Request for Proposal (RFP) for

Understanding decision making and barriers in the Mental Health R&D ecosystem

Summary

Wellcome is a politically and financially independent charitable foundation. We improve health for everyone by funding research, leading policy and advocacy campaigns, and building global partnerships. In 2020, Wellcome announced our new 30-year strategy to tackle three global health challenges: mental health, infectious disease and the impact of climate change on health. For mental health , the vision is a world where no one is held back by mental health problems. To advance this vision Wellcome is seeking to create a step change in early intervention in anxiety, depression, and psychosis.

Vision and Mission

Our Mental Health vision is a world in which no one is held back by mental health problems. To advance this vision, our mission over the next 20 years is to drive a step change in the ability to intervene as early as possible in the course of anxiety, depression, and psychosis, broadly defined, in ways that reflect the priorities and needs of those who experience them.

We recognise that the current diagnostic categories are imperfect but removing all categories or creating new ones also presents difficulties and may limit engagement with the field. Included in our definition of anxiety, depression, and psychosis are all forms of anxiety, depressive and psychotic disorders including obsessive compulsive disorder, post-traumatic stress disorder, post-partum psychosis, bipolar disorder, and schizophrenia.

Wellcome has two core goals:

A) improving the understanding of how the brain, body and environment interact in the trajectory and resolution of anxiety, depression, and psychosis

B) finding new and/or improved usable ways to predict, identify, and intervene as early as possible.

Within 20 years, we hope to have new and improved, practicable, pharmacological, and non-pharmacological interventions that are built on clearer understanding, and which address novel targets with an ability to stratify people to different interventions.

In terms of interventions, we are interested in both pharmacological and non-pharmacological interventions. Interventions may involve any form (e.g., whether self-care or interventions provided by a professional); they may be provided via healthcare systems or via other systems such as societal structures, workplaces, or educational organisations

1. RFP Background & Objectives

There is wide recognition of the unmet treatment gap in mental health both for conditions with the largest burden of disease (depression) and those that are most debilitating (psychosis). This includes cases in which:

- there are currently no effective treatments available;
- treatments exist that may be effective for some groups of people, although our knowledge of how to target these treatments is still limited
- existing treatments are accompanied by intolerable side effects.

The Wellcome Mental Health team has scoped and has a detailed understanding of the scientific challenges that are impeding our advancement in this field. These, on the most part, refer to the clinical development phase of an intervention and include:

- the heterogeneous presentation of mental health problems,
- the limited generalisability of results,
- a limited set of standardised measures of assessment and diagnosis,
- underpowered studies,
- poorly understood intervention mechanisms,
- a perceived lack of validated therapeutic targets and outcomes.

Major advances in neuroscience, genetics, imaging and data science are leading to better phenotyping and new molecular targets which may in part lead to improved interventions however we expect that there exist many other challenges across the mental health R&D ecosystem which could be supported.

2. RFP Specification

We are commissioning a focused piece of analysis to assess and where possible quantify the extent to which scientific and non-scientific challenges create barriers (e.g., gaps, blockages and hurdles) to the development through to approval and initial uptake of mental health interventions currently in the pipeline. (For this analysis, we include initial use of interventions already approved and used to avoid a hard stop, which might exclude relevant insight from, for example: Improving access to psychological therapies (IAPT), brexanolone for postpartum depression, SilverCloud, and Sleepio).

Through this piece we aim to understand:

- the decision-making process that developers of mental health interventions follow across the mental health R&D ecosystem from development and funding, approval/accreditation, entry to market and initial uptake,
- the critical points where the current ecosystem is not serving to support innovative and inclusive/equitable intervention development for mental health
- assess and where possible quantify the extent to which scientific and non-scientific challenges create barriers (e.g., gaps, blockages and hurdles) to the development through to approval and initial uptake of mental health interventions currently in the pipeline
- identify the push/pull factors that exist from regulators, policymakers, investors, end users & advocacy groups and other key stakeholders which influence the mental health R&D Landscape throughout the lifecycle
- assess how such hurdles can be overcome (or not) and/or identify what solutions are available for these barriers or bottlenecks

We recognise that the types of interventions in development are affected in different ways by these challenges and would like the analysis to take this into account. We would also look to the respondents to propose any additional challenges, barriers or hurdles acting upon the intervention's ecosystem, which are not included below, and to propose whether, and how, different factors interact with each other.

