Keizer NF, Jaspers MW: **The value of Retrospective and Concurrent Think Aloud in formative usability testing of a physician data query tool.** *J Biomed Inform.* 2015; **55**: 1–10.
PubMed Abstract | **Publisher Full Text**

Robinaugh DJ, Hoekstra RHA, Toner ER, *et al.*: **The network approach to psychopathology: a review of the literature 2008–2018 and an agenda for future research.** *Psychol Med.* 2020; **50**(3): 353–366.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Schenk PM, Wright AJ, West R, *et al.*: **An ontology of mechanisms of action in behaviour change interventions [version 2; peer review: 3 approved].**

Wellcome Open Res. 2024; **8**: 337.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Seppälä S, Schreiber Y, Ruttenberg A: **Textual and logical definitions in ontologies.** TABLE&OF&CONTENTS, 2014; 35.
Reference Source

Sharp C, Kaplan RM, Strauman TJ: **The use of ontologies to accelerate the behavioral sciences: promises and challenges.** *Curr Dir Psychol Sci.* 2023; **32**(5): 418–426.
Publisher Full Text

Siafis S, Chiocchia V, Macleod MR, *et al.*: **Trace Amine-Associated Receptor 1 (TAAR1) agonism for psychosis: a living systematic review and meta-analysis of human and non-human data [version 1; peer review: 3 approved].** *Wellcome Open Res.* 2024; **9**: 182.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Siafis S, McCutcheon R, Chiocchia V, *et al.*: **Trace Amine-Associated Receptor 1 (TAAR1) agonists for psychosis: protocol for a living systematic review and meta-analysis of human and non-human studies [version 1; peer review: 2 approved].** *Wellcome Open Res.* 2023; **8**: 365.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Smith B, Ceusters W, Klagges B, *et al.*: **Relations in biomedical ontologies.** *Genome Biol.* 2005; **6**(5): R46.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Smoktunowicz E, Barak A, Andersson G, *et al.*: **Consensus statement on the problem of terminology in psychological interventions using the internet or digital components.** *Internet Interv.* 2020; **21**: 100331.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

White R, van den Eijnden M, Donskoy AL, *et al.*: **Lived experience involvement in research funding: taking a more systematic approach.** *Nat Mental Health.* 2023; **1**(3): 157–159.
Publisher Full Text

WHO: **Mental health.** World Health Organization, 2022.
Reference Source

Wright S, Chiocchia V, Elugbadebo O, *et al.*: **The therapeutic potential of exercise in Post-Traumatic Stress Disorder and its underlying mechanisms: a living systematic review of human and non-human studies [version 4; peer review: 1 approved, 2 approved with reservations].** *Wellcome Open Res.* 2025a; **9**: 720.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Wright S, Furukawa TA, Macleod M, *et al.*: **Mechanisms through which exercise reduces symptom severity and/or functional impairment in Post-Traumatic Stress Disorder (PTSD): protocol for a living systematic review of human and non-human studies [version 3; peer review: 2 approved, 1 not approved].** *Wellcome Open Res.* 2025b; **8**: 494.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Wright AJ, Norris E, Finnerty AN, *et al.*: **Ontologies relevant to behaviour change interventions: a method for their development [version 3; peer review: 2 approved, 1 approved with reservations].** *Wellcome Open Res.* 2020; **5**: 126.
PubMed Abstract | **Publisher Full Text** | **Free Full Text**

Open Peer Review

Current Peer Review Status: ❓ ✔ ✔ ❓

Version 3

Reviewer Report 17 September 2025

https://doi.org/10.21956/wellcomeopenres.27402.r130881

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We all are happy with the revisions the author made.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Fidelity, Musculoskeletal health, participatory approaches, stakeholder involvement, Biopsychosocial paradigm, motivation, behavioural psychology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 2

Reviewer Report 19 February 2025

https://doi.org/10.21956/wellcomeopenres.25788.r116802

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Thank you for the opportunity to review this interesting and timely paper, which treats an
important topic with possible clinical implications: create a comprehensive ontology on psychosis,
anxiety and depression to better reflecting the diversity and complexity behind definitions,
establishing links between them and providing with useful resources regarding clinical
implications.

The quality of this work can be further improved on following aspects.

1. Better definition of the perimeter in which this initiative can be usefully implemented in regards
with cultural contexts and use of different classification systems. Indeed, stakeholders come from
different geographical areas, which poses new methodological challenges. While stakeholders
may use western classification systems, not all of them share the same cultural beliefs and
practices and it is unclear whether and how these elements are taken into consideration? The
same goes for the language and representativity of published materials that is going to be used.
This is of high importance, especially in a endeavours that plan to include persons with lived
experience, let alone professionals that are carriers of different cultures and languages.

In addition, some sentences may be misleading, such as '' to capture any population and
intervention''. This may lead the reader think that a universality or a complete representativity is a
given, yet the initiative is based only on western classification systems and paradigms, leaving out
other classification systems and entire geographic zones, such as East Asia, Southeast Asia etc.
While it practically is impossible to include everyone ant take into account absolutely everything, it
is important to acknowledge this limitations and be as clear and transparent about them.

2. Advisory board composition remains blurry and it remains unclear how representativity will be
assured. The same goes for stakeholders.

3. While the inclusion of persons with lived experience is both commendable and necessary, it
remains unclear what framework will be put in place to assure true participation. It is often a big
challenge, when it comes to transdisciplinary collaborations and making sure that environments
conducive to making everyone's voice be heard it is generally useful to refer to some collaboration
framework or guiding principles of user-inclusion. In addition, the precision '' at least one
experiential advisor'' raises questions: is such a low number enough to bring the input needed.

4. Regarding living systematic reviews, it will be important to specify how extracted information
will be organised and further utilised? Authors mention 3 parallel reviews and excel spreadsheets
with annotations. But how those annotations will be structured? What analytical framework is
going to be used to assure that three parallel reviews will obey the same logic? At which point
qualitative analysis will be conducted and how it will be driven?

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Partly

Are sufficient details of the methods provided to allow replication by others?

Partly

Are the datasets clearly presented in a useable and accessible format?

Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Early Intervention in Psychiatry, early psychosis, urban mental health, participatory methodologies.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 13 January 2025

https://doi.org/10.21956/wellcomeopenres.25788.r114717

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Thank you very much for the opportunity to review this interesting and important piece of work. In general, the authors have succeeded in clearly describing the complex process of developing

this new ontology within the scope of mental health, presenting it in a clear and accessible way. This work aims to establish consistent terminology for mental health conditions, thereby enhancing behavioural science research in this area. It is clear that the initial round of reviews has generated many valuable revisions.

We particularly appreciate the high degree of stakeholder involvement throughout the process and the attempt to visualize the process with the aid of figures. We also appreciate the list of definitions presented in Table 1 and throughout the text, which enhances the understanding of the methodology and background.

We do, however, have some concerns that we recommend the authors to address, along with questions for clarification and suggestions that may be useful for future efforts in developing the ontology and refining the protocol.

General comments:
1. **Scope of mental health disorders**
   1.1. We believe that there are some incongruencies in the use of the term "mental health", that require attention. The authors name the ontology a "mental health ontology" and define mental health as "a state of mental wellbeing…". However, the reviews focus on three mental health conditions, which raise the question: should this ontology be defined as an ontology of mental health *conditions*? Furthermore, we wonder whether it can be defined as an ontology of mental health conditions when only three conditions are targeted. We would also suggest more justification as to why those three conditions have been chosen.

   1.2. We suggest adding clear definitions of the three chosen conditions as for example psychosis, can cover a range of different diagnoses with diverse symptoms (schizophrenia, schizoaffective disorders, bipolar disorder, substance-induced psychosis, post-partum etc.).

2. Stakeholder involvement and leadership
We appreciate the attempt to make a thorough stakeholder involvement throughout the developmental process. We have the following suggestions to further enhance the stakeholder involvement :

- Leadership team: what is the distribution across clinicians, experts with lived experience, and researchers (from various fields)? And what counts as clinicians, experts with lived experience (i.e., definition)?
- How often approx. will the advisory board meet? And what will be the distribution across the various types of members?
- Stakeholder consultations: It is a bit unclear whether these are only survey-based? Is there any face-to-face consultation with the group? This is unclear and should be specified. Both would add value in different ways.
- It would be useful with a more iterative consultation phase, where, for example, participants with lived experience take part not in a single consultation but several over time, as these participants often need time to reflect on their lived experiences. An iterative process would allow for participants to refine and expand on their feedback and will therefore provide richer data. This process would foster more engagement, and more in-depth data.
- How will the research team manage disagreements between different stakeholders in

terms of input into the ontology?
  ○ "The updated upper level of the ontology will be presented to the ontology advisory board to verify that the changes to the ontology are appropriate to both academic experts and experiential advisors in mental health." – how will potential discrepancies be handled to inform the ontology?

3. Systematic reviews and ontology development
  ○ Step 2: it is stated "Approximately three systematic reviews on human studies will be conducted per year, completing in January 2026. Each is led by two or three researchers with an MSc or PhD in an area related to mental health." How are the numbers of systematic reviews decided on? It would also be useful with some indication of the topics (indicative titles) for these systematic reviews.

    Please notice that we do not possess qualifications to review parts about repository building or machine learning.

