HYPO RESOLVE

Hypoglycaemia - REdefining SOLutions for better liVEs

Request for Proposal

A series of systematic literature searches to identify studies determining the psychosocial burden of hypoglycaemia (WP6)

HypoRESOLVE Work Package 6 Co-Leaders

Prof Frans Pouwer[1,2] Prof Jane Speight[1,2,3]

1. University of Southern Denmark, Odense, Denmark
2. School of Psychology, Deakin University, Geelong, Australia
3. The Australian Centre for Behavioural Research in Diabetes, Deakin University, Melbourne

INSTRUCTIONS TO CONTRACTORS

1. General

Read these instructions carefully before completing the remaining documentation. Failure to comply with these requirements for completion and submission may result in the rejection of your proposal.

2. Confidentiality

This request for proposal (RFP) should be considered proprietary information to the HypoRESOLVE team[1] and is intended to be used by your organisation ("the contractor") to formulate a response. It may only be shared with an outside organisation, if the organisation's assistance is to be a prerequisite to comply with the request.

All information provided by the contractor(s) will be treated as "Commercial in Confidence" by the HypoRESOLVE team and will not be disclosed to a third party without your written permission. You must not use any information detailed in this document, or provided by us in relation to this RFP, except for the purposes of responding to this RFP and providing a proposal for the services.

3. Proposal

You are invited to submit a proposal for the supply of a series of high quality systematic literature searches to identify studies determining the psychosocial burden of hypoglycaemia. The services are detailed in this document. Please refer to Appendix A for details of what we expect to be included in your proposal. You may submit sales and/or other literature with your proposal response, but answers to the questions in this document should be in the proposal itself.

4. Format and total number of copies required

Please submit one electronic copy of your proposal in Microsoft Word to the following three persons:

- Prof Frans Pouwer (fpouwer@health.sdu.dk)
- Prof Jane Speight (jspeight@acbrd.org.au)
- Dr Jeannette Söderberg (jsoderberg@jdrf.org).

5. Proposal costs

We will not be liable for any costs that you incur in the preparation or submission of your proposal, or for those arising from any consequential demonstration, presentation etc. requested by us prior to the award of the contract.

6. Late proposals

We reserve the right to reject any proposal received after the deadline, particularly if notice and/or reasonable rationale is not provided by the contractor.

7. Evaluation of proposals

All proposals submitted will be subjected to a thorough evaluation. This may result in an award (or awards) of contract or may produce a short-list of the most promising offers.

[1] The HypoRESOLVE team is defined here as the Co-Leaders of WorkPackage 6 (Prof Frans Pouwer and Prof Jane Speight) and any members of their team or the wider HypoRESOLVE project partners who they wish to involve

8. Award criteria

When evaluating which agency proposal that offers the best overall value for money our most important criteria will be as follows:

- Strong track record and clear capabilities in systematic literature review research
- Senior personnel involved and who will be accountable for the quality and timeliness of the work
- Strong internal project management skills
- Price

We will award the project to the contractor(s) whose proposal has been determined as substantially fulfilling the conditions, and which offers the best overall value for money.

9. Our right to accept any proposal or reject any or all proposals

We reserve the right to accept or reject any proposal and to annul the proposal process and reject all proposals at any time prior to award of contract without incurring any liability to the affected contractors.

10. Timelines

- Tuesday 7 Aug 2018 – Request for proposal advertised
- Friday 17 Aug 2018 – Contractor to submit a response indicating the intent to submit a full proposal
- Friday 31 Aug 2018 – Contractor to submit full proposal
- Wednesday 19 Sept 2018 – Decision on outcome of proposal to be advised; contracts to be prepared
- Monday 15 Oct 2018 – Successful contractor(s) to commence project by this date
- Monday 26 Nov 2018 – Successful contractor(s) to submit draft report for Phase 1 (including all requested deliverables) for review by HypoRESOLVE team
- Monday 3 Dec 2018 – Successful contractor(s) to present (face-to-face) to HypoRESOLVE team, to discuss findings and determine any modifications required for final report and slide set
- Wednesday 31 Dec 2018 – Successful contractor(s) to submit final report for Phase 1 (inc all requested deliverables) and final slide set (all revised as needed), enabling WP6 to review the identified literature and write the systematic reviews
- Thursday 31 Jan 2019 – If undertaking Phase 2, successful contractor(s) submit draft report for (inc all requested deliverables) for review by HypoRESOLVE team
- Friday 15 Feb 2019 – HypoRESOLVE team to provide feedback on draft report for Phase 2 (inc all requested deliverables)
- Friday 1 Mar 2019 – If undertaking Phase 2, successful contractor(s) submit final report for Phase 2 (inc all requested deliverables) and final slide set (all revised as needed)

NB You must confirm that you would be able to commit appropriate resources to meet the timeline for this project.

