The active monitoring of oxytocin research evidence (AMORE) platform

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Abstract

Oxytocin, an evolutionarily conserved neuropeptide, plays a crucial role in various physiological and behavioural processes, offering potential therapeutic benefits for several psychiatric and neurodevelopmental conditions. Despite its promise, oxytocin research has been marked by inconsistent results concerning its therapeutic applications and underlying mechanisms. Performing a systematic review and meta-analysis is a popular approach to shed light on mixed findings in a body of literature; however, they can become quickly outdated as new evidence becomes available. Given these challenges, research on oxytocin and its biobehavioural outcomes is ideally positioned for the adoption of 'living' meta-analyses, which allow for the continuous integration of new data and updated conclusions. Here we introduce the Active Monitoring of Oxytocin Research Evidence (AMORE) platform (https://amore-project.org), which is a hub that aggregates articles and materials associated with living meta-analyses for biobehavioural oxytocin research. Developed through consensus among 24 expert researchers, a standardized framework was established that either requires or recommends practices ensuring transparency and rigor in living meta-analyses featured on the AMORE platform. Overall, AMORE has been designed to advance oxytocin biobehavioural research by the timely integration of emerging evidence through transparent living meta-analyses.

Keywords

Living meta-analysis, Systematic Review, Evidence synthesis, Oxytocin, Transparency

Background

Oxytocin is an evolutionarily conserved neuropeptide (Sartorius et al., 2024; Theofanopoulou et al., 2021) that plays a pivotal role in a wide array of physiological and behavioural processes (Jurek & Neumann, 2018). Primarily synthesised by magnocellular neurons in the hypothalamus (Farina Lipari et al., 1995; Farina-Lipari & Valentino, 1993), oxytocin is released both peripherally and centrally, contributing to various functions across the body (Gimpl & Fahrenholz, 2001). Oxytocin binds to G protein-coupled oxytocin receptors located throughout the periphery (Gimpl & Fahrenholz, 2001) and the brain, making this system well positioned to coordinate regulatory processes and behaviour (Quintana et al., 2019). Historically, oxytocin has been referred to as a "maternal hormone" (Carter, 2022) primarily because of its recognised role in promoting maternal behaviours in mammals (Kendrick et al., 1987; Klopfer & Klopfer, 1968; Pedersen & Prange, 1979). A landmark study in 2005 reported that oxytocin administration increases trust behaviour in humans (Kosfeld et al., 2005; but see Declerck et al., 2020), leading to its label as a "social hormone" (Burenkova et al., 2023; Shamay-Tsoory & Abu-Akel, 2016). This new perspective sparked extensive investigations into oxytocin's potential as individualised support or treatment (Rigney et al., 2022; but see Riem et al., 2025) for various psychiatric and neurodevelopmental conditions, such as mood disorders (Ellenbogen et al., 2024; Engel et al., 2019; Wong et al., 2021), eating disorders (Hasselbalch et al., 2020; Maguire et al., 2024; Russell et al., 2018), anxiety disorders (Acheson et al., 2015; Cagna et al., 2019; Guastella et al., 2009), PTSD (Flanagan et al., 2019; Giovanna et al., 2020; Stauffer et al., 2022), drug dependency (Mellentin et al., 2023; Moeini et al., 2019; Woolley et al., 2016), autism (Anagnostou et al., 2012; Audunsdottir et al., 2024; Hollander et al., 2007) and schizophrenia (Buchanan et al., 2017; Feifel et al., 2012; Zierhut et al., 2024).

Despite some promising results and consistent findings—such as reports of oxytocin exerting effects on stress and anxiety responses in humans (Jurek & Neumann, 2018) and decreased amygdala activity in men after intranasal oxytocin in responses to negative valence processes (Kirsch et al., 2005; Wang et al., 2017)—there have been notable inconsistencies in the outcomes of studies exploring its therapeutic application and the more basic mechanisms underlying its effects (Bartz et al., 2011). The literature reporting the effects of oxytocin administration in autistic people exemplifies this issue: while some studies report effects of oxytocin administration on core autism characteristics (Daniels et al., 2023; Watanabe et al., 2015),

others report null findings for the same or similar outcomes (Guastella et al., 2023; Sikich et al., 2021). Similar inconsistencies are found for oxytocin administration for PTSD symptom reduction, reporting both useful reductions in symptoms (Flanagan et al., 2019) and increased startle responses (Stauffer et al., 2022), at least when using a higher 40 international unit dose. Similar complex patterns emerge for other subfields of oxytocin biobehavioral research (Winterton et al., 2021). A systematic review and meta-analysis can serve as a useful method for synthesizing mixed evidence (Borenstein et al., 2009), as it aggregates data related to a specific research question based on predefined inclusion and exclusion criteria, providing summary effect sizes and a framework to evaluate research claims. To date, over 20 meta-analyses on the effects of oxytocin administration alone have been published (Kang et al., 2025), as well as meta-analyses exploring oxytocin genetics (Bakermans-Kranenburg & Van IJzendoorn, 2014; Prata & Silva, 2022) and oxytocin concentrations in peripheral and central fluids (Ferreira & Osório, 2022; Valstad et al., 2017). Other reviewers—although not systematic meta-analyses—have considered whether effects of oxytocin may vary with individual differences such as age or biological sex (Huffmeijer et al., 2012; Procyshyn et al., 2024)

While meta-analysis can be an effective tool for synthesizing findings, a notable limitation is that they can get outdated rapidly as new evidence becomes available. This issue is particularly pronounced in research areas with high activity, such as the field of oxytocin research (Leng & Leng, 2021). Shojania and colleagues (2007) reported a median time lag between last meta-analysis search to publication of 8 months, with 10% of publications experiencing delays exceeding 18 months. Furthermore, there is often a gap of 2.5 and 6.5 years from the publication of a randomised controlled trial to its inclusion in a meta-analysis (Elliott et al., 2014). Alarmingly, it has been suggested that 7% of systematic reviews are outdated before they are published (Shojania et al., 2007). Consequently, as new evidence emerges, meta-analytic outcomes can shift considerably between the final search date and the publication of the review. Collectively, these factors contribute to the finding that within two years, 25% of reviews become obsolete, with this figure increasing to 50% within five years (Winters et al., 2021).

Living meta-analysis is an emerging alternative to traditional meta-analysis, designed to be updated continuously as new evidence becomes available (Simmonds et al., 2017). While living meta-analyses use the same statistical methods as traditional meta-analysis, they are characterised by *a priori* commitments to regular updates, following a specific plan for searches

and analysis (Elliott et al., 2017). Each update builds on the previous by incorporating new evidence, thereby conserving resources by using existing search strategies and analysis plans. Additionally, living meta-analysis can help mitigate parallel reviews on the same topic, allowing research groups to redirect their resources to other areas of inquiry. This approach can also reduce the time lag between article publication and inclusion in a meta-analysis.

