Norwegian Medical Products Agency

Protocol for Health Technology Assessment

Intravenous ketamine for acute suicidal ideation

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Summary

Suicidal ideation refers to thoughts about or planning for suicide, and can be seen as a spectrum of intensity, from a general desire to die without concrete plans, to active suicidal ideation with an intent to act. Treating suicidal ideation is challenging, as it is a complex condition with varying clinical presentation and underlying causes. Furthermore, the current treatment options have clear limitations, e.g., delayed onset of effect and treatment resistance. As such, there is a need for fast-acting treatment options to manage acute suicidal ideation. The anaesthetic drug ketamine is a potential therapy option for acute suicidal ideation in subanaesthetic doses. In Norway, ketamine was recently approved to be used off-label for treatment-resistant depression within the specialist healthcare.

For assessment of relative efficacy and safety, we will perform a systematic search for literature in relevant databases. References will be screened for title, abstract and full-text, and included in accordance with predetermined selection criteria. We will extract and analyse data from the included studies, and the results will be compiled and presented in a report written in English. The risk of bias of the included studies will be assessed, as will the certainty of the evidence, i.e., our confidence in the results. We will also perform a health economic evaluation of ketamine/esketamine compared to standard of care, considering national priority criteria.

The health technology assessment (HTA) will focus on persons with acute clinically relevant suicidal ideation, treated with ketamine or esketamine that is administered orally, intranasally or by injection, at any dose up to 1 mg/kg. Relevant comparators include saline, midazolam, as well as ketamine and esketamine themselves. The primary efficacy outcome will be suicidal ideation as per suicidal rating scales. Outcomes for safety will include adverse events and serious adverse events. We will only include randomised controlled trials.

Title:

Ketamine for acute suicidal ideation: a protocol for a Health Technology Assessment

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Commissioner:
The Ordering Forum in the national system for managed introduction of health technologies within the specialist health care service

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Date commissioned:
28.04.2025

Start date:
27.06.2025

Target date:
27.06.2026

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Sammendrag

Selvmordstanker refererer til tanker om eller planlegging av selvmord, og kan sees som et spektrum av intensitet, fra et generelt ønske om å dø uten konkrete planer, til aktive selvmordstanker med intensjon om å handle. Behandling av selvmordstanker er utfordrende, da det er en kompleks tilstand med varierende klinisk presentasjon og flere underliggende årsaker. I tillegg har de nåværende behandlingsalternativene klare begrensninger, deriblant forsinket innsettende effekt og behandlingsresistens. Det er derfor behov for hurtigvirkende behandlingsalternativer for å kunne behandle personer med akutt selvmordsfare. Det anestetiske legemidlet ketamin er i subanestetiske doser et potensielt behandlingsalternativ for akutte selvmordstanker. I Norge ble ketamin nylig godkjent for bruk utenfor godkjent indikasjon ved behandlingsresistent depresjon innen spesialisthelsetjenesten.

For vurdering av relativ effekt og sikkerhet, skal vi gjennomføre et systematisk litteratursøk i relevante databaser. Referanser vil screenes basert på tittel, sammendrag og fulltekst, og vil inkluderes i henhold til forhåndsbestemte seleksjonskriterier. Vi planlegger å ekstrahere og analysere data fra de inkluderte studiene, og resultatene vil sammenfattes og presenteres i en rapport skrevet på engelsk. Vi vil vurdere risiko for systematiske skjevheter i de inkluderte studiene, i tillegg til vår tillit til resultatene. Vi kommer også til å gjennomføre en helseøkonomisk evaluering av ketamin/esketamin sammenlignet med dagens praksis..

Den fullstendige metodevurderingen kommer til å fokusere på personer med akutt, klinisk relevant selvmordsfare, behandlet med ketamin eller esketamin, administrert oralt, intranasalt eller ved injeksjoner, med alle doser opp til 1 mg/kg. Relevante komparatorer inkluderer saltvann og midazolam, i tillegg til ketamin og esketamin selv. Hovedutfallsmål for effekt kommer til å være selvmordstanker basert på score fra verktøy for vurdering av suicidalvorlighet. Utfallsmål for sikkerhet inkluderer uønskede hendelser og alvorlige uønskede hendelser. Vi kommer kun til å inkludere randomiserte kontrollerte studier.

Tittel:

Ketamin ved akutt suicidfare: en prosjektplan for fullstendig metodevurdering.