Specific comments:

Page 2
Plain language summary:
  ○ Why are 5 steps outlined here and not 8 steps as described in the methods section? Please align these.
  ○ The plain language summary could be more "plain"/lay like. E.g., concepts, entities, classification frameworks are unlikely to be understood by a lay public.
Page 4
1. The "piece by piece approach" to mental health research (Gardner & Kleinman, 2019): Mental health research
  ○ The phrasing "Piece by piece" could lead to the misunderstanding that this phrasing refers to a stepwise process more than a parallel process indicating development in silos. The authors could consider rephrasing the wording "piece-by-piece" – perhaps "piecemeal" approach would be clearer?
  ○ In addition, the authors mention that research happens in silos in different fields. How will they ensure that this is not just a separate "behavioural science" silo and how will they facilitate the availability and use by others?

4. Lack of focus on studying the mechanisms of mental health interventions
  ○ We are unsure whether "biomarkers" and "targets" are the most appropriate outputs for research about mechanisms. We suggest either elaborating on the following "can provide evidence for biomarkers for pharmacological, and targets for psychological and social interventions and" or delete it in order not to be too narrow or misleading in the description.
  ○ "...evaluating existing evidence across animal and human data." Why animal?
  ○ "members from Canada, India, Nigeria, Philippines and Zimbabwe." How come there are no members from Europe?

Page 5
  ○ In the sentence starting with "In the GALENOS project, the…." you are referring to other ontologies. Can you specify exactly which ontologies you are referring to?

○ In the sentence: "Constructs that overlap across systematic reviews can be identified and linked." Does this refer to linkage between various ontologies or reviews?

Page 6:
○ It is a very positive and relevant feature that the upper-level structure will be broad enough to be relevant to any mental health condition.
○ The following sentence is unclear: Mental health classification systems such as DSM-5, ICD and RDoC (Clark et al., 2017) can be explicitly supported through cross-references to relevant ontological entities.

Page 7:
○ When stating "provide upper-level entities and structure to serve as a foundation for developing an extensive ontology of mental health." Do the authors mean a new ontology on mental health in general?

○ ***Step 1: Specifying the scope of the Mental Health Ontology***
Regarding: "Therefore, we will only include detailed entities where required for the associated data extraction of these reviews, focusing on anxiety, depression and psychosis. This scope will be refined during later steps." We believe it is very important to leave the ontology development open for future extensions because the described approach will by the nature of the process limit the amount of entities to the included reviews leaving out potential important aspects, especially regarding promising/evolving new areas within mental health research, that might not be captured by existing reviews.
○ ***Step 2: Identifying, labelling and defining entities needed for living systematic reviews***
Consider being more precise about the minimal criteria instead of a vague description, allowing for large variations in qualifications.
When writing: "These data will be reviewed in an Excel spreadsheet, and a researcher will annotate the categories for which data are extracted, using entities or developing new entities in the ontology." - Does this mean annotating scientific papers? If so, please specify.
○ On page 7, in the first paragraph under Methods, the authors refer to online meetings where members of the Advisory Board will provide feedback. If we understand correctly, members of the Advisory Board will have the role of supervising the development of Ontology and providing their expertise, and stakeholders will include board members as well as other individuals. This could have been made clearer throughout the text as well as in Figure 2 concerning the role of both the Advisory Board and the stakeholder groups.

Page 8
Figure 2. Overview of steps to develop the Mental Health Ontology.
○ This is a nice overview but is it possible to add details about stakeholder involvement - e.g. in different colours depending on the type/number of stakeholders and methods (survey/interview etc) for involvement.
○ Step two continued)
In which cases could the work on this ontology lead to relevant changes in other ontologies? This is a bit unclear to us.
Page 9
Step 3: Identifying and refining entities needed to structure the upper level of the ontology
○ In general, we believe it is very important for the authors to ensure that the upper-level entities sufficiently broad

○ Regarding presenting the first draft of the entities – Would it be feasible for the wider GALENOS team and advisory board to provide suggestions for upper-level entities before they are presented with the first draft. This to make sure that important aspects are not left out early in the process.

Step 4: Iterative stakeholder consultations of the Mental Health Ontology

○ Can the authors specify stakeholder criteria?

○ How will the authors ensure stakeholders are well represented in terms of education level, age and gender etc?

○ Regarding stakeholder survey – consider presenting response options in the protocol paper.

Pages 10-11

○ Step 8 (Evaluating the ontology): More information on the participants is required. Who are they? How many? Which groups will be represented?

○ Do members of the GALENOS team overlap with the author team? Please specify

○ It remains unclear how the researchers responsible for the development of the Mental Health Ontology´s will discuss the feedback and changes suggested by stakeholders (page 10, first paragraph under the heading "Analysis of stakeholder consultations"). This could be briefly clarified in one sentence with supporting references.

Page 11

○ "Applying the ontology to develop tools for data searching, visualising, extraction and synthesis, and partial automation of these processes the Mental Health Ontology will be used for annotations of the 'living evidence' extracted from the literature and stored in the project's online data repository." It is unclear to us what this section means - especially regarding the living evidence. Can the authors please rephrase or clarify?

Is the rationale for, and objectives of, the study clearly described?

Yes

Is the study design appropriate for the research question?

Yes

Are sufficient details of the methods provided to allow replication by others?

Partly

Are the datasets clearly presented in a useable and accessible format?

Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Fidelity, Musculoskeletal health, participatory approaches, stakeholder involvement, Biopsychosocial paradigm, motivation, behavioural psychology

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have

significant reservations, as outlined above.

Author Response 22 Aug 2025
Paulina Margarete Schenk

Thank you very much for the opportunity to review this interesting and important piece of work. In general, the authors have succeeded in clearly describing the complex process of developing this new ontology within the scope of mental health, presenting it in a clear and accessible way. This work aims to establish consistent terminology for mental health conditions, thereby enhancing behavioural science research in this area. It is clear that the initial round of reviews has generated many valuable revisions.

We particularly appreciate the high degree of stakeholder involvement throughout the process and the attempt to visualize the process with the aid of figures. We also appreciate the list of definitions presented in Table 1 and throughout the text, which enhances the understanding of the methodology and background.

We do, however, have some concerns that we recommend the authors to address, along with questions for clarification and suggestions that may be useful for future efforts in developing the ontology and refining the protocol. **Response:** We thank the reviewers for taking the time to review this protocol and providing valuable feedback to strengthen it. **General comments:**
1. **Scope of mental health disorders**
   1.1. We believe that there are some incongruencies in the use of the term "mental health", that require attention. The authors name the ontology a "mental health ontology" and define mental health as "a state of mental wellbeing...". However, the reviews focus on three mental health conditions, which raise the question: should this ontology be defined as an ontology of mental health *conditions*? Furthermore, we wonder whether it can be defined as an ontology of mental health conditions when only three conditions are targeted. We would also suggest more justification as to why those three conditions have been chosen.

Response: We appreciate the feedback. Based on the reviewer feedback in the first round, we would like to note that the protocol has been titled "Towards an ontology of mental health..." This was to emphasise that this work is not intended to develop an extensive ontology for all of the domain of mental health but to provide a starting point for such an ontology. As underlined in the protocol, we are aiming to develop an upper-level structure that helps capture evidence about mental health beyond the three conditions that the GALENOS Project focuses on. However, as the reviewers note, the detailed entities are developed to focus on aspects of anxiety, depression and psychosis as needed for the systematic reviews (see Step 2 of the Methods). On the second point regarding why this ontology is not called an ontology of mental health conditions, this phrase would restrict the intended scope to only the conditions themselves and associated symptomatology. However, the scope of the ontology encompasses protective factors and positive outcomes of mental health in general. Accordingly, the upper level of the ontology needs to accommodate positive aspects of mental health for the current use case and beyond, not only conditions and symptomatology. To make the scope of the ontology clearer, adjustments have been made to Step 1 of the Methods (see in bold):

- ○ *"The preliminary scope of the Mental Health Ontology will cover: (1) human mental health conceptualisations, including constructs representing symptoms, conditions (i.e., diagnoses)* **and wellbeing and promoting mental health rather than merely treating dysfunction with mental health**..."
- ○ *"Therefore, we will only include detailed entities where required for the associated data extraction of these reviews, focusing on* **research questions related to** *anxiety, depression and psychosis."*

For clarity, the title for Step 1 has also been updated to "Specifying the scope of the Mental Health Ontology **within the GALENOS Project**", and the caption of Figure 2 has been updated to "Overview of steps to develop the Mental Health Ontology **within the GALENOS Project**"

1.2. We suggest adding clear definitions of the three chosen conditions as for example psychosis, can cover a range of different diagnoses with diverse symptoms (schizophrenia, schizoaffective disorders, bipolar disorder, substance-induced psychosis, post-partum etc.).
Response: We agree that the three conditions focused on, anxiety, depression and psychosis, cover a range of conditions and diagnoses with diverse symptoms. These conditions are among the top leading causes of global burden of ill mental health (GBD Collaborators, 2019); they were additionally prioritised as research in these areas can be 'triangulated' combining animal and human research to give more comprehensive insights into these areas (Cipriani et al., 2023). These terms are used as organising umbrella topics in the GALENOS Project, with the systematic reviews focusing on more specific topic areas. In most cases, more specific conditions, diagnosis or symptoms, such as social anxiety (Kennett et al., 2025), are investigated within the systematic reviews. We attempt to precisely capture these as labels assigned to people based on pre-specified criteria and, where relevant, we also capture entities for more specific symptoms.   **2. Stakeholder involvement and leadership**
We appreciate the attempt to make a thorough stakeholder involvement throughout the developmental process. We have the following suggestions to further enhance the stakeholder involvement:

- ○ Leadership team: what is the distribution across clinicians, experts with lived experience, and researchers (from various fields)? And what counts as clinicians, experts with lived experience (i.e., definition)?