This analysis will serve to guide decision making and prioritisation on what further activity Wellcome or other parties may fund to help address issues of innovation in mental health interventions and ensure that promising interventions can progress into use. We may look to commission a subsequent piece of work exploring potential solutions in more detail.

2.1. Challenges to consider

We recognise, that scientific and non-scientific challenges are interdependent and cannot be viewed in isolation within an ecosystem. We, therefore, welcome a balanced focus on both scientific and non-scientific challenges. We outline below the types of challenges we expect to see, although anticipate the supplier to offer further depth and breadth to these. We are interested in both challenges which halt the development of interventions as well as challenges specifically encountered in the development of equitable interventions. These two streams should be considered throughout.

- Unmet need
    - Size and characteristics of affected populations and burden of disease
    - Distribution of unmet need across conditions and population subgroups, with attention to marked inequities and disparities (for example, groups with comorbidities)
    - Availability of other treatments or treatments in the pipeline
- Likelihood of developmental success for assets in the pipeline
    - The route to and feasibility of validation
    - The size and difficulty of efficacy/effectiveness trials
    - Enrolling appropriately diverse participants
    - Issues around Intellectual Property
- Acceptability of or demand for intervention by people with Lived experience or end users
    - The process by which input from people with Lived Experience or end users is sought and integrated into decision making across the lifecycle of a new/adapted intervention.
    - Use of appropriate study endpoints/outcomes of interest and side effects profile
- The complex and/or evolving regulatory environment, notably in digital (both in the UK and in international regulatory frameworks)
- Unclear pathway for translational work in innovative / complex areas e.g. using digital or combination therapies
- A lack of demand for new and improved interventions as well as lack of guidance for decision makers to select the most effective treatments/tools
- Value Creation potential
    - Time to market & return on investment
    - Required investment
        - Lack of sufficient investment in innovation across the life cycle of intervention development through to evaluation, approval/accreditation and uptake (in part already documented [1])
        - Challenge of companies (particularly SMEs and start-ups) being able to afford the costs of trials and evidence generation.
    - Commercial feasibility/viability of medical device & digital products. For example, the pressure venture capital firms face to generate profit quickly in order to give return on investment (ROI), whilst trials are seen as a lengthy process that creates a barrier to that ROI.
    - Market access hurdles post authorisation
    - A need to understand existing barriers to adoption, including human factors (such as patient and professional trust in new approaches) and infrastructure challenges (such as service provision and digital literacy) treatment interactions for people with comorbidities which may block use of existing or candidate therapeutics
    - Consideration of equitable access in adoption

[1] https://digitalscience.figshare.com/articles/report/TheInequitiesofMentalHealthResearchIAMHRF/13055897

- Non-financial returns
- Strategic fit (public health fit and organisational fit, portfolio fit and available partners)

We are also interested in the push/pull factors that exist from regulators, policymakers, investors, end users & advocacy groups and other key stakeholders which influence the mental health R&D Landscape throughout the lifecycle from development to market and uptake.
Pushes can include external factors like the Covid-19 pandemic increasing the demand for remote/tele mental health support which may have also brought new opportunities for mental health financing; scientific advances which can open "windows of opportunity" such as the new KarXT drug; or changes in regulatory policies that increase or reduce friction in the ecosystem. Pulls can include any new financial incentives or changes to international/national recommendations.

Inclusions: early stage/prototypes or pilot and proof of concept stage.
Exclusions: detailed consideration of uptake and use beyond initial stages.