Elliot and colleagues (2017) have proposed three criteria for judging whether a living systematic review is appropriate: 1) A systematic review is a priority for decision-making, 2) certainty in the existing evidence is low or very low, and 3) there is likely to be new research evidence emerging. These three criteria arguably apply to oxytocin research. First, oxytocin is suggested to be important for various conditions ranging from mood disorders to schizophrenia, which means that increased knowledge on oxytocin's function can be highly beneficial to better understand and support these conditions. And as systematic reviews are considered the gold standard for evidence (Cooper et al., 2019; Crocetti, 2016; Gopalakrishnan & Ganeshkumar, 2013), systematic reviews investigating oxytocin's role in human health and wellbeing can be considered a priority for decision making, because it affects public health matters such as research funding and prioritization, establishing new or alternative therapeutic options and health care policy decisions. Second, methodological and experimental challenges have raised questions about the validity of existing findings (Leng & Ludwig, 2016; Quintana, 2022; Walum et al., 2016), meaning that the certainty of current evidence base can be considered generally low. Furthermore, overall results in the field have been inconsistent. Third, new research on oxytocin is rapidly emerging (Leng & Leng, 2021). Between 2010 and 2019, 3752 papers were published that included oxytocin as a main research focus, especially the effects of oxytocin administration on biobehavioural outcomes (Leng and Leng, 2021). Therefore, biobehavioural oxytocin research is a good candidate for the living meta-analysis approach.

Although living meta-analyses are not a novel concept, their adoption has been slower than anticipated across most research fields. One reason for this slower than expected uptake, despite the clear advantages of this approach, is that the academic publishing ecosystem and existing researcher incentives are not well suited for living meta-analyses. The prevailing publication and incentive system are suited to the publication of novel individual papers, rather than iterative updates. Most academic publication platforms cannot currently facilitate the versioning of manuscripts (but see the F1000Research platform; https://f1000research.com). While living

meta-analysis updates can be published as individual articles, it can be difficult to have an overview of all updates and the overall status of the living meta-analysis.

Other elements of a living meta-analysis, including the protocol, preregistration, analysis script, and data, are typically fragmented over several platforms, which makes it challenging to have an overview of the entire project. Relatedly, there is a potential for researchers to receive inadequate recognition when each update is assigned an individual Digital Object Identifier (DOI). Conversely, if a living meta-analysis were to be assigned a single DOI for all updates, this could create citation challenges. For instance, if an article references a single living meta-analysis DOI to support a claim, it may inadvertently cite a living meta-analysis whose conclusions have since evolved due to subsequent updates, potentially misrepresenting the evidence. Methodological considerations also arise with living meta-analyses, particularly regarding repeated testing increasing the risk of false positives (Groenwold et al., 2021). While Bayesian meta-analysis can be used (Bartoš et al., 2022), among other emerging approaches, this method is not yet common in the biobehavioural sciences.

To address these challenges, we have created the Active Monitoring of Oxytocin Research Evidence (AMORE) living meta-analysis platform. In this article, we will describe its development and features. AMORE has been designed to host living meta-analysis on oxytocin research investigating its effect on biobehavioural outcomes. Each living meta-analysis project has its own dedicated webpage that displays an abstract and key information and provides direct links to relevant materials and publications. Rather than functioning as an independent publishing system, AMORE acts as an aggregator that connects users to all publications and materials associated with each living meta-analysis. Altogether, AMORE will provide up-to-date evidence for biobehavioural oxytocin research. The name was deliberately chosen to play on the Italian word for ‘love’, reflecting oxytocin’s commonly recognised role as a “love hormone” (Neumann, 2023), while emphasising that our understanding of its diverse functions will continue to evolve as new evidence emerges.

Methods

AMORE is a website platform designed to host living meta-analysis on oxytocin research investigating its effect on biobehavioural outcomes. These outcomes encompass all oxytocin

research spanning across genes, biological markers, behavioural assessment and physiological systems with the specific exclusion of obstetric applications like childbirth, nursing and pregnancy as this is a separate sub-field with a distinct history and research objectives. Contributors to AMORE adhere to a standardized framework for all hosted living meta-analysis. This is to ensure standardisation between meta-analyses. The standardised framework was established by a General expert steering committee with 24 members (Fig. 2). A key feature of the platform is a checklist for researchers planning to publish on AMORE for what information is required for project proposals, so that the checklist can be used actively in the systematic review planning process. This checklist can be downloaded as a PDF file (Supplementary File 1).

Platform development

A general expert steering committee (N = 24) of co-authors was assembled to develop the requirements and recommendations for submitting a living meta-analysis project to AMORE. Authors IAI and DSQ approached potential members via email, who have experience with biobehavioural oxytocin research. The initial invitations were to individuals with a range of experience (e.g., years performing research, meta-analysis expertise), to achieve a more representative sample of researchers. A Delphi approach was used for achieving group consensus on a standardised framework for the AMORE platform (see Figure 1). The process began with authors IAI and DSQ developing the first questionnaire, which was delivered by email to the general expert steering committee. The first questionnaire served as a preliminary assessment of expert panel perspectives. Once the responses were collated, they were analysed and visualised using R (Posit team, 2025).

After the results from the first questionnaire were analysed, authors IAI and DSQ developed the second questionnaire. The second questionnaire balanced three considerations: the level of consensus from the first questionnaire, feedback provided in the open-ended response sections, and alignment with open and reproducible science principles. Items with low agreement often resulted in the proposal of recommendations instead of mandatory requirements.