Response: The leadership described in the Introduction is for the GALENOS Project as a whole, rather than for the ontology work. As indicated in the Introduction, more details about these members can be found online on the GALENOS website: https://www.galenos.org.uk/about. We have added clearer signposting that information about contributors of the project can be found on the website:

- ○ "These contributors include clinicians, researchers and lived experience advisors (mental health activists, campaigners and advocates), with expertise across data science, psychology and psychiatry. *Detailed information about the GALENOS Project* **and its contributors** *can be found on the project website (* *https://www.galenos.org.uk/about)...*"

As this leadership was not involved in the details of the current work, we did not add more information here. However, to provide a better overview of the researchers involved in the current work, we added the following information to the beginning of the Methods section:

○ *"The development of ontology is being led by two researchers with post-graduate degrees in psychology and experience in mental health research (MS & PS). Two senior researchers, both with experience in ontologies and clinical psychology (JH & SM), supervise and regularly provide feedback on the ontology's development and application. The project manager of GALENOS (JP) and two researchers leading systematic reviews within the project (CF & JK) also continuously support the work to refine the ontology and its application. Additional members across the GALENOS Project, such as from the data repository team (DB) and other systematic review team members (SS & SW), also regularly provide feedback to improve this work."*

The lived experience advisors include mental health activists, campaigners and advocates from a range of countries (see https://www.galenos.org.uk/GLEAB). We added a clarification on this in the protocol:

○ *"These contributors include clinicians, researchers and lived experience advisors (**mental health activists, campaigners and advocates**), with expertise across data science, psychology and psychiatry."*

○ How often approx. will the advisory board meet? And what will be the distribution across the various types of members?

Response: The advisory board meets 1-2 times a year, depending on the needs of the project. Details of this has been added to the Methods section "Set up the Mental Health Ontology Advisory Board":

○ *"They will be invited to attend online meetings **once or twice a year, in which they will be given an overview of the methods and progress in developing the ontology. In these meetings, they will be prompted** to provide feedback about the methodology, emerging ontology content and organisation and ontology-structured evidence. They will also be invited to submit feedback to written documents that will inform ontology development **and join the formal stakeholder consultation to refine the ontology content (see Step 4) and usability evaluations of the ontology's application (see Step 8)."***

As various advisory board members work across interdisciplinary fields, an exact breakdown of their expertise is not possible. However, additional details have been added to provide a better overview of the board's composition:

○ *"Many advisory board members have expertise in more than one discipline (e.g., clinical experience and health psychology research experience), with some focusing on specialised topics such as paediatric traumatic stress, pain and chronic illness, physical activity, mood disorders and various others. The members include 14 with professor, associate or assistant professor roles at universities (with some also working as clinicians),* a research fellow (JK) *and two lived experience advisors with undergraduate or post-graduate degrees related to psychology."*

○ Stakeholder consultations: It is a bit unclear whether these are only survey-based? Is there any face-to-face consultation with the group? This is unclear and should be specified. Both would add value in different ways.

Response: The stakeholder consultations were planned to be primarily survey based. However, the methods planned for the upper level evolved to include a second round of feedback from the advisory board. Relevant sections in Step 4 have been updated to communicate this:

○ *"This consultation will primarily be conducted through a Qualtrics survey, followed by a*

second round of feedback from advisory board members, involving an online meeting and then written input over email (see details in 'Analysis of stakeholder consultations')."

○ *"The updated upper level will be presented to the ontology advisory board **in a meeting** to verify that the changes to the ontology are appropriate to both academic experts and lived experience advisors in mental health. **Following the meeting, advisory board members will be invited to share additional comments via email to allow them more time to provide feedback on the changed entities. Drawing on these comments, any disagreements and potential updates will be discussed by the ontology development team, with a transparent log being kept showing how each comment was addressed**. These logs, recording how each piece of feedback is addressed, will be shared on Open Science Framework."*

It should also be noted that we adjusted the planned work of the stakeholder consultation to only focus on the upper level's improvements. Instead, the usability work in the later stages will investigate the clarity and usefulness of the entities mapped to systematic reviews and therefore included in the repository. This was done to focus more on the usability of the ontology's application within the repository, instead of conducting a separate stakeholder review for the entities that will be used in the repository (without the relevant context). The relevant sections were removed from Step 4. Instead, the usability section has been updated to more clearly reflect the work (see Step 8):

○ *"In line with stakeholder consultations on ontologies (3–29 participants) as part of the BCIO (Michie et al., 2020; Norris et al., 2020) and relevant usability studies (Bruun & Stage, 2015), we will aim to recruit at least 10 participants. As the repository is likely to be used by people interested in data synthesis, the criteria will be for participants to have experience contributing to scoping or systematic reviews or applying review evidence in work related to mental health. To ensure that we include participants from a range of backgrounds, we will ask the lived experience advisors of the GALENOS Project to circulate invitations to their networks.*

Participants will first be given an overview of the data repository by a researcher and then will be prompted to engage with the data in the repository based on their interests (e.g., finding a living systematic review, and data on a specific category, such as mean age). After participants have explored the repository on their own, a researcher will provide them with use cases about finding specific ~5 categories within the repository, visualising the data within these categories and engaging with the ontology classes mapped to the categories. To provide a wider range of different categories to engage with, the researchers will randomly select the ~5 categories from the full list of extracted categories for each participant. We will use think-aloud methods to explore the usability and acceptability of the repository interface (McDonald et al., 2012; Peute et al., 2015), including whether entity labels and definitions used for the systematic reviews are sufficiently clear. Following, the interviews, we will ask participants to fill out around 10 survey questions, adapted from the System Usability Scale (SUS) on the usability of digital systems (Brooke, 1996). The think aloud method and the survey questions are expected to take around 45-60 minutes to complete."

○ It would be useful with a more iterative consultation phase, where, for example, participants with lived experience take part not in a single consultation but several over time, as these participants often need time to reflect on their lived experiences. An iterative process would allow for participants to refine and expand on their feedback and will therefore provide richer data. This process would foster more engagement, and more in-depth data.

Response: We appreciate the suggestion for a more iterative consultation phase. We have adjusted the consultation of the upper level to include more iterative feedback on the updates from advisory board members (see Step 4: Iterative stakeholder consultations of the Mental Health Ontology):

- *"The updated upper level will be presented to the ontology advisory board **in a meeting** to verify that the changes to the ontology are appropriate to both academic experts and lived experience advisors in mental health. **Following the meeting, advisory board members will be invited to share additional comments via email to allow them more time to provide feedback on the changed entities. Drawing on these comments, any disagreements and potential updates will be discussed by the ontology development team, with a transparent log being kept showing how each comment was addressed**. These logs, recording how each piece of feedback is addressed, will be shared on Open Science Framework."*

Unfortunately, the team does not have enough capacity to include iterative reviews for all parts of the ontology. Lived experience advisors, who are part of the project, have limited capability to be involved in the project as well, creating challenges for a more in-depth process than the proposed one. Please note that this section was updated from the previous round of review to make this work more realistic, and further adjustments needed to be made to focus more on the usability step (see Step 8), as indicated above.

- How will the research team manage disagreements between different stakeholders in terms of input into the ontology?

Response: The descriptions in Step 4 have been updated to specify more clearly how disagreements will be addressed for each round of feedback:

- "*In these discussions, the team will consider how the feedback will be addressed and review disagreements between stakeholder comments, documenting the rationale for implementing relevant changes in a log.*"
- "*Following the meeting, advisory board members will be invited to share additional comments via email to allow them more time to provide feedback on the changed entities. Drawing on these comments, any disagreements and potential updates will be discussed by the ontology development team, with a transparent log being kept showing how each comment was addressed.*"

In response to another reviewer's comments, we also added detail to more clearly communicate our aim to make the upper level as inclusive as possible:

- "*To ensure that the ontology's upper level captures a range of geographical and social contexts, we will aim to update the entities and their structure to be as inclusive as possible. Examples include updating entity labels and definitions to be broader to capture wider contexts or adding specific entities to better capture aspects of mental health that were previously insufficiently represented.*"

The final decisions about the updates to the ontology classes will be made by the research team. Decisions on the changes will be logged, along with the feedback received, to provide a transparent trail of the decisions made. The explanation of this log has been updated to explain that the relevant log will be included on OSF:

- "*We will record decisions regarding how each piece of feedback will be addressed**, sharing this log on Open Science Framework**.*"

- "The updated upper level of the ontology will be presented to the ontology advisory board to verify that the changes to the ontology are appropriate to both academic

experts and experiential advisors in mental health." – how will potential discrepancies be handled to inform the ontology?