The definition of the R&D ecosystem for the purposes of this RFP, will be defined jointly by Wellcome and the supplier as part of the research. Parameters to consider will include

- **The time period** to be included as part of the desk-based research
- **Conditions** to be included are limited to depression, anxiety and psychosis (as defined in the Mental Health Strategy) but open to learn from breakthroughs or unsuccessful examples in other areas
- **The types of interventions** This RFP should include both pharma and non-pharma interventions as well as digital and hardware (eg neuromodulation tools) Jointly with Wellcome the supplier may decide to include/exclude certain interventions as they may share barriers and may benefit from similar solution sets
- **Interventions** This RFP is focused on intervention and not diagnostics or prognostics.
- **Stage of development** – Included in this RFP are the areas of inception, development, evaluation, accreditation, entering the market/initial uptake

2.2. Geographic Coverage
The UK will be a key area to focus on with additional locations to be suggested by the supplier from the below list. We expect the report to touch on at least 3-4 locations in total and at least one LMIC location. Countries of interest include Australia, Canada, Colombia, Ecuador, Egypt, Germany, Ghana, India, Indonesia, Israel, Japan, Kenya, Morocco, Romania, Senegal, South Africa, Switzerland, Tanzania, Vietnam, USA and UK. We anticipate it could be an asset if the supplier has in-country partners for the target countries, so please identify these where relevant in the proposal.

The review should reach out to a range of stakeholders including (but not limited to):

- Developers of interventions (large, established companies, small and mid-sized companies, start-ups, biotech organisations, academia/government developers)
- People with lived experience
- Policy makers
- Regulators

Wellcome will facilitate introduction to networks as much as possible and use its convening power.

2.3. Outputs/Research areas

We will ask the successful supplier to evaluate the following:

2.3.1. **Characterisation of the ecosystem.**

- Provide a systematic literature review of the mental health research and development ecosystem for depression, anxiety and psychosis[2] and identify preliminary barriers, bottlenecks or hurdles for intervention development from early-stage development through to late stage and initial use. As with section 2.1 please include both challenges which halt the development of interventions as well as challenges specifically encountered in developing equitable interventions.
- Develop an approach to grouping different types of interventions in order to facilitate analysis of how they interact with the current ecosystem. This might include grouping interventions in more than one way and/ or complementing analysis of types of interventions with individual case studies of interventions. We are also interested in the value of retrospective consideration of interventions that have already reached later stage development, or which have stalled. (Examples of categories of interest: by disease; type of asset pharma vs. non-pharma vs. digital; prescribed vs self-administered; software vs. hardware; over the lifecycle: development, evaluation, accreditation, uptake; or by type of developer)
- Estimate the anticipated size and nature of markets for types of interventions. In particular, we would like to explore what different assumptions are used by developers of interventions in assessing potential market and return on investment especially where there are gaps or issues with available data. We would like to understand the points where potential market is considered as new intervention candidates progress in the pipeline, and what tips the balance between a go/no-go investment decision. This may include risk or liability issues. We would particularly like to understand whether (and how) end user priorities and perspectives are incorporated. We would not anticipate the creation or commissioning of any new data relating to a specific intervention, intervention type or market, where there is inadequate information, this should be presented as a finding.

2.3.2. **Analysis of mental health intervention developer decision-making & prioritisation of universal barriers or bottlenecks**

- Propose a methodology for and provide clear analysis for each challenge identified on whether and to what extent it represents a barrier for interventions and equitable interventions in development. The methodology should include both quantitative and qualitative aspects as analysis of whether barriers exist will sometimes be based on data and sometimes on insights from relevant stakeholders.
- How do developers make decisions to continue or discontinue intervention development?
    - When are decisions made and what triggers the need for a decision?
    - Which are the most influential factors?
    - How do the factors change over time?

[2] We recognise that the current diagnostic categories are imperfect but removing all categories or creating new ones also presents difficulties and may limit engagement with the field. Included in our definition of anxiety, depression, and psychosis are all forms of anxiety, obsessive compulsive disorder, post-traumatic stress disorder, post-partum psychosis, bipolar disorder, and schizophrenia.