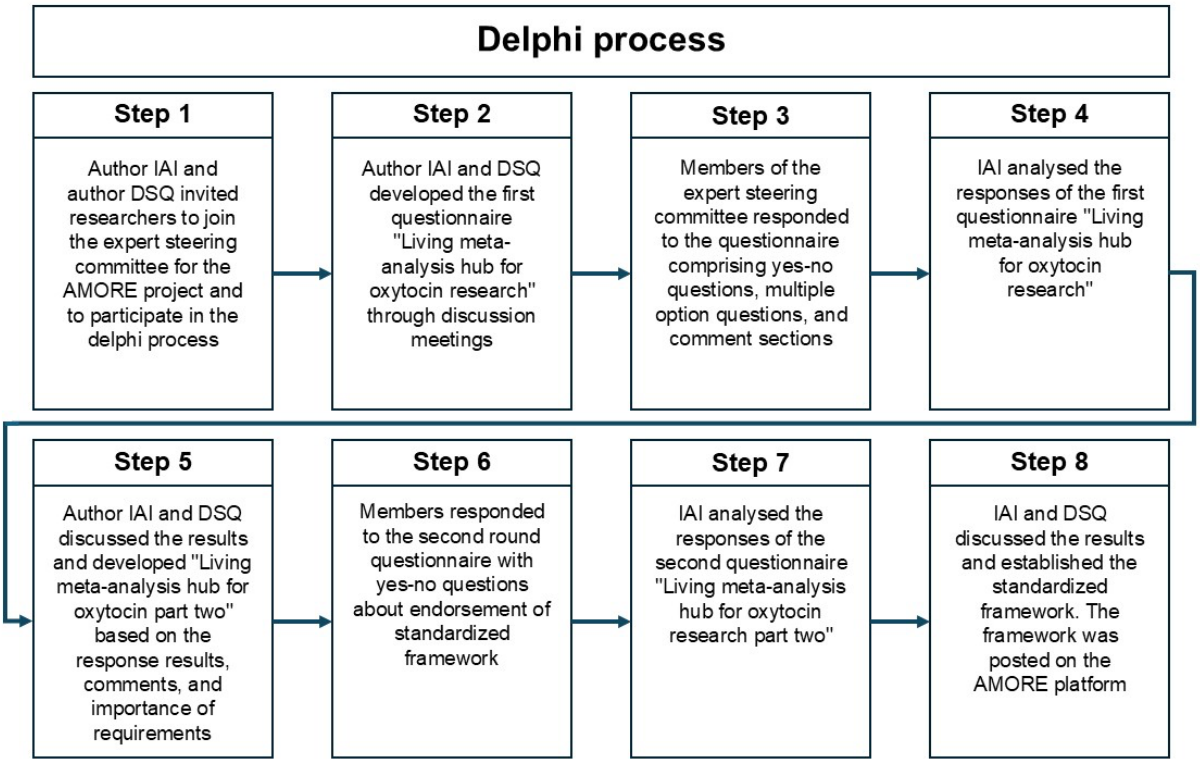

Figure 1. The Delphi process. The steps conducted to reach consensus with the general expert steering committee on a standardized framework.

Expert Steering committee

The general expert steering committee resulted in 24 members (Figure 2), including authors IAI and DSQ. A core expert steering committee is tasked with evaluating project proposals, confirming whether they fall within the remit of the AMORE platform. A core group of members serves a one-year term. This core group consists of six members, including four active members and two reserve members in cases with conflict of interest or if active members are on leave. The core group is led by author DSQ. The expert steering committee can also provide methodological guidance if requested by project proposers. Once a living meta-analysis is accepted for inclusion, members of the expert steering committee can voluntarily contribute with verification of computational reproducibility, review protocol adherence and cross-check analysis to preregistration, and report deviations from protocol.

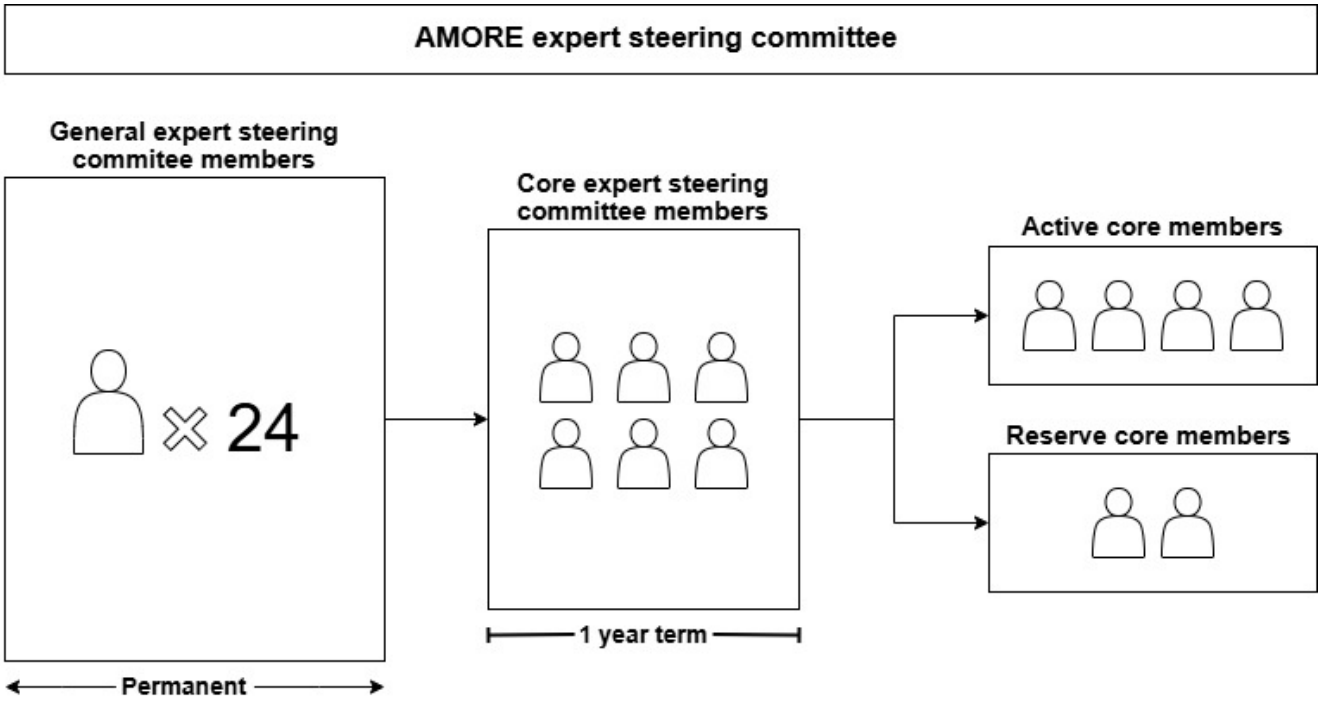

Figure 2. Formation of AMORE expert Steering Committee. The General expert Steering Committee comprises all 24 co-authors including authors IAI and DSQ.

Results

First questionnaire

The first section from the first questionnaire examined demographic attributes of the expert steering committee members (Fig. 3). Over half of the members had passed 7 years or more since they completed their PhD (Fig. 3a). Most of the expert committee members have experience with meta-analysis having been a co-author on a published article for meta-analysis (Fig. 3b). A majority of the members are comfortable with interpreting Bayesian meta-analysis results (Fig. 3c), which is becoming an accessible approach with the recent development of reproducible point-and-click analysis (Bartoš et al., 2022).