Response: The following details have been added to the section on "Analysis of stakeholder consultation" to show how these comments are being addressed:

- "*Following the meeting, advisory board members will be invited to share additional comments via email to allow them more time to provide feedback on the changed entities. Drawing on these comments, any disagreements and potential updates will be discussed by the ontology development team, with a transparent log being kept showing how each comment was addressed."*

3. Systematic reviews and ontology development

- Step 2: it is stated "Approximately three systematic reviews on human studies will be conducted per year, completing in January 2026. Each is led by two or three researchers with an MSc or PhD in an area related to mental health." How are the numbers of systematic reviews decided on? It would also be useful with some indication of the topics (indicative titles) for these systematic reviews.

Response: The number of the systematic reviews is guided by the GALENOS Project proposal and decided on by the leadership team. The plan was to generate about three systematic reviews per year, as this was deemed feasible given the capacity within the project. The ontology development responds to the needs of the project, integrating the evidence of the resulting systematic reviews. A table has now been added to provide an overview of the topics covered as part of the living systematic reviews planned (see Table 2).

Please notice that we do not possess qualifications to review parts about repository building or machine learning. **Response:** Thank you for noting this.

Specific comments:

Page 2

Plain language summary:

- Why are 5 steps outlined here and not 8 steps as described in the methods section? Please align these.

Response: Thank you for the suggestion. We have updated the plain language summary to better align with the overall abstract; see the updates to the method specified within the plain language summary:

- "*The ontology will be developed and applied by (1) specifying what it aims to cover, (2) identifying concepts that are needed in GALENOS Project's systematic reviews (e.g., information on people's ages and their diagnosis), (3) identifying broad concepts relating to mental health, such as 'people' or 'mental health intervention', that help organise more detailed concepts (e.g., 'age' organised as information relevant to people), (4) seeking feedback from mental health experts and people with lived experience to improve the ontology, (5) linking concepts by specifying their relationships (e.g., 'age' is a characteristic of 'people'), (6) making the ontology computer-readable and available online, (7) using the ontology to structure evidence from different systematic reviews in an online repository, and (8) evaluating whether this online repository is useable."*

- The plain language summary could be more "plain"/lay like. E.g., concepts, entities, classification frameworks are unlikely to be understood by a lay public.

Response: We appreciate the feedback. In line with the suggestion, we have changed 'concept' to 'category'. The term 'entity' was removed as it is not essential within the plain

language summary. We changed the term 'classification system' to 'categorisation system'. We have attempted to simplify the language; the updated version attempts to balance the need to reflect the work simply, clearly and accurately.   **Page 4**

1. The "piece by piece approach" to mental health research (Gardner & Kleinman, 2019): Mental health research

- The phrasing "Piece by piece" could lead to the misunderstanding that this phrasing refers to a stepwise process more than a parallel process indicating development in silos. The authors could consider rephrasing the wording "piece-by-piece" – perhaps "piecemeal" approach would be clearer?

Response: We changed the phrasing to "Silos in mental health research" in the Introduction (p. 4) to be clearer.

- In addition, the authors mention that research happens in silos in different fields. How will they ensure that this is not just a separate "behavioural science" silo and how will they facilitate the availability and use by others?

Response: Ontologies should be designed to cross disciplinary boundaries and this is also the focus of the GALENOS Mental Health Ontology and the Behaviour Change Intervention Ontology. The current ontology will be aligned with the Behaviour Change Intervention Ontology, including some broad and overlapping entities (e.g., about interventions). However, the extent to which the Mental Health Ontology will be used across disciplines beyond the social and behavioural sciences will depend on dissemination and on providing tools and resources to facilitate this. The APRICOT (Advancing behavioural and social sciences through ontology tools) Project will help disseminate ontologies (including the Mental Health Ontology) and related tools across disciplines. A sentence reflecting this has been added to the Conclusion:

- "The Mental Health Ontology will be developed and maintained as part of the GALENOS Project, but beyond this project, the ontology will also be maintained alongside the BCIO as part of the **APRICOT (Advancing behavioural and social sciences through ontology tools) Project,** a 5-year long US National Institutes of Health (NIH) grant (https://reporter.nih.gov/project-details/10938088). During this time, any issues on the ontology that are reported on GitHub will be tracked, responded to and, where needed, addressed by updating the ontology. **In addition, this project will support the dissemination of the ontology, introducing it to ontology developers and users interested in structuring knowledge about mental health across disciplines."**

4. Lack of focus on studying the mechanisms of mental health interventions

- We are unsure whether "biomarkers" and "targets" are the most appropriate outputs for research about mechanisms. We suggest either elaborating on the following "can provide evidence for biomarkers for pharmacological, and targets for psychological and social interventions and" or delete it in order not to be too narrow or misleading in the description.

Response: The reference to 'targets' was made to more generally refer to mechanisms, which are targets within interventions. 'Biomarkers' are relevant within pharmacological interventions and relate to studying mechanisms, but we agree that the language around these could be clearer in the relevant point's title. In line with the current comment, we have updated the relevant title to read as follows (see bolded phrase for changes):

- "*Lack of focus on studying the mechanisms **and biomarkers** within mental health interventions*"

○ "…evaluating existing evidence across animal and human data." Why animal?

Response: Evaluating and integrating evidence across animal and human data is part of the GALENOS Project's overarching aims; these types of data produce evidence with different systematic errors and biases and triangulating them allows more comprehensive insights into the chosen topic area (Cipriani et al., 2023). However, as indicated in Step 1 (Specifying the scope of the GALENOS Mental Health Ontology), the ontology itself will focus on human data.

○ "members from Canada, India, Nigeria, Philippines and Zimbabwe." How come there are no members from Europe?

Response: Members from Europe are already well represented in the leadership team (as indicated in the early part of the selected sentence). The aim of the Global Lived Experience Advisory Board is to integrate a wider range of perspectives into the decision-making process of the GALENOS Project as a whole.

Page 5

○ In the sentence starting with "In the GALENOS project, the…." you are referring to other ontologies. Can you specify exactly which ontologies you are referring to?

Response: Thank you for the comment. The sentence is from the Introduction, so only a small edition has been made for clarity adding "where relevant":

○ "*In the GALENOS Project, the ontological entities are developed or reused from other ontologies, **where relevant**, to organise constructs for which data are extracted in the systematic reviews.*"

We provide more details about the methods for identifying relevant ontologies in the Methods Section, including examples of the ontologies we are planning to draw on, please see in Step 2:

○ *"Entities from other ontologies will be identified by using specialist ontology databases, e.g., the Ontology Lookup Service (European Bioinformatics Institute, 2019), and where appropriate, these entities will be reused or cross-referenced in the Mental Health Ontology. For example, we will reuse relevant parts from the Behaviour Change Intervention Ontology (BCIO; Michie et al., 2020), the Mental Functioning Ontology (MFO; Hastings et al., 2012), Emotion Ontology (MFOEM; Hastings et al., 2011) and Information Artifact Ontology (IAO; Ceusters & Smith, 2015)."*

○ In the sentence: "Constructs that overlap across systematic reviews can be identified and linked." Does this refer to linkage between various ontologies or reviews?

Response: Thank you for noting this. The sentence has been updated to be clearer:

○ "*Constructs that overlap across systematic reviews can be identified and linked **by mapping these to the Mental Health Ontology and organising them in an online repository structured by the ontology**.*"

Page 6:

○ It is a very positive and relevant feature that the upper-level structure will be broad enough to be relevant to any mental health condition.

Response: Thank you for the positive feedback on this. We have also updated the aims of the stakeholder consultation to more clearly indicate that we intend to be inclusive enough to capture positive and negative mental health experiences:

○ *"This consultation on the upper-level entities aims to ensure that the ontology's broader structure: (1) clearly reflects broad entities important to specify **people having positive or negative experiences related to their mental health**"*

○ The following sentence is unclear: Mental health classification systems such as DSM-5, ICD and RDoC (Clark et al., 2017) can be explicitly supported through cross-references to relevant ontological entities.

Response: To be clearer, the relevant sentence has been changed to:

○ ***"In the future, the ontology can be linked to existing** mental health classification systems such as DSM-5, ICD and RDoC (Clark et al., 2017) **by associating ontological entities with** cross-references **to relevant DSM/ICD/RDoC concepts or categories (e.g., diagnosis).**"*

Page 7:

○ When stating "provide upper-level entities and structure to serve as a foundation for developing an extensive ontology of mental health." Do the authors mean a new ontology on mental health in general?

Response: The aim refers to the upper-level entities and structure can be used to expand the ontology to cover aspects of mental health more extensively in the future. It has been updated to be clearer:

○ "...*provide upper-level entities and structure to serve as a **foundation for expanding this ontology into** an extensive ontology of mental health*."

○ ***Step 1: Specifying the scope of the Mental Health Ontology***
Regarding: "Therefore, we will only include detailed entities where required for the associated data extraction of these reviews, focusing on anxiety, depression and psychosis. This scope will be refined during later steps." We believe it is very important to leave the ontology development open for future extensions because the described approach will by the nature of the process limit the amount of entities to the included reviews leaving out potential important aspects, especially regarding promising/evolving new areas within mental health research, that might not be captured by existing reviews.