    - How are the factors different by type of developer?
    - What criteria drive the decision to outsource components of work such as clinical validation?
- What are the most relevant challenges that create barriers (i.e., gaps, blockages and hurdles) from early to late-stage development, to licensure and initial use of mental health intervention candidates?
    - What are the root causes of those barriers?
    - Which type of developer is most affected by each barrier?
    - Which type of intervention is affected by each barrier; which barriers affect all interventions and are universal?
    - How do the barriers affect influential factors in continuing or discontinuing development of interventions of interest?
    - Which barriers or bottlenecks are most relevant in slowing/ending development of interventions of interest?
- We would like the impact of the different barriers to be broken down by cost in time and/or money (this could relate to costs for developers/companies or the cost to the healthcare system), the feasibility of reducing that barrier, the potential for delay or stalling of intervention development, other relevant factors should also be included. We recognise that estimates and basic models may need to be used.
- Given that the mental health interventions ecosystem is dynamic, we would like an analysis of how different barriers in the system interact with each other. e.g., how likely size of market may link to perceived feasibility of conducting trials, manufacture of product or development of software platform.
- The analysis will need to assess both current and future progress through the pipeline, drawing out any actual or predicted waste in the process (e.g., delays, rework, redundancy etc.)
- Taking the above analysis, give an overall representation and, where possible, quantification of the barriers in the mental health intervention market. We would like an assessment to be made of the relative importance of different factors to the overall functioning of the mental health intervention development ecosystem recognising that some of the barriers may be anticipated rather than already evidenced issues.

2.3.3. Identification of solutions

- Which are the priority barriers or bottlenecks that, if addressed, could significantly improve the ecosystem for development of new mental health interventions of interest?
- What are the currently ongoing solutions to these prioritised barriers? Are there solutions to these barriers in other fields the mental health field could learn from?
- Which prioritised barriers require additional solutions?
- Map current initiatives aimed to support mental health intervention development and assess the extent to which these have successfully reduced or mitigated issues in the mental health ecosystem. This can include the role of WHO and other initiatives (eg OneMind, MQ, NIHR's £30m investment in mental health), work to reduce the burden of clinical trials.
- Provide an initial proposal that identifies, and puts forward a case for, those solutions most likely to address issues identified in the mental health intervention ecosystem, including feasibility, cost and potential impact.

2.4. Other requirements

We expect the supplier's team to be diverse in membership, inclusive in practice and have experience of working across a range of global settings. We anticipate it could be an asset if

the supplier has in-country partners for the target countries, so please identify these where relevant in the proposal.

3. Deliverables from the supplier:

3.1. A brief **inception report**, which will confirm:

- The detailed scope of work;
- The final list of research questions and sub-questions to be pursued;
- The proposed methodology for answering these research areas;
- The supplier's proposals for collecting, managing, analysing and reporting on information;
- The milestones within the study, between the completion of the inception report and the delivery of the draft final report.
- We will communicate with the successful supplier to help them develop the inception report.
- We would like the work to be informed by insights from key actors and participants, so the methodology should detail how this will be achieved. There is no restriction on the methodology used as long as all tools are used with the consent of participants, the results can be anonymised and that they are used in accordance with Wellcome's data protection policies, in compliance with UK and EU data protection regulations.

3.2. A **full report** that answers the research areas set out above, and an executive summary (maximum of 4 pages). We are open to different timetables for the work but ideally would like to see it completed in around 9 months from contract start date. This will be delivered in two stages:

- A **draft final report**, which will be shared with Wellcome in advance of the end date to allow Wellcome staff time to discuss feedback, raise questions, and make recommendations for further improvement.
- A **final report**: a clean and final copy which will be delivered one week after the receipt of feedback from Wellcome. This final report will include detail on the methods of analysis and findings including any caveats or assumptions, this should also include clear visual or graphical representations of the findings. The final report should be openly licensed (e.g. CC-BY) and be published on an open platform indexed in PubMed. Where appropriate, data underpinning the final report should be shared openly on a community-recognised repository, or behind managed access solution if sensitive data.
- A **slide deck** of summary findings
- A **presentation of the findings** to the Mental Health Translation team. Note that other Wellcome members of staff may be invited to the presentation.