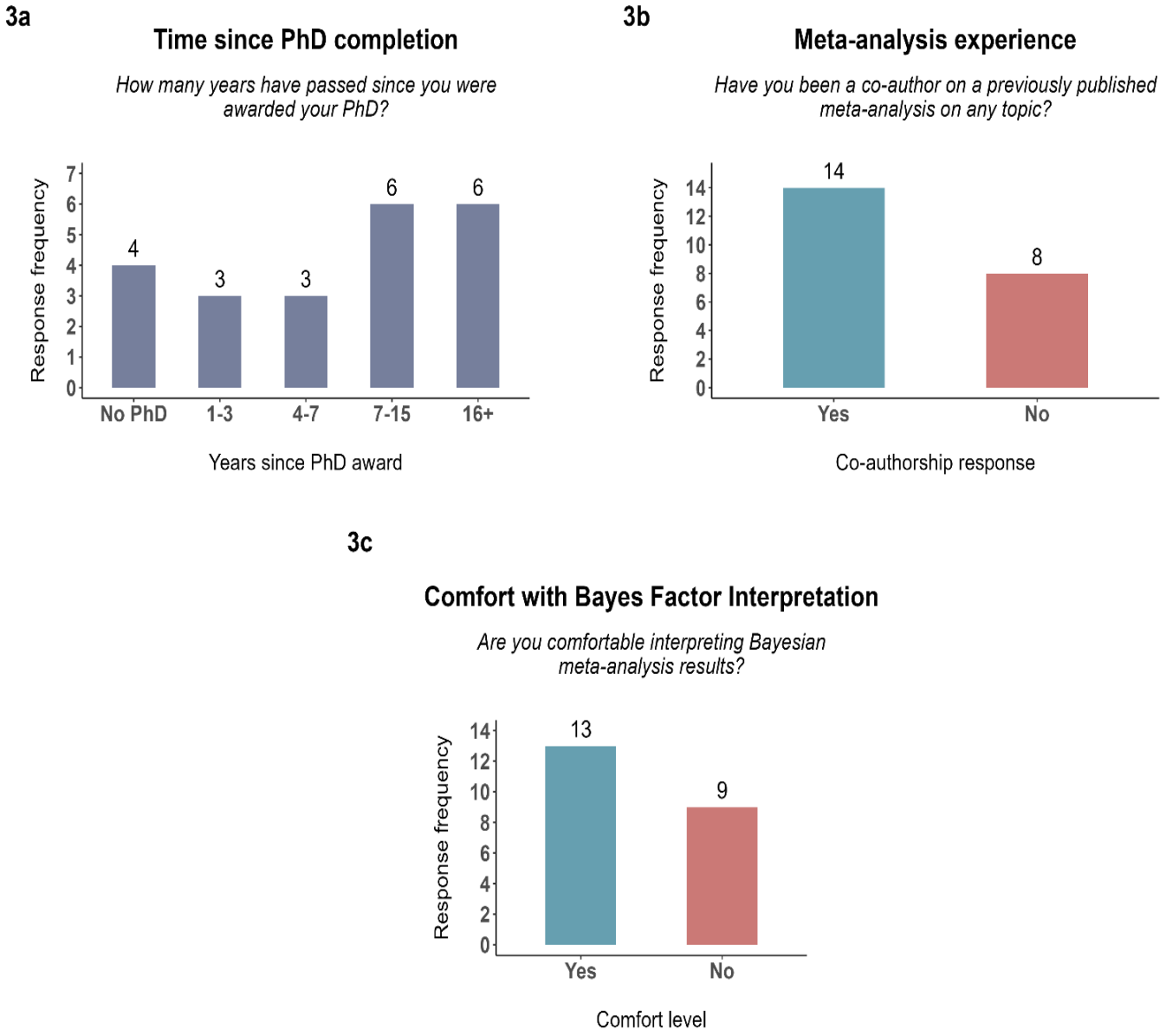

Figure 3. Demographic results from the first questionnaire. Questionnaire items are shown under each subtitle. (n = 22).

Questionnaire items from the first questionnaire with multiple response options are presented as bar graphs to clearly display the response options and results, while binary questions are reported as percentage endorsement in Table 1.

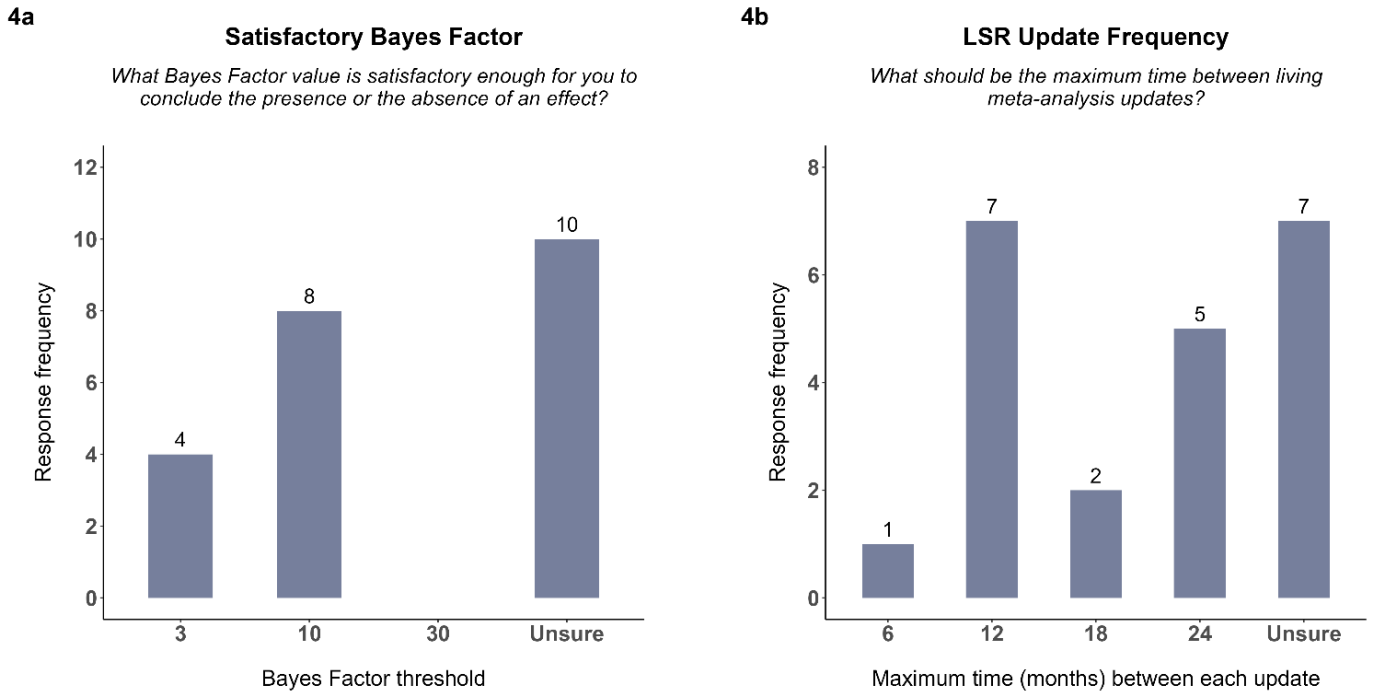

Figure 4**. Questionnaire items from the first questionnaire with multiple response options.** Questions are shown under each subtitle (n = 22). LSR = Living systematic review. Bayes Factor = statistical measure comparing how well competing hypothesis explains the data. Bayes Factor can quantify evidence for *both* presence and absence of an effect.

