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**Place of enrolment:** University of Copenhagen, Faculty of Health and Medical Sciences

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**Title of project:** HypoBar: Unravelling Post-Bariatric Hypoglycaemia towards Improving Healthcare and Inspiring New Glucose Lowering Therapies

## **ABSTRACT**

Obesity and diabetes are major public health concerns that have been exponentially growing in prevalence in the last decades. Obesity and its co-morbidities such as Type 2 diabetes, hypertension, hyperlipidaemia, obstructive sleep apnoea, osteoarthritis and cardiovascular disease threaten to reverse the gains in life expectancy experienced during the 20th century, with cardiovascular comorbidities as main cause for morbidity and mortality in this patient population. The single effective long-term treatment to induce weight loss and diabetes remission with proven reduction of morbidity and mortality is bariatric surgery. The Roux-en-Y gastric bypass (RYGB) is one of the most popular and effective bariatric procedures worldwide. However, with the increasing number of RYGB procedures worldwide, physicians are increasingly facing with complications such as post-bariatric hypoglycaemia (PBH), which is the development of symptomatic hypoglycaemia (typically post-prandial) after bariatric surgery. PBH is most often reported after RYGB, significantly impairs patient quality of life, and can be life-threatening in certain situations. Hence, PBH merits further investigations. Our knowledge so far on PBH arises from small scale observational studies. The following topics are still a mystery: (1) what are the preoperative risk factors for PBH; (2) whether there is a role for glucose absorption in PBH pathophysiology; (3) in what way gut-secreted factors are involved in the counterregulatory response to hypoglycaemia; (4) how effective are currently available treatment options for PBH. In this PhD project, we designed specific tasks to target all the above questions, making it, to the best of my knowledge, the first comprehensive study dedicated to PBH.

In particular, we will pursue a cross-sectional study for phenotyping patients with PBH and identifying risk factors (Task 1); a proof-of-concept study for assessing glucose absorption role in PBH by blockage of  $\alpha$ -glucosidase or SGLT1 (Task 2); a dual approach for describing gut-hormone profile under hypoglycaemia and impact of substrate availability, by profiling gut and pancreatic secretion under extreme hypoglycaemia using intestinal perfusions (Task 3.1) and by describing adaptive counterregulatory responses to hypoglycaemia prompted by RYGB (Task 3.2); and a head-to-head randomised controlled trial on treatment options for PBH (Task 4). This is therefore a multidisciplinary project which will be led by Carolina Brito Lobato, a medical doctor with research background on PBH. The project will combine basic, translational, and clinical research tasks, in a pioneer collaboration between world-class research centres at University of Copenhagen and Imperial College London. The anticipated outcomes of the project will aid physicians in providing better healthcare for patients dealing with PBH, and thus positively impact patient well-being.