Oppdragsgiver:
Bestillerforum for nye metoder

Bestillingsdato:
28.04.2025

Startdato
27.06.2025

Leveringsfrist:
27.06.2026

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Godkjent av:
Martin Lerner, *enhetsleder, DMP*

Commission

On 28th April 2025, the Norwegian Medical Products Agency (NOMA) was commissioned by the Regional Health Authorities (RHA) Ordering Forum (Bestillerforum) within the National System for Managed Introduction of New Health Technologies in the Specialist Health Care Service in Norway (Nye metoder) to conduct a national health technology assessment (HTA) regarding the use of ketamine for acute suicidal risk.

The HTA is intended to act as a basis for decision-making for the RHA Decision Forum. The work on this HTA was officially initiated on 27th June 2025.

The HTA-work will be a collaboration between NOMA, clinical experts from the RHA, and patient representatives.

Project group

Project leader at NOMA:	Ingrid Kristine Ohm
Internal project group at NOMA:	Ingrid Kristine Ohm Annette Vogt Flatby Anna Stoinska-Schneider Elisabet Hafstad
External clinical experts:	Andreas Wahl Blomkvist; *University Hospital of North Norway* Peder Olai Skjeflo Holman; *Oslo University Hospital* Arne Einar Vaaler; *St. Olavs Hospital/Norwegian University of Science and Technology* Lars Lien; *Innlandet Hospital*
Patient representatives:	Guro Skottene; *Mental Helse* Lise Aareskjold; *LEVE*

Glossary and abbreviations

Term/abbreviation	Explanation
CI	Confidence interval
C-SSRS	Colombia-Suicide Severity Rating Scale
GRADE	Grading of Recommendations, Assessment, Development and Evaluation system
HTA	Health Technology Assessment
i.m.	Intramuscular
i.n.	Intranasal
i.v.	Intravenous
ICD-10	International Classification of Diseases and related health problems, 10th edition (ICD-10
INAHTA	International Network of Agencies for Health Technology Assessment
MADRS item 10	Montgomery And Åsberg Depression Rating Scale, where item 10 relates to suicidal ideation
MeSH	Medical Subject Headings
NOMA	Norwegian Medical Products Agency
NMDA receptor	N-methyl-D-aspartate receptor
PICOS	Population, Intervention, Comparator, Outcomes, Study design
RCT	Randomised Controlled Trial
RHA	Regional Health Authority
s.c.	Subcutaneous
SI	Suicidal Ideation

1. Introduction

1.1 Suicide and suicidal ideation

Suicide is the conscious and deliberate act of self-harm that causes the person to die, while suicidal ideation refers to thoughts about or planning for suicide (1;2). Suicidal ideation can be seen as a spectrum of intensity, that ranges from a general desire to die without any concrete plan or action, to active suicidal ideation with detailed plans and a determined intent to act on them (1;2).

1.1.1 Aetiology and epidemiology

Suicide and suicidal ideation are often linked to (severe) mental health disorders, especially in high-income countries such as Norway (3). Still, the aetiology is more complex, as suicidal ideation is associated with an interrelated constellation of psychological, biological, genetic, social/cultural, and environmental factors (1;4).

Although prevalent in all regions of the world, suicide and suicidal ideation are more prevalent among certain vulnerable groups, such as members of the LGBTQ+ community, refugees, migrants and minorities (3). Furthermore, men have overall a higher risk of suicide than women, especially in Western countries, e.g., Norwegian men had over twice as high risk of suicide as Norwegian women in 2023 (2;5).

As there are no numbers on how many people in Norway experience suicidal ideation at any given time, rates of suicide and attempted suicide would be the closest proxy to attempt at giving an estimation of the relevant population. It is important to note however, that having suicidal ideation is not a prerequisite for suicide, as most suicide attempts are impulsive acts rather than a result of lengthy considerations (2;6).

Norway does not have any systematic recordings of attempted suicides, though it is estimated to be around 4000-6000 attempts each year (7). In contrast, suicidal deaths are recorded in the Cause of Death Registry (Dødsårsaksregisteret). In 2023, 707 suicides were registered in Norway, i.e., a rate of 12.9 per 100,000 persons, which is similar to that of Sweden, Denmark and Iceland, lower than Finland, but higher than the average suicide rate in Europe (5). Globally, there are almost 730,000 deaths by suicide each year, which equals to almost 1 suicide every 40 seconds (3). Still, suicidal deaths may be underreported due to stigma surrounding mental health and suicide, illegality of suicide in some countries, as well as poor-quality mortality data, where suicide is not adequately reported (3).