Response: The title for Step 1 has been updated to "Specifying the scope of the Mental Health Ontology **within the GALENOS Project**". We need to reflect the scope to be realistic within the current project. As indicated, the detailed entities that will be added will focus on the application of the ontology, while the upper level of the Mental Health Ontology will accommodate the addition of entities on more varied topics in the future.

○ ***Step 2: Identifying, labelling and defining entities needed for living systematic reviews***
Consider being more precise about the minimal criteria instead of a vague description, allowing for large variations in qualifications.
When writing: "These data will be reviewed in an Excel spreadsheet, and a researcher will annotate the categories for which data are extracted, using entities or developing new entities in the ontology." - Does this mean annotating scientific papers? If so, please specify.

Response: Thank you for the comment. The paragraph refers to the extraction templates that are used in the systematic reviews, which will be used to inform the entities in the

ontology. To be clearer, several changes have been made to the Step 2 description. We described the purpose of this step earlier on:

○ "*To ensure the ontology is fit for structuring the GALENOS online repository, entities will be identified to capture the data extracted in the GALENOS Project's living systematic reviews. The project's ontology development and systematic review teams will work together to identify and refine these ontological entities.*"

We also rephrased the paragraphs describing the mapping process to identify ontological entities to capture the categories for which data is extracted in the systematic reviews:

○ "*Once each review is completed, the ontology development team will review the data extracted within the systematic reviews from published papers (e.g., mean age and mental health outcomes) in an Excel spreadsheet. The team will focus on formally capturing the categories for which data is extracted (e.g., mean age) in the ontology, rather than capturing the entire extracted dataset (e.g., a study's mean age being 45) in an ontological format. These categories (e.g., mean age) are captured through a mapping exercise, in which one or two researchers (MS & PS) map ontology entities onto these categories, developing new entities where needed (see example in Figure 3).*

For the mapping exercise, the ontology development team will first check if a relevant entity is already included in the Mental Health Ontology...."

○ On page 7, in the first paragraph under Methods, the authors refer to online meetings where members of the Advisory Board will provide feedback. If we understand correctly, members of the Advisory Board will have the role of supervising the development of Ontology and providing their expertise, and stakeholders will include board members as well as other individuals. This could have been made clearer throughout the text as well as in Figure 2 concerning the role of both the Advisory Board and the stakeholder groups.

Response: As the reviewer suggested, the Advisory Board will have a consulting role in providing feedback on the methods and development of the ontology. The stakeholder consultation will include advisory board members, but we will also make an effort to recruit a wider range of people to provide feedback. To be clearer, the details about the Advisory Board's role and work has been updated to read as:

○ "*They will be invited to attend online meetings **once or twice a year, in which they will be given an overview of the methods and progress in developing the ontology. In these meetings, they will be prompted** to provide feedback about the methodology, emerging ontology content and organisation, and ontology-structured evidence. They will also be invited to submit feedback to written documents that will inform ontology **development and join formal stakeholder consultation to refine the ontology content (see Step 4) and usability evaluations of the ontology's application (see Step 8).**"*

○ Figure 2 has been updated to illustrate who will be involved in the different steps.

Page 8

Figure 2. Overview of steps to develop the Mental Health Ontology.

○ This is a nice overview but is it possible to add details about stakeholder involvement - e.g. in different colours depending on the type/number of stakeholders and methods (survey/interview etc) for involvement.

Response: Figure 2 has been updated to illustrate who will be involved in the different steps. However, we attempted to keep the figure simple. The details about the GALENOS members involved in the ontology's development have been added under a new section

titled " Developers and contributors to the ontology and its application in the GALENOS Project":

- *"The development of ontology is being led by two researchers with post-graduate degrees in psychology and experience in mental health research (MS & PS). Two senior researchers, both with experience in ontologies and clinical psychology (JH & SM), supervise and regularly provide feedback on the ontology's development and application. The project manager of GALENOS (JP) and two researchers leading systematic reviews within the project (CF & JK) also continuously support the work to refine the ontology and its application. Additional members across the GALENOS Project, such as from the data repository team (DB) and other systematic review team members (SS & SW), also regularly provide feedback to improve this work."*

The details about the Advisory Board's involvement have been updated, as described above:

- *"They will be invited to attend online meetings **once or twice a year, in which they will be given an overview of the methods and progress in developing the ontology. In these meetings, they will be prompted** to provide feedback about the methodology, emerging ontology content and organisation, and ontology-structured evidence. They will also be invited to submit feedback to written documents that will inform ontology **development and join formal stakeholder consultation to refine the ontology content (see Step 4) and usability evaluations of the ontology's application (see Step 8).**"*

Step 4 (the stakeholder consultations) and Step 8 (usability evaluation) have also been updated to provide an overview on the number of participants and methods earlier:

- *"We aim to recruit at least 10 participants, with broad theoretical knowledge and expertise relating the mental health field, lived experience of mental health conditions or ontologies. The number of participants is considered appropriate based on the development of ontologies part of the BCIO, which included 3–29 participants in their stakeholder consultations. Participants will be recruited by (1) inviting members of the Mental Health Ontology Advisory Board, (2)* asking these members to suggest individuals or groups with relevant expertise, with the two lived experience advisors being asked separately to share the invitation with their networks*, and (3) advertising the study through the UCL Centre of Behaviour Change and GALENOS Project's official social media accounts (LinkedIn and X). The inclusion criteria will be having professional or volunteering experience on mental health project, being able to read and write in English and having access to an electronic device."* (Step 4)

- *"In line with stakeholder consultations on ontologies (3–29 participants) as part of the BCIO (Michie et al., 2020; Norris et al., 2020) and relevant usability studies (Bruun & Stage, 2015), we will aim to recruit at least 10 participants. As the repository is likely to be used by people interested in data synthesis, the criteria will be for participants to have experience contributing to scoping or systematic reviews or applying review evidence in work related to mental health. To ensure that we include participants from a range of backgrounds, we will ask the lived experience advisors of the GALENOS Project to circulate invitations to their networks."* (Step 8)

- Step two continued)
  In which cases could the work on this ontology lead to relevant changes in other ontologies? This is a bit unclear to us.

Response: The work on the ontology will not directly lead to changes in other ontologies, as these are often led by different development groups. We indicate that we will submit

changes for the consideration of other ontology developers in the following sentence in Step 2, but this sentence has been updated to be clearer:

- ○ "*Where we identify that* changes are needed to an external ontology, *we will log the* **suggested** *changes on the ontology's GitHub repository* **for the external developers' consideration**."

Page 9

Step 3: Identifying and refining entities needed to structure the upper level of the ontology

- ○ In general, we believe it is very important for the authors to ensure that the upper-level entities sufficiently broad

Response: Thank you for the feedback. Our aim is to have entities that are broad enough to capture evidence about mental health across various contexts and studies.

- ○ Regarding presenting the first draft of the entities – Would it be feasible for the wider GALENOS team and advisory board to provide suggestions for upper-level entities before they are presented with the first draft. This to make sure that important aspects are not left out early in the process.

Response: We received feedback on the first draft of the upper level in a meeting with the advisory board and by sharing the upper level to the wider GALENOS team, which included asking them whether we missed any entities. The format allowed us to structure the discussion. However, in the future, a more open-ended format could be used to allow stakeholders to suggest initial entities. This limitation will be communicated in the future paper on developing the upper level of the GALENOS Mental Health Ontology.   ***Step 4: Iterative stakeholder consultations of the Mental Health Ontology***

- ○ Can the authors specify stakeholder criteria?

Response: We added this information on the criteria to Step 4 in the protocol:

- ○ "*The inclusion criteria will be having professional or volunteering experience on mental health project, being able to read and write in English and having access to an electronic device.*"

- ○ How will the authors ensure stakeholders are well represented in terms of education level, age and gender etc?

Response: We do not have specific requirements regarding the representativeness regarding education level, age and gender. A key consideration during recruitment will be on encouraging people from underrepresented geographies to participate. We will contact the two lived experience advisors on our Advisory Board to forward the invitation to their networks for this. To specify this more clearly, the following addition has been made for the recruitment strategy:

- ○ *Participants will be recruited by (1) inviting members of the Mental Health Ontology Advisory Board, (2) asking these members to suggest individuals or groups with relevant expertise,* **with the two lived experience advisors being asked separately to share the invitation with their networks** *…"*

- ○ Regarding stakeholder survey – consider presenting response options in the protocol paper.

Response: Details on the response options in the stakeholder consultation have been added to the Methods Section Step 4:

- ○ "*Participants will be able to indicate which entities need changing by clicking options*

'Change label' or 'Change definition' for the respective entities and providing open-ended feedback on how these should be changed. They will also be able to indicate that entities are missing or that relationships need changing in an open-ended response format. Finally, participants will be asked if they have any additional feedback which was not prompted by other survey questions."

Pages 10-11
- Step 8 (Evaluating the ontology): More information on the participants is required. Who are they? How many? Which groups will be represented?