Figure 4 displays the questionnaire items from the first questionnaire which had multiple response options and was used in the process of developing the standardized framework. The AMORE goal is presenting updated evidence, and it was therefore considered an advantage to have a Bayes factor threshold agreement on what is sufficient evidence for an alternative or null hypothesis. A Bayesian approach is better suited for accumulating evidence than frequentist tests (Bartoš et al., 2022; Quintana & Williams, 2018). Most members responded 'Unsure' to the Bayes factor question (Fig. 4a). The first questionnaire also sought to explore opinions regarding meta-analysis update frequency, for which expert steering committee members had to consider the best balance between up-to-date evidence and the resources it takes to perform an update (Fig. 4b). The response with the most votes was split between 12 months of maximum time between meta-analysis updates and the response option 'Unsure' (Fig. 4b).

Question	Percent who endorsed 'Yes'
Are you comfortable interpreting bayesian meta-analysis results?	59.1%
Should it be mandatory that authors require a plan to evaluate evidence for a null hypothesis?	86.4%
Should it be mandatory that these meta-analysis are pre-registered?	72.7%
Should it be mandatory that authors require a plan to deal with 'accumulation bias' issues when using a frequentist framework?	77.3%
Should it be mandatory that the manuscript describing results from the initial meta-analysis to be deposited on a recognised pre-print server, such as Open Science Framework?	77.3%
Should it be mandatory that meta-analyses adhere to the PRISMA reporting guidelines?	90.9%
Should it be mandatory that the meta-analyses data is depositied in a recognised repository (e.g., Open Science Framework, Zenodo)?	95.5%
Should it be mandatory that the meta-analyses analysis script or analysis file using free software is deposited in a recognised repository?	95.5%
Should it be mandatory that if there are any protocol deviations, these should be reported in a seperate supplementary document attached to the meta-analysis manuscript?	95.5%

Table 1. Living meta-analysis hub for oxytocin research: Questions and responses. Summary table of questions and responses to binary questions from the first questionnaire (n = 22).

All binary questions and the percentage of the sample who endorsed ‘Yes’ from the first questionnaire is presented in Table 1. Questions regarding evaluating evidence for a null hypothesis, making preregistration mandatory, requiring the researchers to handle accumulation bias when using a frequentist framework and requiring initial results to be published as a preprint were the questions with the lowest agreement levels.

The final item on the first questionnaire addressed visualisation requirements and was designated as optional. Among the 22 participants, 15 provided responses to this question

(Fig. 5a). Non-responses were interpreted as indication that participants did not consider visualisation to be essential as part of the requirements. However, the questionnaire design omitted a response option which would have explicitly expressed this. Analysis of response patterns from the 15 participants who addressed this question (Fig 5b) revealed a strong preference for forest plots, with 8 participants selecting at least forest plots and 7 participants indicating a preference for both forest and funnel plots. Notably, no participants selected funnel plots as their sole visualization preference.

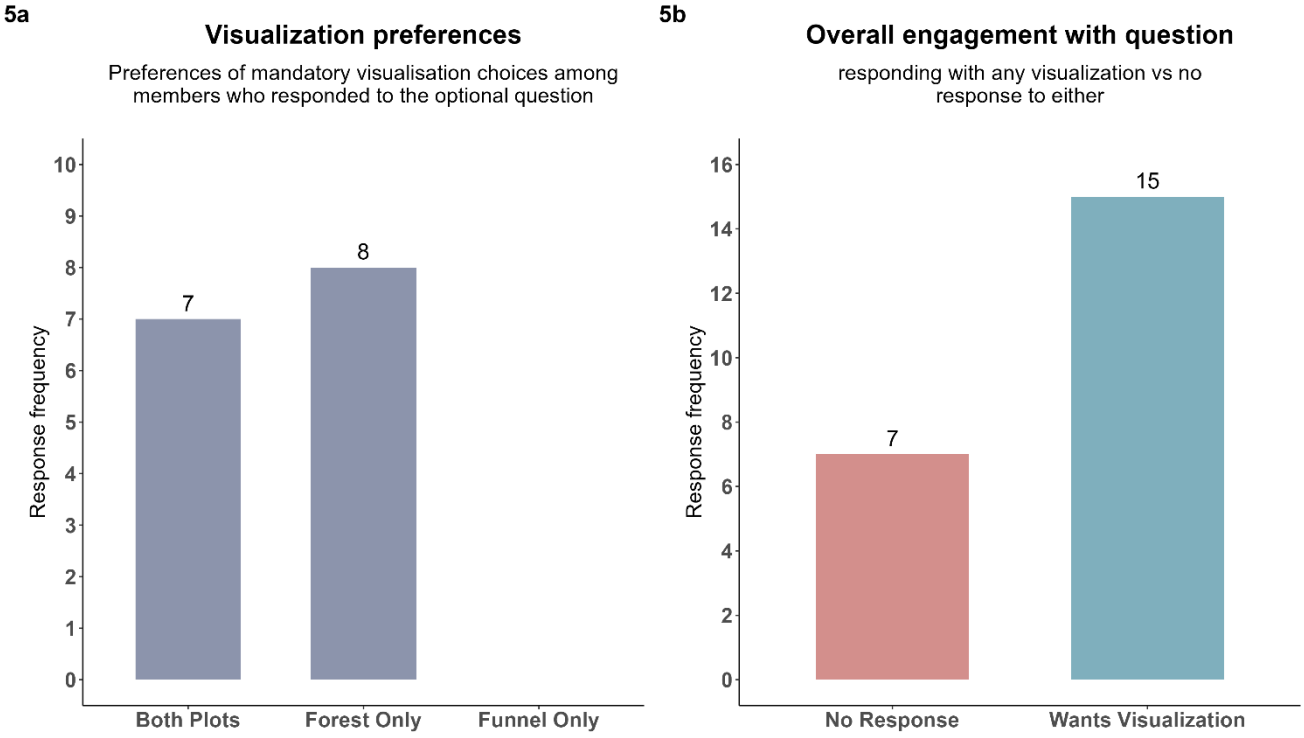

Figure 5: **Meta-analysis Visualization Preferences**. Questionnaire items from the first questionnaire with multiple response options. (n = 22). The responders of the first questionnaire had the optional question “Which of these meta-analysis visualisations should be mandatory? (Select any that you think should be mandatory)”. The response options were Forest plot and Funnel plot.