4. RFP Timetable

#	Activity	Responsibility	Date
1	RFP issued to Suppliers	WT	14/09/22
2	Submission of expression of interest and Supplier Q&A to Wellcome Contact	Supplier	12/10/22
4	Return of Supplier Q&A to Suppliers	WT	26/10/22
5	Submission of RFP Response	Supplier	23/11/22
6	RFP Evaluation Period	WT	24/11/22 to 07/12/22
7	Supplier Presentations	Supplier	08/12/22 to 14/12/22
9	Notification of Contract Award	WT	December 2022

10	Contract Negotiation	WT & Supplier	December 2022-January 2023
11	Contract Start Date	WT & Supplier	End of January/Start of February 2023

5. Response Format

The following headers support the timetable by providing further detail of the key steps.

5.1. Expression of Interest

Suppliers are asked to submit a short expression of interest by e-mail to the Wellcome Contact in accordance with the RFP timetable. There will not be a shortlisting stage, but suppliers must have submitted an EOI to be considered. The EOI should consist of the following:

- Whether you are an individual or a company (including full company name and number and registered company address)
- Provide a non-binding cost estimate as a single figure, excluding VAT
- Provide a list of countries the research will cover.

We recognise one organisation or individual may not feel equally able to deliver all strands of this analysis and we are therefore happy to accept expressions of interest from a group of partner organisations or individuals. We ask that one of these organisations or individuals is identified as the lead contact in the expression of interest. In a successful multi-partner bid the lead organisation/individual will be contracted and must be prepared to sub-contract partner organisations/individuals.

5.2. Supplier Q&A

Prior to the submission of your RFP response, Suppliers are provided the opportunity to submit any questions they have about the exercise. All questions are to be submitted to the Wellcome Contact by e-mail along with your Expression of Interest in accordance with the RFP timetable.

5.3. RFP Proposal

Suppliers are required to submit proposals which respond to the following sections;

	Question	Max pages
Team		
1	A brief overview of your organisation, including your track record and expertise relevant to analysis of the type outlined in this RFP. Please also include a brief description of who would be involved in the project team, their qualifications and their main responsibilities.	1

2	What makes you best placed to fulfil Wellcome's requirements set out in the RFP?	1
Approach		
3	Your proposed approach to this work, including the proposed: • Methodology (for particular questions around methodology, see section 2, RFP Specification) • Timeframes • Management plan, including role of team members • Plan for engagement with Wellcome during contract • Plan for production of final report, including copy editing, formatting and graphics. Plan for outputs management and sharing • Diversity and inclusion planning (how you will ensure that: the literature reviewed, and interviews conducted will be inclusive to different groups of people and locations; your methodology does not introduce bias) • How will you involve people with lived experience at multiple stages of this project (e.g. during project design, literature scanning and data collection, analysis, toolkit design) (300 words). • Justification of chosen countries to focus on as part of this research.	6-7
4	Case studies of where you have successfully provided similar services to those described in this RFP	1
5	Highlight any risks you foresee in meeting the RFP requirements and any mitigation you will undertake (both related and not related to Covid-19)	1
Costs		
6	Cost proposal detailing and justifying the proposed costs to meet our requirements	1
Other		
	Provide details of any existing restrictions that may impact your ability to meet Wellcome's requirements. These should include (but not be limited to): • Conflicts of interest with other clients • Conflicts of interest with internal Wellcome staff • Restrictions on your licence to operate in certain jurisdictions	1

5.4. Proposal Scoring

Your proposal will be scored out of 100% and it will be assessed against the following criteria

Assessment Criteria	Weighting
Team and Project management	20%
Understanding of requirements of RFP	20%
Methodology – data collection, including D&I	25%
Methodology – analysis	25%
Costing	10%

5.5. Contract Feedback

This section allows Suppliers to provide specific feedback to the contractual agreement which will be used should their proposal be successful. Contract feedback is to be incorporated into your proposal as an annex and in the following format;

Clause #	Issue	Proposed Solution/Comment

Suppliers submitting proposals as a registered company should review this document.
Individuals submitting proposals as a sole trader (not registered) should review this document.
Individuals submitting proposals through their own personal services company please highlight this to the Wellcome contact immediately (see point 8 below).