Response: Details on the prospective participants has been added to Step 8 on the usability evaluation:

- "*In line with stakeholder consultations on ontologies (3–29 participants) as part of the BCIO (Michie et al., 2020; Norris et al., 2020) and relevant usability studies (Bruun & Stage, 2015), we will aim to recruit at least 10 participants. As the repository is likely to be used by people interested in data synthesis, the criteria will be for participants to have experience contributing to scoping or systematic reviews or applying review evidence in work related to mental health. To ensure that we include participants from a range of backgrounds, we will ask the lived experience advisors of the GALENOS Project to circulate invitations to their networks.*"

- Do members of the GALENOS team overlap with the author team? Please specify

Response: The ontology development team include Micaela Santilli, Janna Hastings, Susan Michie and Paulina Schenk, while Jennifer Potts is the project manager of the GALENOS Project, and Jaycee Kennett and Claire Friedrich are leads on systematic reviews. Initials have been added throughout to provide more clarity on the authors' involvement in various steps.

- It remains unclear how the researchers responsible for the development of the Mental Health Ontology´s will discuss the feedback and changes suggested by stakeholders (page 10, first paragraph under the heading "Analysis of stakeholder consultations"). This could be briefly clarified in one sentence with supporting references.

Response: The discussions will be informed by the specific feedback received; they will involve how the feedback will be addressed and why we have opted for this approach. The sentence has been updated to more clearly reflect this:

- "*The relevant feedback and proposed changes will be discussed among the researchers leading the Mental Health Ontology's development (JH, MS, SM & PS). **In these discussions, the team will consider how the feedback will be addressed and review disagreements between stakeholder comments, documenting the rationale for implementing relevant changes***."

Page 11
- "Applying the ontology to develop tools for data searching, visualising, extraction and synthesis, and partial automation of these processes the Mental Health Ontology will be used for annotations of the 'living evidence' extracted from the literature and stored in the project's online data repository." It is unclear to us what this section means - especially regarding the living evidence. Can the authors please rephrase or

clarify?

Response: Thank you for noting this. We updated the title to reflect that we will not be able to develop automated extraction systems at this stage: "Applying the ontology to develop tools for data searching, visualising and synthesis, and partial automation of these processes" The first sentence has also been updated to be clearer:

- *"The Mental Health Ontology will be used to organise the evidence extracted from the literature in the living systematic reviews and stored in the project's online data repository (see Steps 2, 7 and 8)."*

We deleted the following sentence to reduce confusion and reflect the scope of the work more realistically:

- *"In conjunction with machine learning algorithms and the data from living systematic reviews carried out early in the GALENOS Project's lifecycle, the ontology will also be applied to develop and test structured search strategies for later systematic reviews."*

References Bruun, A., & Stage, J. (2015). An Empirical Study of the Effects of Three Think-Aloud Protocols on Identification of Usability Problems. In *Human-Computer Interaction – INTERACT 2015: 15th IFIP TC 13 International Conference* (pp. 159–176). https://doi.org/10.1007/978-3-319-22668-2_14 Brooke, J. (1996). SUS-A quick and dirty usability scale. *Usability evaluation in industry*, *189*(194), 4-7. Cipriani, A., Seedat, S., Milligan, L., Salanti, G., Macleod, M., Hastings, J., ... & Elliott, J. H. (2023). New living evidence resource of human and non-human studies for early intervention and research prioritisation in anxiety, depression and psychosis. *BMJ mental health*, *26*(1). Collaborators, G. M. D. (2022). Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet Psychiatry*, *9*(2), 137-50. Kennett, J., Friedrich, C., Chiocchia, V., Blackwell, S. E., Furukawa, T., Carlbring, P., ... & Cipriani, A. (2025). Cognitive bias modification for social anxiety: protocol for a living systematic review of human studies and meta-analysis. *Wellcome Open Research*, *9*, 657.

Competing Interests: No competing interests were disclosed.

Reviewer Report 24 December 2024

https://doi.org/10.21956/wellcomeopenres.25788.r111650

✔️ **Carla Sharp**
    University of Houston, Houston, USA

The authors have been sufficiently responsive to my comments.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Classification, assessment, treatment development.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 20 June 2024

❌ **Carla Sharp**
University of Houston, Houston, USA

The goal of this paper is to outline the steps that the GALENOS project will engage in to develop a Mental Health Ontology. Drawing on Wright et al. (2022) which in turn, drew on several other indexed by this group (see any Michie articles on the development of the BCIO), the current paper outlines 6 steps that if completed will have resulted in the development of a Mental Health Ontology.

In all, the goal of this work is much needed and of great potential significant. The paper is clearly written and the steps for ontology development broadly mirror best practices for ontology development. I think the paper can be improved by address what I perceive to be some gaps that may negatively affect buy-in of this project - which we know is a significant prerequisite for ontology development and use (see recent NASEM report on the use of ontologies to accelerate behavioral sciences).

1) It is not clear why the focus is on anxiety, depression and psychosis. Broadly speaking these three classes of disorders represent (however, not fully) an internalizing dimension of psychopathology, as well as psychoticism. Disorders representing the externalizing spectrum are not included; in addition, there is much debate about where personality disorders fit in into any of these dimensions, as well as somatoform disorders. Given high comorbidity between internalizing, externalizing, psychoticism, somatoform, personality, and trauma-related disorders, the applicability of a mental health ontology focused on depression, anxiety and psychosis is not clear to me. Other classes of disorders such as neurocognitive disorders are also not considered, calling into question the overall legitimacy of a mental health ontology that is very selective, thus neglecting to articulate relationships between specified (and missing) entities in the ontology.

2) Related, the paper as it stands, seem to be unaware of the significant tensions between the clinical science the paper appears to rely on (HiTOP, or the personality-psychopathology spectrum approach) and other approaches to psychiatric nosology. If the authors are not aware of these tensions it may be important to become aware of them otherwise their selection of stakeholders

and domain experts may be biased such that only a small portion of the clinical science community's views will be represented. Much of what Hi TOP proposes is interesting, but much work is still to be done before this framework becomes the sole guidance to the development of a mental health ontology.

3) Related, I do not think 10 members provide enough options to fully represent views. It may be that the authors intend to make this a HiTOP-like ontology only, which is fine, and in which case 10 may be enough, but they will need to know that there may have to articulate commitment to this lens with the associated caveats that come with that.

4) The timeline is unclear. To my mind, what the authors propose is highly ambitious, and it would be good to have a better sense of timeline, and the exact processes stakeholders and content experts will be engage in. Wright is reference, which in turn references the BCIO development, so this is a bit circular, and I'm wondering if other gold standard approaches to ontology development could strengthen (or expand) on the current proposed steps.

5) A goal of the proposed mental health ontology is to explicate mechanisms. While I agree this is an important gap, I'm not sure what entities would be considered mechanisms given the broader literature (HiTOP) covered in the paper. I'm struggling to connect the dots with the type of descriptive psychiatry the authors espouse with a desire to also elucidate mechanisms.

6) I was curious why the authors did not reference the recent NASEM report on the use of ontologies to accelerate behavioral sciences. The recommendations of the report, which single out BCIO as a strong example for the development of behavioral ontologies, would be in alignment with the proposed work.

Is the rationale for, and objectives of, the study clearly described?
Partly

Is the study design appropriate for the research question?
Partly

Are sufficient details of the methods provided to allow replication by others?
Partly

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Classification, assessment, treatment development.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 06 Nov 2024

Paulina Margarete Schenk

The goal of this paper is to outline the steps that the GALENOS project will engage in to develop a Mental Health Ontology. Drawing on Wright et al. (2022) which in turn, drew on several other indexed by this group (see any Michie articles on the development of the BCIO), the current paper outlines 6 steps that if completed will have resulted in the development of a Mental Health Ontology.

In all, the goal of this work is much needed and of great potential significant. The paper is clearly written and the steps for ontology development broadly mirror best practices for ontology development. I think the paper can be improved by address what I perceive to be some gaps that may negatively affect buy-in of this project - which we know is a significant prerequisite for ontology development and use (see recent NASEM report on the use of ontologies to accelerate behavioral sciences).
Response: We thank the reviewer for their feedback about this paper. All comments made by the reviewer have been addressed and implemented where appropriate.

1) It is not clear why the focus is on anxiety, depression and psychosis. Broadly speaking these three classes of disorders represent (however, not fully) an internalizing dimension of psychopathology, as well as psychoticism. Disorders representing the externalizing spectrum are not included; in addition, there is much debate about where personality disorders fit in into any of these dimensions, as well as somatoform disorders. Given high comorbidity between internalizing, externalizing, psychoticism, somatoform, personality, and trauma-related disorders, the applicability of a mental health ontology focused on depression, anxiety and psychosis is not clear to me. Other classes of disorders such as neurocognitive disorders are also not considered, calling into question the overall legitimacy of a mental health ontology that is very selective, thus neglecting to articulate relationships between specified (and missing) entities in the ontology.
Response: The ontology's scope and focus of development are shaped by that of the broader GALENOS Project. At this stage, we are focusing on developing an ontology that is sufficient for evidence synthesis in the GALENOS Project. We have made changes to this protocol's Introduction to describe the GALENOS Project more clearly, as well as the role of the ontology within this project and how it will be applied. The reason that the ontology will initially focus on anxiety, depression and psychosis is due to the GALENOS Project's focus on these areas. These three broad conditions were selected for the GALENOS Project as they have been identified as having the highest prevalence among mental health conditions and high mortality rates associated with them. We will also develop a broader upper-level structure so that we or others can develop other parts of the ontology relevant to different conditions over time (see the Methods section Step 3). We have reframed the title and content of the protocol to better reflect that we are working towards an ontology of mental health through addressing these specific focus areas first, rather than aiming to develop a fully comprehensive ontology at this stage. This project is now framed as the first step towards a more comprehensive ontology, which more realistically reflects the scope of the current work and presents the ontology's development as primarily serving a particular use case at this stage. As the reviewer points out, anxiety, depression and psychosis are very broad conditions with some disagreements as to what "disorders" fall underneath them. Our intention is to remain agnostic regarding any specific classification system, to represent

conditions as diagnoses rather than disorders to remain compatible with different diagnostic systems, and to explicitly indicate symptoms where we can. Thereby, the ontology will remain open to the possibility that diagnoses of mental health conditions may be assigned based on different classification frameworks in different contexts. Entities will be developed as broadly as is needed to fulfil the objective of capturing, comparing and integrating evidence based on the research questions of the systematic reviews in the GALENOS Project. Feedback from a broader group of stakeholders will be used to further develop and refine entities.