Second questionnaire

Questions and endorsement measured in percentages from the second questionnaire are presented in Table 2. The questionnaire consisted of 11 questionnaire items, of which six received 100% endorsement. These six items included two items regarding recommendations and four

items regarding requirements. The recommendations pertained to creating a plan to evaluate the evidence for a null hypothesis and handling accumulation bias issues and the requirements to adherence to PRISMA, sharing of data and analysis scripts from free software, and supplying

Question	Percent who endorsed 'Yes'
Based on the panel's responses, would you consider it satisfactory that a Bayes Factor of 10 is the recommended value to conclude about the presence or absence of an effect?	90.5%
Based on the panel's responses, would you consider it satisfactory to have a mandatory bar of 24 months as the maximum time between living systematic reviews update, and a recommendation of updating every 12 months?	95.2%
Based on the panel's responses, would you consider it satisfactory that we highly recommend authors to create a plan to evaluate the evidence for a null hypothesis?	100%
Based on the panel's responses, would you consider it satisfactory that pre-registration is mandatory for the meta-analysis?	90.5%
Based on the panel's responses, would you consider it satisfactory that we highly recommend authors to develop a plan to deal with accumulation bias issues when using a frequentist framework?	100%
Based on the panel's responses, would you consider it satisfactory that it is mandatory for authors to publish a manuscript describing the results from the initial meta-analysis on a recognised pre-print server, such as Open Science Framework?	90.5%
Based on the panel's responses, would you consider it satisfactory that it is mandatory for authors to adhere to the PRISMA reporting guidelines?	100%
Based on the panel's responses, would you consider it satisfactory that it is mandatory for meta-analysis data to be deposited in a recognised repository (e.g. Open Science Framework, Zenodo)?	100%
Based on the panel's responses, would you consider it satisfactory that it is mandatory for analysis scripts using free software to be deposited in a recognised repository?	100%
Based on the panel's responses, would you consider it satisfactory that it is mandatory for authors to supply a deviation report in a separate supplementary document attached to the meta-analysis manuscript?	100%
Based on the panel's responses, would you consider it satisfactory that we recommend authors to use visualisations (e.g., forest plot and funnel plot)?	95.2%

Table 2. Questions and endorsement percentages for the second questionnaire**. (n=21).**

the manuscript with deviation reports. Additionally, two items received 95% endorsement, i.e., the item regarding frequency of updating the living meta-analysis with a mandatory maximum time of 24 months and a recommended time of 12 months between updates and the item recommending authors to use visualisations. Further, three items received 90.5% endorsement, i.e., the item regarding recommended use of a Bayes Factor of 10 for concluding presence or absence of an effect; and the items regarding required preregistration of the analysis and publishing of the preprints.

Standardized framework

The final standardized framework (Table 3) was developed by balancing three key considerations: expert committee endorsement levels from the second questionnaire, open-ended feedback, and alignment with transparent, reproducible science principles. Six of the 11 proposed framework elements received unanimous expert committee endorsement and were included with minimal modification. The broader goal for the application of PRISMA reporting guidelines (Page et al., 2021) was for authors to report their meta-analysis with transparency and detail that will enable other scientists to replicate and better understand their work. The requirement to use PRISMA was modified from use of PRISMA only to also include MOOSE (Brooke et al., 2021) or MARS (Appelbaum et al., 2018) as alternatives to accommodate different types of meta-analyses (e.g., intervention studies, observational studies). In addition to using PRISMA, providing deviation reports when departing from initial protocols (Galuchie et al., 2021), developing plans to manage accumulation bias (Ranganathan et al., 2016), creating plans to evaluate null hypotheses (Harms & Lakens, 2018), and sharing data and analysis scripts in recognized repositories received unanimous endorsement and was included without any modification. Since the design of the questionnaire, a modified version of PRISMA for living systematic reviews was published (Akl et al., 2024), which will now be required for reporting meta-analyses of intervention studies instead of the regular PRISMA checklist.

Five elements received strong (but not unanimous) support, with endorsement levels between 90.5% and 95.2%. The decision to include these requirements was based on their fundamental importance to transparent research. Notably, the two items that received 90.5% endorsement were the requirement for preregistration and preprint publication. It was decided that the importance of these requirements in facilitating timely meta-analysis updates

independent of journal publication timelines, combined with their high endorsement rates, justified their inclusion in the AMORE standardized framework.

	Mandatory requirements
Update frequency	Maximum 24 months between updates, with a recommendation of updating every 12 months
Preregistration	The meta-analysis must be preregistered
Preprint	Initial results must be published on a recognised preprint server (e.g. Open Science Framework)
Guidelines adherence	Meta-analysis must follow PRISMA or equivalent guidelines (e.g. MOOSE, MARS)
Data repository	Meta-analysis data must be stored in a recognised repository (e.g. Open Science Framework, Zenodo)
Analysis scripts	Analysis scripts using free software must be deposited in a recognised repository
Deviation report	Authors must supply a deviation report in a separate document attached to the meta-analysis manuscript
	Recommended practices
Null hypothesis	It is highly recommended to create a plan to evaluate the evidence for a null hypothesis
Accumulation bias	It is highly recommended to develop a plan to deal with accumulation bias issues
Effect determination	Bayes factor of 10 is the recommended value to conclude about the presence or absence of an effect
Visualisations	It is recommended to use visualisations (e.g. forest plot, funnel plot)

Table 3.The AMORE standardized framework.

The requirement regarding updating frequency received 95.2% endorsement and was incorporated into the standardized framework following a consensus-building process that resolved initial disagreement. The responses to the first questionnaire from panel members (n = 22) are as follows (Figure 4b): Seven members favoured 12-month updates, five preferred 24-month updates, and seven were uncertain about appropriate intervals. Open-ended comments revealed conflicting concerns about being either too strict (potentially deterring authors) or too lenient (compromising the timeliness of evidence). The second questionnaire addressed these competing priorities through a dual approach: a mandatory bar of 24 months between each update, with a recommendation of updating every 12 months. The 95.2% endorsement of this modified item represents both a relatively successful resolution of the initial disagreement and an endorsement rate high enough to justify inclusion.