Suicide rates increase with increasing age, especially for men. In 2023, the suicide rates among Norwegian men increased from 15 to 25 per 100 000 persons, from the age groups 15-24 years to ≥75 years, respectively (5). In contrast, the suicide rates for Norwegian women were more stable across most age groups (from 15 to 75+ years), and were highest among 45-74 year olds, at about 9 per 100,000 persons (5). It was only among the youngest age groups, i.e., up to 14 years old, that the suicide rates were somewhat similar between men and women, albeit very low (5). Although the median age for suicide is around 40-50 years in Norway, suicide is still one of the leading causes of death among youth and young adults worldwide (3-5). In Norway, almost a third of all deaths among 1 to 29-year-old men and women are caused by suicide (8).

1.1.2 Prevention and treatment

The World Health Organization recognize suicide as a serious public health problem that requires a public health response and multisectoral national strategies for suicide prevention (3). In 2020, the government of Norway published an action plan for prevention of suicide with a goal of zero suicides (“nullvisjon”), and committing to work on the basis that we have no one to lose (9). However, prevention of suicide proves to be difficult, and there are no single theories that accurately predict suicide. Moreover, the therapy strategy for suicidal ideation is also challenging, as it is a complex condition with varying clinical presentation and underlying causes. The first priority in treating acute suicidal ideation is to ensure the patient’s safety, i.e., implementing safety measures that reduce the

risk of suicide, e.g. hospitalisation (voluntary or involuntary) and close observation over a certain period of time (4;6;10-12). Furthermore, treatment strategies in general typically involve managing (underlying) symptoms such as despair, hopelessness, anxiety, and insomnia with pharmacological interventions, in addition to psychotherapy (4;6;10-12). Clear limitations with these treatment options include treatment resistance, as well as a delayed onset of effect, during which patients may act on their suicidal thoughts (13). As such, there is a need for fast-acting treatment options to manage acute suicidal ideation.

1.2 Ketamine

Ketamine (a racemic mix of R-and S-enantiomers) is a well-known, highly effective anaesthetic drug that has been commercially available since the 1970s (14;15). Due to its rapid onset effect, short half-life and general lack of clinically significant respiratory depression, ketamine has remained as a desirable anaesthetic, especially for emergency surgical procedures (14-16). Ketamine has also been known to have analgesic as well as antidepressive effects, where subanaesthetic doses of ketamine is used off-label as a therapy option for treatment-resistant depression and acute suicidal ideation (14-17). However, due to the dissociative effects with distortion of sensory input and thought processes at even low doses, and a potential for abuse, such off-label treatments with ketamine remain somewhat controversial (16-18).

While the anaesthetic effect of ketamine is primarily attributed to it acting as a noncompetitive antagonist blocking N-methyl-D-aspartate (NMDA) receptors, the mechanism of action for its possible anti-suicidal effect is largely unknown (14-16).

1.2.1 Ketamine in Norway

Ketamine is only authorised for use in Norway as an anaesthetic for brief diagnostic and/or surgical procedures, and as a supplement to other anaesthetics (14). However, ketamine in subanaesthetic doses is being used off-label as analgesia, especially for treating severe pain, e.g. in palliative care (14;17;19;20). Furthermore, ketamine was recently (25.08.2025) approved by the Regional Health Authority (RHA) Decision Forum (Beslutningsforum) within the National System for Managed Introduction of New Health Technologies in the Specialist Health Care Service in Norway (Nye metoder), to be used off-label for treatment-resistant depression within the specialist healthcare (21).

In contrast, the S-enantiomer of ketamine: esketamine, was awarded marketing authorisation in 2020 as an antidepressant used for adults with treatment-resistant depression (in combination with other antidepressive drugs) (22). However, the esketamine-drug Spravato has currently not been approved for financing by the Norwegian specialist health care in the RHA Decision Forum, due to low quality evidence and high costs (23).

1.3 Why is it important to do this HTA

The commission for this HTA was based on a proposal from Østfold Hospital HF and the previous HTA commission of ketamine for treatment-resistant depression (ID2022_018) (24). The proposal argued that ketamine is a low-cost drug, with fast and significant therapeutic effect and few side effects (25). According to the Act relating to specialist health care (Spesialisthelsetjenesteloven), the regional health authorities must organize their service in line with priority criteria relating to benefit, resource use and severity (26). All new medical technologies (i.e., medical products and indications for use) that the Norwegian specialist healthcare service are expected to finance, must therefore first be assessed in an HTA relating to the priority criteria. As such, it is important to assess the relative efficacy and safety, as well as to perform a health economic evaluation of treatment with ketamine for this patient group.