11. Queries and requests for clarification

If you have any questions regarding this invitation to proposal, please contact: Prof Frans Pouwer (fpouwer@health.sdu.dk) or Prof Jane Speight (jspeight@acbrd.org.au)

NB. We reserve the right to copy questions received, and answers provided, to all potential contractors.

PROJECT BACKGROUND

HypoRESOLVE is a unique public-private partnership. Our overall objective is to alleviate the burden and consequences of hypoglycaemia among people with diabetes. This requires finding answers to questions which, nearly 100 years after the discovery of insulin, still need to be answered.

To help address these questions, we have assembled a unique consortium of leading experts in basic, clinical, psychological/behavioural and economic aspects of hypoglycaemia research, who will work collaboratively with industry partners and other stakeholders. We aim to tackle these challenges through a comprehensive, multi-level approach. The first approach in terms of understanding the psychological impact and personal burden of hypoglycaemia is to undertake a series of systematic reviews.

- Diabetes is a major non-communicable threat to global health and affects around 1 in 10 of the European population.[1] Despite different underlying causes and approaches to treatment, both type 1 and type 2 diabetes (T1D and T2D) can have devastating consequences and continue to impair both quality and quantity of life. Maintaining glucose levels substantially in the 'normal' range reduces the risk of long-term microvascular complications, macrovascular disease and mortality.[2,3] However, treatment with insulin and certain oral hypoglycaemic agents (e.g. sulphonylureas) is associated with an increased risk of hypoglycaemia (low blood glucose), the occurrence of which may cause acute cognitive dysfunction, confusion, coma, seizures, cardiac arrhythmias and, rarely, sudden death. Repeated episodes of hypoglycaemia have also been associated with significant end-organ disease, particularly of the heart and brain and are of major concern to both healthcare professionals and people with diabetes.

- Episodes of hypoglycaemia can frighten both the individual and their family members, interfere with their school/work, independence and social activities. This cumulative experience not only impairs quality of life for the individual and their family, but also has important societal and economic consequences. People with insulin-treated diabetes are particularly vulnerable to hypoglycaemia as their susceptibility to hypoglycaemia increases, both due to defective hormonal defences to hypoglycaemia (particularly loss of glucagon) and reduced symptomatic awareness of impending hypoglycaemia (impaired awareness of hypoglycaemia, IAH). IAH affects approximately 25% of individuals with type 1 diabetes and ~10% of those with type 2 diabetes using insulin, which increases their risk of severe hypoglycaemia by up to six- and 17-fold, respectively. As a result, many people with diabetes adjust their lifestyle and/or their self-management strategies, choosing glucose targets that are higher than recommended, which increase their risk of long-term complications.

- Technological advances in insulin design (e.g. analogues), insulin delivery (e.g. pumps) and glucose monitoring (e.g. real-time continuous glucose monitoring, RT-CGM) have helped to improve overall glucose control. However, real-world studies show that severe hypoglycaemia is unrelated to HbA1c.[4,5] Furthermore, rates of both non-severe and severe hypoglycaemia remain high in everyday clinic practice (largely unchanged over several decades[4,6]) and well above those observed in clinical trials. Thus, hypoglycaemia arguably remains the major barrier in preventing people with diabetes achieving glucose levels necessary to avoid serious long-term complications.

- The World Health Organisation (WHO) defines quality of life (QoL) as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. QoL is a broad concept, widely acknowledged to be subjective (known only to the individual), dynamic (changing over time), and multi-dimensional (e.g. encompassing aspects of life, such as the person's physical health, emotional well-being, level of independence, social relationships, finances, sleep, daytime functioning). Also of relevance are cognitive functioning (e.g. attention, concentration, memory) and other psychological outcomes (e.g. fear of hypoglycaemia, psychological conflict, diabetes distress, diabetes stigma).