The remaining two items [i.e., use of a Bayes factor of 10 to conclude about presence or absence of an effect (90.5% endorsement); and inclusion of visualisations (95.2% endorsement)] were included as recommendations rather than requirements. Recommendations require a lower consensus threshold because they maintain author autonomy and acknowledge that panel members hold less unanimous or strong opinions about their necessity. It is important to stress that the AMORE standardized framework reflects strong collective endorsement rather than 100% agreement across all members for all items. We acknowledge that individual panel members may hold different views on some elements of the standardized framework.

Demonstration of platform use

We demonstrate the use of the platform with two projects that are currently at different publishing stages. The first project (Moxnes et al., 2025) is in its preliminary phase, having been preregistered but not having yet completed any analysis or published any preprints or articles (Supplementary Fig. 1). The second project was originally preregistered as a conventional meta-analysis and has published its first preprint and article (Kang et al., 2025). It is now transitioning into a living meta-analysis through protocol modifications incorporating search and analysis update details (Supplementary Fig. 2). We have also prepared an instructional video

introducing the platform, which can be found on the AMORE Open Science Framework page https://osf.io/tuva2/files/osfstorage/68b827002dec0717e5ef9701.

Discussion

AMORE is a centralized hub for living meta-analyses investigating oxytocin and its biobehavioural outcomes in humans. The platform implements a standardized framework that all hosted meta-analyses must adhere to, developed through consultation with an expert steering committee using a Delphi process. A smaller core steering committee provides ongoing consultation and contributes to AMORE by reviewing project proposals and offering voluntary methodological guidance. Instead of relying on scattered publications and files for investigating a research question via living meta-analysis, AMORE consolidates materials in comprehensive project pages. The platform promotes transparency through default requirements including preregistration, publication of preprints, sharing data, and analysis scripts, following consistent reporting guidelines and providing deviation reports. By enhancing both rigor and visibility of ongoing evidence synthesis for biobehavioural oxytocin research, AMORE complements traditional publishing systems while addressing the challenge of conventional meta-analysis becoming obsolete.

The two-round Delphi process established a standardised framework with strong consensus across 24 experts. This process yielded seven mandatory requirements focused primarily on open science practices, and four recommendations centred around statistical/methodological considerations. Overall agreement levels were remarkably high with the lowest agreement level at 90.5% (recommendation of using Bayes factor of 10, mandatory preregistration and mandatory publication of preprints), and six out of ten items received a 100% consensus. Key areas of unanimous support included data sharing in recognised repositories, sharing analysis scripts using open software (e.g., R, JASP), deviation reporting, and adherence to reporting guidelines. The strategic shift from mandatory to recommended practices proved useful for building acceptance amongst the expert committee and helped to provide an acceptable balance between methodological rigor and preserving researcher autonomy.

Analysis revealed patterns in how researcher experience influenced responses to open science requirements (Supplementary fig. 3). Senior researchers (7+ years or more since PhD conferral) were the only group consistently represented in the “No” response (six

instances) across all four controversial items: preprint requirement, preregistration requirement, handling accumulation bias and creating a plan to evaluate evidence for null hypothesis, followed by early career (three instances) and no PhD (one instance). This pattern raises important questions about whether these differing views from some senior researchers reflects wisdom gained through experience or less familiarity with newer research practices. Senior researchers might have encountered more practical challenges with open science implementation, developing realistic expectations about potential complications, such as the additional time needed to implement new practices (Hostler, 2024). Conversely, early-career researchers may possess more theoretical knowledge about the problems open science may address (e.g., reducing researcher flexibility), but lack practical experience with implementation challenges. Given the small sample sizes within each group (n= 4-12 per experience level) these patterns should be interpreted with caution, as a single individual changing the response could substantially alter the observed trends.

Another notable pattern emerged in the identical “Yes” to “No” shifts that occurred for preprints and preregistration between the first and second questionnaire (Supplementary fig. 3a and 3b). Both preprints and preregistration remained as mandatory requirement items even after the results from the first questionnaire with 23% opposition for mandatory publication of preprint and 27% opposition of mandatory preregistration. The second questionnaire asked, “Based on the panel’s responses, would you consider it satisfactory that...". This wording asked respondents to evaluate whether implementation was satisfactory given the panels collective responses, rather than soliciting their personal opinions on the requirements. Respondents who shifted from “Yes” to “No” between the first and second questionnaire may have found this an insufficient justification for mandatory requirements. They may have expected a higher consensus level before imposing strict demands. Conversely, expert respondents who shifted from “No” to “Yes” between the first and the second questionnaire may have different consensus expectations, viewing majority support as adequate justification for mandatory requirements. An alternative explanation for these shifts is that simply respondents changed their mind after additional reflection between questionnaires. Shifting responses and varying consensus thresholds ultimately highlight a critical question: on what grounds were preregistration and preprint publication deemed essential enough to remain mandatory despite expert dissent? Ultimately, the 90.5% consensus achieved in the second

questionnaire for preregistration and preprint publication requirements was considered adequate endorsement for such critical elements. This decision recognises the crucial role of preregistration in combating *post hoc* analysis and publication bias. A concern is that preregistration and deviation reports require additional administrative work (Hostler, 2024). However, this cost is likely outweighed by credibility issues that can be associated with meta-analyses that are not preregistered. Moreover, preregistration with robust protocols may in fact reduce workload by establishing one comprehensive protocol for all updates, eliminating repeated rounds of methodological reconsiderations, re-decisions, and re-discussions. Preregistration, therefore, should not be considered solely as a resource cost. Lastly, another concern raised by preregistration of living meta-analysis regards stifling innovation (Garzino Demo, 2025; Klonsky, 2025), but see Frankenhuis & Nettle (2018). Preregistration is not a protocol that rigidly prohibit changes, rather, it requires documentation of methodological decisions and deviations. Thus, preregistration should not be viewed as discouraging methodological innovation, but a transparent record of decisions taken during the process.

Mandatory preprint publication also received sufficient endorsement at 90.5%. The primary rationale for inclusion of this process as recommendation in the platform stems from the limited publishing options available to living meta-analysis and the benefits of rapidly sharing research results. Traditional publishing venues are generally not designed to accommodate multiple updates, whereas preprints can be published almost instantly, ensuring continuity for living meta-analysis projects. Additionally, preprints enhance transparency with publication of complete analytical results without the constraints of journal word limits. Preprints also ensure that negative or null results will be disseminated even when academic journals decline to publish these results.