2) Related, the paper as it stands, seem to be unaware of the significant tensions between the clinical science the paper appears to rely on (HiTOP, or the personality-psychopathology spectrum approach) and other approaches to psychiatric nosology. If the authors are not aware of these tensions it may be important to become aware of them otherwise their selection of stakeholders and domain experts may be biased such that only a small portion of the clinical science community's views will be represented. Much of what Hi TOP proposes is interesting, but much work is still to be done before this framework becomes the sole guidance to the development of a mental health ontology.

Response: We appreciate the tensions in clinical science between traditional diagnostic approaches and the dimensional approaches that focus on experiences within context (e.g., as proposed by HiTOP, or the symptom network approaches). We understand that there remains work to be done to develop these alternative approaches. Our objective is to provide a framework that can be used in an integrative fashion. The reason for explicitly noting classification systems and frameworks with differing perspectives was to represent entities that can be used to integrate evidence from a wide range of different sources. However, we appreciate the need for the project scope to be more realistic within the specified timeframe. We have removed the mapping work to classification systems (specified in Step 3) from the workflow and protocol. In the Conclusion section, we have noted that future work can involve mapping the ontology to existing classification systems to improve cross-referencing to these systems and to ensure that entities relating to mental health are comprehensively captured.

3) Related, I do not think 10 members provide enough options to fully represent views. It may be that the authors intend to make this a HiTOP-like ontology only, which is fine, and in which case 10 may be enough, but they will need to know that there may have to articulate commitment to this lens with the associated caveats that come with that.

Response: We have currently 17 advisory board members from 10 different countries and have been inviting additional people to join when additional expertise or perspectives are identified. Members include people with expertise from various domains, including psychiatry, clinical psychology and health psychology, as well as lived experience. Additions have been made to the section "*Set up the Mental Health Ontology Advisory Board*" to provide an overview of current advisory board members. The stakeholder consultations will allow us to receive additional feedback from a wider range of people. For the stakeholder reviews, we are aiming to have feedback from at least 10 participants, as the tasks can be long and require considerable expertise in some cases (e.g., a good grasp of both the mental health domain and ontologies). This can make recruiting more participants quite challenging. We appreciate that feedback from more people would help ensure that the ontology is more representative of wider views in mental health. In addition to the stakeholder consultations

and advisory board, ontologies are meant to be updated based on feedback over time. Updates have been made to the Methods section Step 4 to more clearly specify the stakeholder consultations. Finally, the GitHub repository, where we will maintain the ontology, allows users to report issues with the ontology. This functionality allows us to track issues with the ontology over time and ensure that the ontology is updated in line with wider perspectives. An additional project on developing related ontologies has been funded for 2024-2029 and we will be tracking any issues with the Mental Health Ontology throughout this period and making updates accordingly. Updates have been made to the Conclusion sections of the protocol to explain the plans for the ontology's maintenance.

4) The timeline is unclear. To my mind, what the authors propose is highly ambitious, and it would be good to have a better sense of timeline, and the exact processes stakeholders and content experts will be engage in. Wright is reference, which in turn references the BCIO development, so this is a bit circular, and I'm wondering if other gold standard approaches to ontology development could strengthen (or expand) on the current proposed steps.
Response: The timeline of the project, three years, will be added to the protocol (see Methods section Step 2). As we appreciate that the proposal was highly ambitious, we have updated the workflow to be more realistic within the given timeline. For example, the work to map the ontology to mental health classification systems has been removed from our Methods, as this work was not essential for the ontology's use case in the GALENOS Project. As the reviewer suggests, stakeholder consultations every 6-9 months was too ambitious given the resources available, and therefore, we have adjusted our timelines. For each set of three systematic reviews conducted annually, stakeholders will be asked to provide feedback on the clarity of entities mapped onto these reviews, as these will be used to structure the GALENOS data repository. However, stakeholders will only be asked to review entities that have not been included in a previous consultation. In addition, we will have one stakeholder consultation on the upper level of the ontology. Updates have been made to the Methods section Step 4 in the protocol to reflect this change. A key difference of this work to the BCIO development process is that we are working on an ontology to be fit for a specific use case in the GALENOS Project. The overview of the Methods section will be updated to clarify this difference, and emphasise the application of the Mental Health Ontology in the context of the GALENOS Project.

5) A goal of the proposed mental health ontology is to explicate mechanisms. While I agree this is an important gap, I'm not sure what entities would be considered mechanisms given the broader literature (HiTOP) covered in the paper. I'm struggling to connect the dots with the type of descriptive psychiatry the authors espouse with a desire to also elucidate mechanisms.
Response: We will draw on diverse perspectives about mental health, without trying to position the ontology as linked to a particular perspective. The protocol has been updated to avoid any confusion resulting from references to HiTOP. In the upper-level structure of the ontology, we will include an entity for "mental health intervention mechanisms of action" to conceptually structure the ontology and allow users to describe or synthesise evidence about mechanisms. We conceptualise mechanisms as processes that bring about the effect of an intervention on an outcome (e.g., beliefs, opportunities, bodily processes). As intervention outcomes can be very different in mental health interventions, such mechanisms can be extremely diverse as well. We will prioritise developing entities for

mechanisms of action that are identified as part of the living systematic reviews in the GALENOS Project, but construct these in such a way that they can be extended to other conditions over time.

6) I was curious why the authors did not reference the recent NASEM report on the use of ontologies to accelerate behavioral sciences. The recommendations of the report, which single out BCIO as a strong example for the development of behavioral ontologies, would be in alignment with the proposed work.
Response: As the reviewer suggests, the reference was added to the Introduction, as it is highly relevant to the current work.   We thank the reviewer for their useful suggestions, and the questions they raised.

Competing Interests: No competing interests were disclosed.

Reviewer Report 06 May 2024

https://doi.org/10.21956/wellcomeopenres.22909.r79166

? **Maya Braun** (iD)

Department of Experimental-Clinical and Health Psychology, Ghent University, Gent, Belgium

The GALENOS project aims to develop a Mental Health Ontology to facilitate knowledge aggregation and evidence synthesis. Their methodology for ontology is based on existing classification frameworks and stakeholder consultation.

The paper is a highly relevant roadmap for researchers interested in using ontologies within the behavioural sciences. It provides an outlook on the GALENOS project and the development of the mental health ontology. As a protocol for ontology development, some information could be provided in more detail.

Methodology
The project uses a methodology based on existing classification systems, systematic reviews and stakeholder involvement, similar to processes in existing ontologies created in the context of the Human Behaviour Change Project. The methodology seems largely suited for this project, though some aspects remain unclear.

First and most importantly, is not clear to me how the finalised ontology will be evaluated and what the maintenance plan is for the ontology.

Second, it is unclear to me which GALENOS teams there are, and what the background of the researchers in the different teams is. Please provide more information on this, or link to further

information. Similarly, it is not clear to me how many systematic reviews there are, and what they focus on.

Third, preliminary information regarding the external ontologies you are planning to link to would be valuable, particularly since you incorporate collaboration with the ontology developers. Working together closely with developers of external ontologies might not always be possible. How will reuse of entities be handled if close collaboration is not possible?

Background
In general, the background of the project is clearly described, albeit short. I believe the background would benefit from some revisions to further clarify the goal of the project.
First, the choice of anxiety, depression and psychosis specifically is not sufficiently justified in the background text. Relatedly, the focus shift from "anxiety, depression and psychosis" to "a broad range of aspects of mental health" is unclear to me. Do I understand correctly that the ontology covers all mental health related diagnoses, but the reviews focus on anxiety, depression and psychosis? It is also unclear to me how the mental health ontology relates to non-human animals. Please clarify this in the text.

Second, the introduction uses a lot of technical terms that readers with a behavioural sciences background might not be familiar with. Vocabulary regarding ontologies are not sufficiently clarified. Please provide some further information on what ontologies are and why they should be used in this context. It is also unclear to me how the cross-references between different diagnostic systems will work, and how this will improve upon current classification systems. Please also provide additional information regarding the planned "reliable machine learning" – does this refer to the language models mentioned on page 9?