1.4 Aim

The aim of this HTA is to systematically identify, assess and analyse available research regarding efficacy and safety of ketamine and esketamine for hospital-based treatment of adults with acute suicidal ideation, and to conduct a health economic evaluation of the intervention.

1.5 External project group

Before the work on this HTA was officially initiated, we recruited external project group members consisting of clinical experts appointed by Nye Metoder, as well as patient representatives. The external project group will contribute to the work by giving their input and suggestions on information regarding Norwegian clinical practice, inclusion criteria (i.e. PICOS) based on the research question drafted in the commission, suggestions of relevant publications, as well as reading and giving their input on the report draft.

2. Efficacy and safety - method

We plan to conduct the work in our HTA in accordance with the handbook “Slik oppsummerer vi forskning”, by the National Institute of Public Health (27) and Cochrane handbook (28).

2.1 Selection criteria

Our framework, i.e., inclusion and exclusion criteria, for searching for and selecting relevant literature for our HTA is outlined in *Table 1*.

Table 1: Selection criteria (PICOS)

PICOS	Inclusion	Exclusion
Population (P)	Adults with acute clinically relevant suicidal ideation	Psychosis, schizophrenia, pregnant, post-partum depression, severe personality disorders (especially emotionally unstable personality disorder), alcohol or drug dependence
Intervention (I)	Drug: ketamine, esketamine Dose: all up to 1 mg/kg Administration forms: i.v., s.c., i.m. oral, i.n. Frequency: single dose and multiple doses	
Comparator (C)	Saline, midazolam, ketamine*, esketamine*	
Outcome (O)	Primary outcome: Suicidal ideation as per suicidal rating scales (e.g., C-SSRS or MADRS item 10). Secondary outcomes: hospital admission rate, hospital admission length of stay, Safety outcomes: adverse events, serious adverse events	
Study design (S)	Randomised controlled trials, including cross-over studies	Conference abstracts, all other study types, e.g., one-armed studies, cohort studies, systematic reviews, etc.

C-SSRS: Colombia-Suicide Severity Rating Scale, i.m.: intramuscular, i.n.: intranasal, i.v.: intravenous, MADRS item 10: Montgomery And Åsberg Depression Rating Scale, where item 10 relates to suicidal ideation, s.c.: subcutaneous
**ketamine and esketamine are listed as both intervention drugs and comparator drugs for potentially compare dose and/or administration forms.*

2.1.1 Exclusion criteria

Papers written in other languages than English, or any of the Scandinavian languages will be excluded. A list of publications excluded based on language alone in the full-text screening will be listed separately.

2.2 Literature search

An information specialist (EH) will be responsible for the search and collaborate with the project group to plan the searches aimed at identifying completed and ongoing studies that meet the predefined criteria for the assignment. The search plan and strategies will be reviewed and approved by another information specialist before the searches are conducted. The entire search process will be thoroughly documented in the final HTA report to enhance transparency and reproducibility.

As a first step we will search for ongoing and completed HTAs in the International HTA database supplemented with relevant HTA organisations' websites. We will also search the Epistemonikos database for published systematic reviews on the topic. For the main search, we will then use the following sources:

- Embase (Ovid)
- MEDLINE (Ovid)
- Clinicaltrials.gov (National Institutes of Health)
- International Clinical Trials Registry Platform (World Health Organization)

The search strategies for the electronic bibliographic databases will be adapted to the interface of each individual database. The search strategy will comprise thesaurus terms, (Medical Subject Headings (MeSH) and Emtree), author keywords and free text terms, for the population and intervention concepts. Search terms will be combined with Boolean logical operator "OR", and the search concepts with "AND". We will not restrict the search by language or publication year. We will limit the searches in MEDLINE and Embase to randomized controlled trials using validated search filters.

The search results from bibliographic databases and trials registries will be exported to the reference management tool EndNote (29). Here, we will correct any errors (e.g., records with missing titles, publication years, etc.) and remove duplicates. The unique records will then be uploaded to the web-based screening tool Rayyan (30) to assess their relevance based on the selection criteria.

We will review studies and study reports included in relevant reviews and HTAs, using a literature search conducted no later than January 2022, to evaluate their relevance. Additionally, we will consult the experts involved in this HTA to identify any further relevant publications that may have been missed in our searches. Finally, during data extraction, we will check reference lists of included publications.