While much of oxytocin research addresses clinical outcomes, AMOREs inclusive scope of all biobehavioural outcomes, including mechanistic research that contributes to theory building and future research directions, may not equally satisfy the criterion of importance for decision making. This suggests that some of the future project proposals for living meta-analysis might be better suited as traditional meta-analysis, given the substantial resource demands required for maintaining a living meta-analysis. This is a point the expert steering committee members should consider when reviewing and approving project proposals.

Fundamental tension in the discussion around living meta-analysis pertains to sustainability and cost-benefit considerations. Living meta-analyses aim to reduce research waste by encouraging researchers to invest in a single, continuously updated meta-analysis that reuses established analysis plans and search strategies; this contrasts with the current practice of conducting multiple, often parallel, meta-analyses on the same topic that quickly become outdated, each requiring new protocol development, analysis plans, and comprehensive methodological frameworks. However, this resource-saving potential depends on the research context. In cases where evidence remains sparse or when conclusions are consistent, conventional meta-analyses may offer greater resource efficiency. Therefore, researchers should thoughtfully consider if their systematic review is suited as a living systematic review or better suited as a conventional meta-analysis. Elliot and colleagues' (2017) criteria can provide a useful starting point for these considerations. Since it can be difficult to determine in advance which topics offer optimal value as living compared to conventional meta-analysis, establishing frameworks for evaluating return on investment and establishing retirement criteria can offer potential future solutions for this dilemma.

While AMORE offers the advantages of a centralized hub for living meta-analysis in oxytocin research, these benefits must be weighed against the flexibility of conducting independent living meta-analyses. AMORE provides several advantages, such as increased visibility through a centralised hub, cross-project connectivity within the oxytocin research community, comprehensive project pages linking all relevant documents and materials, enhanced credibility through the standardized framework and access to methodological support from an expert steering committee. However, these benefits come at the cost of autonomous decision-making, as researchers must adhere to standardized framework requirements including preregistration, preprint publication, open data and script sharing, and compliance with reporting guidelines. Notably, while the framework mandates open scientific practices, it preserves considerable methodological flexibility by not prescribing specific analytical approaches, with one key exception: the requirement for analysis updates at least every two years.

AMORE's standardised framework encourages living meta-analysis for oxytocin research to maintain high methodological quality and transparent research practices. A central achievement during the platform's development was striking a balance that upholds these standards without deterring participation through excessive strictness. The recommendation

structure for items like accumulation bias planning provides flexibility while raising awareness of important statistical considerations. For accumulation bias specifically, while living meta-analyses involve multiple updates that could increase Type I error risk (Ranganathan et al., 2016), the AMORE framework's recommendation encourages researchers to consider these issues while still accommodating different analytical approaches. Rather than potentially excluding valuable research contributions through restrictive requirements, our approach promotes methodological awareness.

It is noteworthy that the Delphi approach, while effective, lacked some predetermined specifications. Although it was decided that the first questionnaire would collate responses and the second questionnaire would assess agreement with the consensus results, the criteria for defining and formulating these "consensus responses" were not established beforehand. Between questionnaires, some items were reclassified from requirements to recommendations, but this decision emerged during the process rather than following predetermined protocols for handling varying agreement levels. Similarly, no threshold levels of endorsement were established in advance for determining inclusion and exclusion of the standardized framework. Instead, decisions were made after collecting and reviewing all responses. Despite this, the process succeeded because endorsement levels were high, minimizing potential conflict. This approach also benefited from treating responses as guidelines rather than absolute directives, allowing for pragmatic interpretation.

One issue specific to living meta-analyses involves citation issues stemming from traditional publishing infrastructure not designed for iterative updates. The conventional DOI model assumes one publication equals one final, static version. This creates fundamental problems for living meta-analyses. A single DOI approach generates confusion when content changes significantly. For example, studies citing the living meta-analysis may find their citations pointing to conclusions that no longer support their original claims. Conversely, multiple DOIs, while systematically differentiating between versions and enabling safe citation practices, can fragment impact measurement. A living meta-analysis project might accumulate hundreds of citations across several DOIs, with each individual DOI appearing to have minimal influence, while a traditional single-publication meta-analysis concentrates all citations under one DOI, seemingly demonstrating greater impact. However, this is a solvable

problem, with platforms like F1000 providing a DOI that resolves to the latest version of an article, which is encouraged for citations, along with DOIs for specific article versions.

Preregistrations, preprints and publications receive separate DOIs. AMORE can assist by organizing these different DOIs on their respective project pages. This way, AMORE can track and manage versioning. However, this does not solve the problem of fragmented impact. One potential solution involves assigning each AMORE project its own overarching DOI, perhaps via an Open Science Framework project. However, this deviates from standard citation practices that reference single paper versions. This approach could create inconsistent citation behaviours, with some referencing the versioned DOI, others the overarching DOI, and others a combination of both, potentially causing confusion and diluting citations for authors. Given these limitations, we have opted to gather existing DOIs, rather than creating new DOIs.

Conclusion

Biobehavioural oxytocin research has garnered considerable research interest over the past two decades. However, findings have been inconsistent, with new evidence continually emerging. Consequently, the field is particularly well-suited for living meta-analyses, which can incorporate new evidence that will help draw up-to-date conclusions. In response to this need, we have developed a new online platform designed to facilitate living systematic reviews for biobehavioural oxytocin research. The platform's key features were established through a consensus process of 24 expert researchers in the field, enhancing its relevance and usability. The level of AMORE's success will largely depend on how widespread its use becomes within the oxytocin research community. We are hopeful that this article can serve as a catalyst for its adoption. While primary oxytocin research studies have notably benefited through methodological improvements, such as the use of replications studies (Declerck et al., 2020) and a closer consideration of intranasal administration practices (Guastella et al., 2013) to increase robustness, the AMORE platform presents an improved approach for advancing meta-analysis methods in the field. By embracing the living meta-analysis format and mandating rigorous standards, AMORE will help ensure that the most up-to-date findings are used to draw conclusions in the field of oxytocin research.

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Conflict of interest

EAL receives grant support and research study drug from Tonix Pharmaceuticals and receives royalties from UpToDate. EAL and/or immediate family member holds/recently held stock in Thermo Fisher Scientific, Zoetis, Danaher Corporation, Intuitive Surgical, Merck, West Pharmaceutical Services, Gilead Sciences, and Illumina. EAL is an inventor on PCTUS2025/030536 entitled, “Oxytocin-based therapeutics to improve cognitive control in individuals with attention deficit hyperactive disorder” filed on May 22, 2025. No other authors have any potential conflicts of interest to report.

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