THE PROJECT

We are seeking to conduct five related systematic reviews. Each one will focus on the impact of hypoglycaemia (including its frequency, severity, and timing (while awake or asleep)) on the quality of life, related psychosocial outcomes and expressed care needs[2] of a particular population:

1) children/adolescents with type 1 diabetes
2) adults with type 1 diabetes
3) adults with type 2 diabetes
4) parents/caregivers of children/adolescents with type 1 diabetes
5) family members of adults with type 1 or type 2 diabetes

In **Phase 1**, **the contractor(s) will** conduct five systematic searches (as noted above) according to Cochrane standards. Search protocols (including search terms, databases, inclusion/exclusion criteria, and data sources) will be developed and agreed with the HypoRESOLVE team[3]. All types of empirical studies will need to be identified; these will likely include both qualitative and quantitative research, such as interview studies, focus groups, surveys, cohort studies, observational studies and randomised controlled trials. The contractor(s) will conduct the searches and screen abstracts, producing definitive lists of studies to be included in the five reviews, and a summary of the nature of those studies.

In **Phase 2**, **the contractor(s) will** prepare tables summarising key characteristics and findings of the studies. The results of Phases 1 and 2 will provide the basic findings with which the HypoRESOLVE team can conduct the review in Phase 3.

In **Phase 3**, **the HypoRESOLVE team will** synthesise the findings and appraise the quality of the empirical studies identified for each of the five searches. This may involve conducting meta-analysis of quantitative data, meta-synthesis of qualitative data or other narrative synthesis. Conceptual models will also be developed to identify direct and indirect impacts of mild and severe hypoglycaemia on QoL, distinguishing proximal from distal impact, and predictors of psychological burden/resilience. In **Phase 3**, the HypoRESOLVE team will work with the contractor(s) to publish the findings.

ROLE OF CONTRACTOR(S)

Phase 1 of the project (see above) is compulsory. Please note that this involves developing a protocol, conducting systematic searches, screening abstracts (and full-text articles as needed), and providing a list of full-text articles for the HypoRESOLVE team to include in each review. It does not include review or critical appraisal of literature obtained.

The contractor(s) have the option to include delivery of Phase 2 in their proposal.

The contractor(s) may be invited to co-author[4] publications in Phase 3. This would involve reviewing and contributing to draft manuscripts prepared by the HypoRESOLVE team. Fees are not payable for involvement in publications.

For further details, see Appendix A.

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[2] The expressed care needs may or may not require a separate search strategy from the search related to quality of life and related psychosocial outcomes

[3] The HypoRESOLVE team is defined here as the Co-Leaders of WorkPackage 6 (Prof Frans Pouwer and Prof Jane Speight) and any members of their team or the wider HypoRESOLVE project partners who they wish to involve

[4] This assumes that key personnel from the contractor(s) organisation fulfil the international criteria for authorship; otherwise acknowledgements will be offered

APPENDIX A: What we would like to see in your proposal

Our primary objective is to select a contractor that has the capability to perform the scope of services.

The contractor shall describe how services will be performed, including resources, tools, and processes. We expect the contractor to **share ALL budget assumptions, such as data sources, meetings, pass through costs and expenses**.

The proposal must incorporate the following information in a clear and precise fashion:

1) Explain your methods and rationale

- Key words and search terms
- The search strategy
- Databases to be investigated
- Inclusion & exclusion criteria
- Processes for abstract selection, including number of reviewers at each stage, the qualifications/experience and seniority of individuals involved and the software to be used
- Quality processes for ensuring the accuracy and completeness of the searches
- *If you plan to apply a different methodology with a significant corresponding additional cost (access and/or analysis), please propose in a separate option and describe the pros and cons for this method accordingly.*

2) A proposed table of contents for your report

3) A preliminary search (<u>in order to estimate the workload</u>)

- The search strategy; proposed search terms; number of hits per search term, and per string combinations; the estimated number of titles/abstracts to be fully analysed; the estimated number of articles to be retained

4) Quality control

- Provide details of how your full search will differ from the preliminary search.
- Provide details of how you have conducted quality control of similar projects (your processes) previously.

5) Milestones / project timeline

- Detail your milestones, deliverables and timeline.
- Explain the milestones and input / agreement needed from the HypoRESOLVE team at each stage / deliverable.
- If necessary, challenge the timeline and deliverables proposed in this Request for Proposal.