The project team will consider the need for supplementary searches to provide further data on health economic evaluations, quality of life and health utility weights or complications, long-term side effects and other safety aspects when the main inclusion and data extraction processes are complete. If necessary, we will consult with the experts before deciding whether more information is needed or not.

2.3 Selection of studies

We will select studies found in the literature search in a two-step selection strategy:

1) Screening: two researchers (AVF and EH) will independently screen titles and abstracts (where available) using the Rayyan software (30) to include or exclude articles based on their relevance to our research question. When in doubt, full-text version will be included.
2) Full-text assessment: two researchers (AVF and IKO) will independently read the full-text articles to assess which will be included in our HTA.

Both steps will adhere to the eligibility criteria listed above (***Feil! Fant ikke referansekilden.***). Disagreements in either of the two steps will be resolved through discussion, or by consultation with a third researcher.

Systematic reviews and records from trial registries will be screened separately from the journal articles. Conference abstracts and preprints reporting results from randomized controlled trials will only be reviewed if there is considerable uncertainty related to effect estimates in the included studies, and we judge data from conference abstracts and preprints may contribute to clarifications.

2.4 Assessment of risk of bias

Two researchers (AVF and IKO) will independently assess the risk of bias for primary outcomes reported in the included RCTs by using the Cochrane Risk of Bias Tool for RCTs 2 (31;32). Any potential differences will be resolved through discussion between the researchers, or by consultation with a third researcher.

2.5 Data extraction

Relevant data will be extracted from the full-text articles to a self-made Excel-sheet, by one researcher. The extracted data will be verified by a second researcher. Any potential disagreements will be resolved through discussion, or by consultation with a third researcher. The researchers will also try to use a large language model (LLM) to help extract data more effectively. All data extracted by this model will be verified by a researcher.

If necessary (e.g., if data are unintelligible, etc.), we will attempt to contact the authors for them to provide us with sufficient information to use in our HTA. Information to be extracted is presented in *Table 2*.

Table 2: Data to be extracted from included studies.

About	Information to be extracted
The study	Authors, publication year, study design, country, clinical identification number, eligibility criteria, follow-up time, funding,
The participants	Numbers of participants in each group, age, sex, diagnosis, ethnicity, previous suicide attempts, baseline SI severity score, hospitalisation,
The interventions and comparators	Treatment name, information related to posology, e.g. dosage, administration, treatment cycles, etc.
The outcome	All outcome-data relevant for our HTA (see Outcome in *Table 1*)

HTA: Health Technology Assessment, SI: suicidal ideation

2.6 Analysis

The data synthesis will depend on the data provided in the included articles. If possible, we will synthesise the data in pairwise-meta-analyses (33). As we cannot assume that populations, interventions and outcomes are identical across the included studies, we will use a random-effects model in our meta-analyses. If the included studies present both adjusted and non-adjusted effect estimates, we will use the adjusted estimates. If a meta-analysis cannot be performed (e.g., if we have too heterogeneous studies, too few studies, etc.) we will present the data in a narrative synthesis. Regardless, all outcomes will be presented in forest plots (where possible) and summary-of-findings tables. For analysis of outcomes that are dichotomous, we will use effect measures such as relative risk, odds ratio or hazard ratio, with 95% confidence intervals (CI). Continuous data outcomes will be presented as absolute or relative mean difference between groups. If the included studies are using different scales to measure the same outcome, we will use standardised or weighted mean difference, with 95% CI. Where possible, the primary outcome will be subjected to subgroup (e.g., age group, etc.) or sensitivity analysis, with respect to risk of bias. Heterogeneity will be tested for using I^2-test (33). All data will be analysed using the Review Manager software (34).

2.7 Assessment of certainty of evidence

We will assess the certainty of evidence for each selected outcome using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system (28). In brief, the GRADE system evaluates the certainty of evidence through assessment of several criteria, downgrading the certainty of evidence, due to a) study limitations (risk of bias), b) inconsistency of results, c) indirectness of evidence, d) imprecision, and e) publication bias (28). The GRADE approach results in an assessment of the certainty of evidence in one of four grades, as presented in *Table 3*.

Table 3: Certainty of evidence classification

GRADE level	Symbol	Definition
High certainty	⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty	⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty	⊕⊕◯◯	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

GRADE level	Symbol	Definition
Very low certainty	⨁◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Two researchers (AVF and IKO) will independently GRADE effect estimates for each outcome extracted. Any potential disagreements will be resolved through discussion, or by consultation with a third researcher.