5.6 Information Governance

Suppliers are asked to complete the TPSRA2 assessment before the RFP submission deadline for Wellcome to assess how you handle data.

6. About Wellcome

Wellcome supports science to solve the urgent health challenges facing everyone. We support discovery research into life, health and wellbeing, and we're taking on three worldwide health challenges: mental health, global heating and infectious diseases. Find out more about Wellcome and our work at: wellcome.org.

7. Non-Disclosure and Confidentiality

Prospective Suppliers should be aware that inappropriate publicity could have a serious effect upon Wellcome's business. The information contained within this document or subsequently made available to prospective suppliers is deemed confidential and must not be disclosed without the prior written consent of Wellcome unless required by law.

8. Prospective Suppliers Personnel - IR35 and Off Payroll Working Rules

Before the RFP response deadline, Prospective Suppliers must make the Wellcome Contact aware if they are intending to submit a proposal where the services will be provided by any individuals who are engaged by the Prospective Supplier via an intermediary i.e.

- Where the Prospective Supplier is an individual contracting through their own personal services company; or
- The Prospective Supplier is providing individuals engaged through intermediaries, for the purposes of the IR35 off-payroll working rules.

9. Independent Proposal

By submission of a proposal, prospective Suppliers warrant that the prices in the proposal have been arrived at independently, without consultation, communication, agreement or understanding for the purpose of restricting competition, as to any matter relating to such prices, with any other potential supplier or with any competitor.

10. Funding

For the avoidance of doubt, the output of this RFP exercise will be funded as a **Contract** and not as a Grant.

11. Costs Incurred by Prospective Suppliers

It should be noted that this document relates to a Request for Proposal only and not a firm commitment from Wellcome to enter into a contractual agreement. In addition, Wellcome will not be held responsible for any costs associated with the production of a response to this Request for Proposal.

12. Sustainability

Wellcome is committed to procuring sustainable, ethical and responsibly sourced materials, goods and services. This means Wellcome seeks to purchase goods and services that minimise negative and enhance positive impacts on the environment and society locally, regionally and globally. To ensure Wellcome's business is conducted ethically and sustainably, we expect our suppliers, and their supply chains, to adhere to these principles in a responsible manner.

13. Disability Confident

The Wellcome Trust is proud to be a Disability Confident Employer (DC Level 2) and we encourage all our partners and suppliers to do the same. More information about this can be found on the government website Disability Confident employer scheme and guidance - GOV.UK (www.gov.uk). Disability Confident is creating a movement of change, encouraging employers to think differently about disability and take action to improve how they recruit, retain and develop disabled people.

14. Accessibility

Wellcome is committed to ensuring that our RFP exercises are accessible to everyone. If you have a disability or a chronic health condition, we can offer adjustments to the response format e.g. submitting your response in an alternate format. For support during the RFP exercise, contact the Wellcome Contact.

If, within the proposed outputs of this RFP exercise, specific adjustments are required by you or your team which incur additional cost then outline them clearly within your commercial response. Wellcome is committed to evaluating all proposals fairly and will ensure any proposed adjustment costs sit outside the commercial evaluation.

15. Diversity & Inclusion

Embracing diversity and inclusion is fundamental to delivering our mission to improve health, and we are committed to cultivating a fair and healthy environment for the people who work here and those we work with. As we learn more about barriers that disadvantage certain groups from progressing in our workplace, we will remove them.

Wellcome takes diversity and inclusion seriously, and we want to partner with suppliers who share our commitment. We may ask you questions related to D&I as part of our RFP processes.

16. Wellcome Contact Details

The single point of contact within this RFP exercise for all communications is as indicated below;

Name: Olivia Donovan
Role: Procurement Officer
Email: RFP@wellcome.org