Is the rationale for, and objectives of, the study clearly described?
Partly

Is the study design appropriate for the research question?
Partly

Are sufficient details of the methods provided to allow replication by others?
Partly

Are the datasets clearly presented in a useable and accessible format?
Not applicable

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Using ontologies in behaviour change (physical activity) interventions

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 06 Nov 2024

Paulina Margarete Schenk

The GALENOS project aims to develop a Mental Health Ontology to facilitate knowledge aggregation and evidence synthesis. Their methodology for ontology is based on existing classification frameworks and stakeholder consultation.
The paper is a highly relevant roadmap for researchers interested in using ontologies within the behavioural sciences. It provides an outlook on the GALENOS project and the development of the mental health ontology. As a protocol for ontology development, some information could be provided in more detail.
Response: We thank the reviewer for their feedback about this paper. All comments made by the reviewer have been addressed and implemented where appropriate.

Methodology
The project uses a methodology based on existing classification systems, systematic reviews and stakeholder involvement, similar to processes in existing ontologies created in the context of the Human Behaviour Change Project. The methodology seems largely suited for this project, though some aspects remain unclear.
First and most importantly, is not clear to me how the finalised ontology will be evaluated and what the maintenance plan is for the ontology.
Response: The Mental Health Ontology is being developed for a particular application to help integrate the data from the different living systematic reviews of the GALENOS Project in the associated data repository. The method described in the protocol has been updated to better reflect the application focus of the ontology. We will evaluate the usability of the ontology-structured data repository; information about this has now been added to the protocol as Step 8 in the Methods section. Furthermore, the ontology will be evaluated through stakeholder reviews as described in the protocol. The Mental Health Ontology will be maintained alongside the wider Behaviour Change Intervention Ontology as part of a 5-year NIH grant on increasing the usability of ontologies. The ontology will be open to feedback on GitHub, and the research team associated with the grant will monitor the comments to make appropriate updates. Information about this has been added to the Conclusion section of the protocol. The ontology's application as part of the data repository will be maintained by the relevant team, Future Evidence, of the GALENOS Project.

Second, it is unclear to me which GALENOS teams there are, and what the background of the researchers in the different teams is. Please provide more information on this, or link to further information. Similarly, it is not clear to me how many systematic reviews there are, and what they focus on.
Response: The goal of the GALENOS project is to carry out systematic reviews in sets of around three per year for human studies and three per year for animal studies until the completion of the project (planned as January 2026). However, the exact number of the systematic reviews has not been specified. This information has been added to the Methods section Step 2 in the current protocol. The researchers are based in countries spanning several continents, with backgrounds in psychiatry, psychology, data science and expertise relating to lived experience. The reviews are led by researchers with an MSc or PhD relating to psychology or psychiatry. Each stage of the review received input from the leadership team and Global Lived Experience Advisory Board. The leadership team includes members from Australia, several European countries, Japan and South Africa. Global Lived Experience

Advisory Board includes members from Canada, India, Nigeria, the Philippines and Zimbabwe. The project members are clinicians, experts by lived experience, and researchers with expertise across data science, psychology and psychiatry. Detailed information about the GALENOS Project can be found on the project website (https://www.galenos.org.uk/about), as well as in the protocol for the overarching project (https://mentalhealth.bmj.com/content/ebmental/26/1/e300759.full.pdf). This information has been added to relevant parts of the Introduction and Methods section Step 2 in the current protocol.

Third, preliminary information regarding the external ontologies you are planning to link to would be valuable, particularly since you incorporate collaboration with the ontology developers. Working together closely with developers of external ontologies might not always be possible. How will reuse of entities be handled if close collaboration is not possible? **Response:** We are reusing relevant parts of the Behaviour Change Intervention Ontology (BCIO), the Mental Functioning Ontology (MFO), Emotion Ontology (MFEOM), Information Artifact Ontology (IAO) and where necessary, a small number of classes from other ontologies available on the EMBL-EBI Ontology Lookup Service (https://www.ebi.ac.uk/ols4/). Information about this has been added to the Methods section Step 2. As the reviewer points out, close collaboration might be difficult with external ontology developers, both due to their time constraints and the current project's timelines. We will submit feedback on the appropriate GitHub issue trackers for the developers of other ontologies to address, in cases where we are reusing entities, but these entities need some updates. In some cases, we may decide not to reuse entities (e.g., if they do not capture the intended meaning of a construct in a review or do not fit into the ontology's structure), instead developing more fitting entities. Where relevant (e.g., entities closely overlap with entities in external ontology), we will inform the external ontology developers via GitHub. Details about this approach have been added to the Method section Step 2. Any mentions of 'collaboration' have been removed where close collaboration is not possible, in order to avoid confusion. In cases where the external ontologies are co-developed by members of the project team (BCIO, Mental Functioning and Emotion Ontologies), we expect good collaboration to be possible. In addition, we have good experiences of collaboration with the developers of ontologies that are actively maintained and participate in communities such as the Open Biological and Biomedical Ontology (OBO) Foundry.

Background
In general, the background of the project is clearly described, albeit short. I believe the background would benefit from some revisions to further clarify the goal of the project. First, the choice of anxiety, depression and psychosis specifically is not sufficiently justified in the background text.
Response: Additions have been made to more clearly describe the GALENOS Project in the Introduction section. The reason for focusing on anxiety, depression and psychosis within the GALENOS Project is the high prevalence and impact of these mental conditions globally. As this is the focus of the broader project as a whole, the Mental Health Ontology will also focus on these three conditions, but the upper-level structure of the ontology will be developed in a way that is compatible with other conditions as well. The title and framing of the protocol have been updated to better reflect that the work involves a step towards an ontology of mental health in the context of the GALENOS project's focus areas (anxiety,

depression and psychosis), rather than developing a comprehensive ontology of mental health. This reframing will better show the scope of the current work and help illustrate the development of the ontology mostly within the context of a particular use-case, structuring and integrating evidence regarding anxiety, depression and psychosis.

Relatedly, the focus shift from "anxiety, depression and psychosis" to "a broad range of aspects of mental health" is unclear to me. Do I understand correctly that the ontology covers all mental health related diagnoses, but the reviews focus on anxiety, depression and psychosis?
Response: As noted above, the Mental Health Ontology is being developed so that the upper-level structure (e.g., upper levels, such as human population, mental health intervention) can be used for all mental health conditions. As the reviewer correctly noted, the framing of the protocol needs to be updated to better reflect that this ontology will be developed within a use-case. The GALENOS Project's systematic reviews focus on anxiety, depression and psychosis. Accordingly, the content of the ontology will also primarily relate to these conditions and the research questions that are associated with the reviews. We have clarified in the Introduction that ontologies are always in development, and that what we are doing is creating an overall structure for representing knowledge about mental health but elaborating in detail three areas relevant to mental health: anxiety, depression and psychosis.

It is also unclear to me how the mental health ontology relates to non-human animals. Please clarify this in the text.
Response: The GALENOS Project is piloting an innovative approach in which each living systematic review includes relevant evidence based on human studies as well as evidence based on animal studies. Accordingly, both human and non-human content will be included in the online data repository and may be annotated to the ontology terms where possible. However, as animal-specific research is already included in the scope of other ontologies in the biomedical domain, animal-specific entities will not be explicitly included in the Mental Health Ontology. To avoid confusion, this part of the protocol has been omitted.

Second, the introduction uses a lot of technical terms that readers with a behavioural sciences background might not be familiar with. Vocabulary regarding ontologies are not sufficiently clarified. Please provide some further information on what ontologies are and why they should be used in this context.
Response: More details have been added to the Introduction to clarify what ontologies are and how the current ontology will be useful in context of the GALENOS Project. A figure (see newly added Figure 1) illustrating the link between the ontology development and application within the context of the GALENOS Project has also been added.

It is also unclear to me how the cross-references between different diagnostic systems will work, and how this will improve upon current classification systems.
Response: Categories from different diagnostic systems can be mapped onto the same entity in the ontology where relevant, and these categories can be signposted using an appropriate "cross-reference" annotation for an entity. The ontology does not intend to replace existing classifications systems. Instead, the ontology will enable evidence that has been gathered in multiple of those classification systems to be integrated and inter-related.

The ontology will propose an unambiguous definition for each entity, with concepts from different systems integrated into the ontology. We have removed Step 3 (Identifying and refining entities and their structure based on existing classification systems) from the protocol, in response to other comments on the scope and timeline of the work. For the current phase of the project, our focus is on the entities that are required for the data repository. In the Conclusion, we have noted that further work will be required to comprehensively map the ontology onto existing classification systems to improve cross-referencing and ensure that entities relating to mental health are well captured in the ontology.

Please also provide additional information regarding the planned "reliable machine learning" – does this refer to the language models mentioned on page 9?
Response: The phrase "reliable machine learning" is used to describe machine learning algorithms that have been tested and found to produce reliable results. To reduce confusion, the phrase "reliable machine learning" has been amended to "machine learning algorithms". In addition, as the reviewer points out, the phrase "language models" on page 9 is used to describe one of the machine learning approaches that can be used with ontologies. For consistency, we have updated the phrase "language models" to the more general phrase "machine learning algorithms" on page 9. The computer science team will test out different machine learning approaches depending on the needs of the project. A clarification has been added to the protocol that this will be an iterative process, depending on the evolving deliverables of the GALENOS Project (see section "*Applying the ontology to develop tools for data searching, visualising, extraction and synthesis, and partial automation of these processes*").   We thank the reviewer for their useful suggestions, and the questions they raised.

Competing Interests: No competing interests were disclosed.