3. Health economics - method

To assess the health economic impact of treatment with ketamine/esketamine for treatment of patients with acute suicidal ideation, we will estimate and describe all costs and effectiveness related to this treatment option and the comparator(s) relevant in the Norwegian context. Efficacy estimates will be based on the results of the systematic literature review, and we will make final decisions about the appropriate methods and the time horizon for the health economic evaluation once the efficacy results become available. Type of analysis, underlying assumptions and input parameters will be based on the available evidence on efficacy, safety, feedback from clinical experts, Norwegian cost databases, registers, and literature. All cost data will be expressed in Norwegian kroner. In the analyses, we will use an extended health care perspective, which is relevant for prioritization of interventions within a fixed health care budget. This is in line with the guidance from the Priority-setting White Paper (35).

4. Other assessments

4.1 User involvement

The patient representatives recruited as external project participants will provide their input on aspects on ketamine and esketamine therapy for acute suicidal ideation, that are important for patients and their relatives. We will collect this information through a survey that will be sent by e-mail, as well as an informal interview. Similarly to clinical experts and other external team members, the patient representative(s) will be given the opportunity to read and comment on the protocol and the HTA report before submitting it to the commissioner.

4.2 Clinical expert opinions

The clinical experts recruited as external project participants, will provide their input on clinical aspects of ketamine and esketamine treatment. Their involvement extends to all stages of the project, in particular the establishment of PICO(S), and review of the protocol and HTA report drafts. If clinical disagreements regarding this treatment become apparent, we will attempt to elucidate the differing opinions.

5. Deliverables and publication

5.1 Delivery

The end product of this project will be an HTA report, intended as a decision-making tool for the Ordering Forum in the national system for managed introduction of health technologies within the specialist health care service (Nye Metoder), which consists of the RHA Ordering forum (Bestillerforum) and the RHA Decision forum (Beslutningsforum). However, the finished report will be published and available to the public and should therefore be readable for a larger audience. The report will be written in English, in clear language, with a Norwegian summary and key points. We will publish the report on the web pages of NOMA (www.dmp.no), as well as on the web pages of the RHA-forum (www.nyemetoder.no). We are also open to publish the whole or parts of the report as one or more articles in scientific journals. Abstracts may be submitted to relevant conferences. The approved protocol will be published on the web pages of NOMA (www.dmp.no) along with a short description of the commission, as well as in the INAHTA database.

5.2 Peer-review

5.2.1 Protocol

A finalised draft of the protocol will be submitted to internal peer-review by co-workers at NOMA, before being sent to the entire external project group, i.e., clinical experts and patient representatives, for input. The protocol will then be approved by the head of the unit for HTA medical devices at NOMA.

5.2.2 HTA

When the report draft is finalised, it will be submitted to internal peer-review, before being sent to the entire external project group for input. If necessary, we will submit the report draft to external peer-review. The report will subsequently be approved by the head of the unit for HTA medical devices at NOMA.

5.3 Time frame

Start date: 27.06.2025

End date: 27.06.2026

Step	**From date**	**To date**
Protocol	27.06.2025	31.10.2025
Literature search	27.06.2025	06.08.2025
Screening references	06.08.2025	03.09.2025
Assessment of risk of bias	01.10.2025	31.10.2025
Data extraction	15.09.2025	31.10.2025
Analysis	01.11.2025	01.12.2025
Assessment of certainty of evidence	01.12.2025	31.12.2025
Preparatory work for health economic evaluation / data collection	01.06.2025	31.10.2025
Health economic analyses	01.11.2025	31.03.2026
Draft report	15.10.2025	31.03.2026
Peer-review	01.04.2026	10.05.2026
Assess and complete report draft	20.04.2026	15.06.2026
Approval of report	15.06.2026	26.06.2026
Send to commissioner	26.06.2026	26.06.2026
Publish	03.07.2026	03.07.2026

5.3.1 Measures to be taken in the event of delays/unforeseen developments

If conditions arise that may affect the deadline for the HTA report more than the framework for this project allows for, we will implement relevant measures, e.g.:

- Increased staffing.
- Replacing project members upon long-term disease or absence.
- Limiting the selection criteria.
- Extending the deadline, after agreement with the commissioner.

Examples of such conditions may include, but are not limited to, unforeseen long-term absences among the project members, larger number of hits to screen following the literature search, or larger number of included studies to extract data from.

6. Related NOMA projects/publications/studies

- ID2022_018 Ketamine for treatment-resistant depression (24)

7. References

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