6) Meetings

- Detail any proposed meetings required (face-to-face, teleconference, videoconference) and the purpose of each meeting
- For each milestone, review the deliverables and describe the process proposed

- If review is needed by the HypoRESOLVE team, the contractor must send the proposed document no later than 3 working days prior to the meeting
- The agenda and minutes of all meetings will be prepared by the contractor(s)
- Plan for a face-to-face presentation of the results in London or Copenhagen

7) Budget

- Detail the budget by task (project management with daily rate and task description). Provide a table showing the different job categories (Project Leader, Statistician, etc.) involved in the project, with the number of hours estimated and the hourly billing rates.
- Detail any optional services (e.g. involvement in reviewing future publications) that you anticipate you could provide to add value.
- If some tasks are allocated a significant additional cost (access and/or analysis), please propose it as a separate option.
- Split your budget by agency fees and pass through costs. Estimate ALL pass through costs related to the scope of services. Pass through costs will be capped by the major type of expenses, such as travel, accommodation, copyright. Please indicate the maximum potential amount of pass through costs.
- Please detail your budget in EURO.
- Please provide your reference banking account.

8) Project team

- Identify the Project Manager(s) who will be responsible for, and our key contact, for the project. The role and responsibility of each staff member involved in the project is also required.
- Highlight any external experts, affiliates or advisory board members that you would propose to involve in this project.

9) Your track record

- Demonstrate your experience in the field of conducting systematic reviews. The contractor will specify the projects (number and type) that the designated team members have conducted in the past, the therapeutic area (particularly in the context of diabetes and/or quality of life research), the deliverables provided, the target audience, and a list of any peer-reviewed systematic review publications in the academic literature.

10) Deliverables

a. Summaries of, and action points arising from, face-to-face meetings and teleconferences

b. A systematic review protocol document of the pilot search

c. The flowchart of exclusion/inclusion publications

d. Documents (e.g. Endnote database or Excel spreadsheet) including:

- a list of all citations retrieved from the original search
- the list of included abstracts after reviewing and reasons for inclusion
- the list of excluded abstracts after reviewing and reasons for exclusion

- the list of included full-text publications after reviewing and reasons for inclusion
- the list of excluded full-text publications after reviewing and reasons for exclusion

e. Two interim reports and a final report (according to PRISMA statements) in Word format including (but not limited to) the following content:
   - Executive summary
   - Objectives
   - Methods
     i. Reference databases
     ii. Key words of search strategies
     iii. Inclusion / exclusion criteria used to select articles
     iv. Publication dates covered
     v. Definitions used
     vi. Studies considered
     vii. Details on search(es) performed
   - Results
     i. Phase 1: Flow chart(s) of included / excluded publications for each of the five systematic reviews
     ii. Phase 1: List of included empirical studies for each of the five systematic reviews
     iii. Phase 2: Brief summary of the nature of the studies identified for each of the five systematic reviews
     iv. Phase 2 (optional): Tables summarising the characteristics and key results of included studies

f. A PowerPoint slide set including key messages in the comment sections

g. Presentation: A senior team member will present the summary findings using the above PowerPoint slide set during a face-to-face meeting in London/Copenhagen

h. Full-text articles (PDF format, electronic only) of the articles selected for inclusion.

REFERENCES

[1] IDF Diabetes Atlas, 7th Edition. 2015. Available at: http://www.diabetesatlas.org

[2] The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med, 1993; 329: 683-689

[3] Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med, 2008; 359: 1577-1589

[4] Hendrieckx C, Halliday J, Bowden J, Cohen N, Colman PG, Jenkins A, Speight J. Severe hypoglycaemia and its association with psychological well-being in Australian adults with type 1 diabetes attending specialist tertiary clinics. *Diabetes Research and Clinical Practice*, 2014; 103: 430-436

[5] Speight J, Holmes-Truscott E, Harvey DM, Hendrieckx C, Hagger VL, Harris SE, Knight BA, McIntyre HD. Structured type 1 diabetes education delivered in routine care in Australia reduces diabetes-related emergencies and severe diabetes-related distress: the OzDAFNE program. *Diabetes Research and Clinical Practice*, 2016; 112: 65-72

[6] Frier BM. How hypoglycaemia can affect the life of a person with diabetes. *Diabetes Metabolism Research and Reviews*, 2008; 24(2): 87-92