This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 847879.
Insulin dysregulation: much more than diabetes

- In our body, the hormone **insulin regulates the levels of sugar** (glucose) in the blood. It does this by stimulating cells to take up, process and store sugars after eating a meal.

- **Dysregulation of the biological processes related to insulin**, such as insulin resistance, causes problems with metabolism and blood sugar levels. This is linked to **type 2 diabetes, metabolic syndrome, and/or obesity**.

- In the brain, insulin also plays important roles in the functioning and survival of brain cells. **Insulin resistance is linked to cognitive impairments and Alzheimer’s disease.** New research also links insulin dysregulation to autism spectrum disorders and obsessive-compulsive disorder (OCD).
Physical and mental problems frequently occur together

- Diseases such as type 2 diabetes and metabolic syndrome frequently co-occur with mental problems. Having type 2 diabetes increases your risk of Alzheimer’s disease. Similarly, individuals with OCD run a higher risk of developing diabetes, compared to those without OCD.

- This co-occurrence (either at the same time, or later in life) is called **comorbidity** or **multimorbidity**. We don’t yet fully understand why these diseases co-occur. We think that changes in how the body regulates insulin plays an important role.

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**PRIME starts from the hypothesis that the co-occurrence of multiple mental and physical diseases is caused by dysregulated insulin signalling**

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Older people with type 2 diabetes are over 50% more likely to develop dementia, compared to elderly without type 2 diabetes

The first study from PRIME found a genetic overlap between OCD, OCD-like symptoms and measures related to insulin signalling

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Molecular mechanisms of insulin multimorbidity

PRIME researchers investigate the molecular mechanisms underlying the co-occurrence of multiple insulin-related mental and physical diseases.

One key molecule for insulin signalling is **KCNQ1**. PRIME is studying this molecule because genetic links between KCNQ1 and OCD, type 2 diabetes, and Alzheimer’s disease have previously been found.

**People with Romano-Ward Syndrome** (a rare heart condition) can have a slightly altered gene for KCNQ1. They often also have type 2 diabetes, but not much is yet known about their cognitive characteristics.

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New tools for diagnosis, treatment and prevention

Insulin-related diseases present a major health, societal, and economic burden and are mostly chronic with limited or no curative treatments.

PRIME aims to develop tools for early diagnosis, improved clinical care, and prevention of insulin-related multimorbidities

Worldwide, 463 million adults are living with diabetes. The global direct and indirect costs of diabetes are estimated to be over 1 trillion euro per year.
PRIME uses very large **population and genetic databases** to study associations between different conditions, including type 2 diabetes, Alzheimer’s disease and OCD).

By changing the activity of specific genes, we can measure how these genes influence brain cells, brain, functioning and behavior. For this, PRIME uses **animal models and brain cells derived from human induced stem cells**.

PRIME measures cognitive characteristics of individuals with **Romano-Ward Syndrome**. This provides new insights into the role of the KCNQ1 gene in diabetes and in brain functioning.

With **smartphone apps**, PRIME monitors how diet and physical activity influence cognition in people with type 2 diabetes. We also use **computer models** to predict multimorbidity and treatment success, and to screen for new drug targets.

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WHO ARE WE?

PRIME is a research consortium funded through EU’s Horizon 2020 programme
• 17 partner organisations from all over Europe contribute to PRIME
• The project was granted 6 million Euro funding for 5 years (2020 – 2025)
• Project leader: Prof. Dr. Barbara Franke (Radboudumc Nijmegen, The Netherlands)
Find out more about PRIME:

• Website: www.prime-study.eu

• Twitter: @PRIME_H2020

• Facebook: www.facebook.com/PRIMEhorizon2020

• LinkedIn: www.linkedin.com/company/PRIME-horizon2020

• Sign up for our newsletter: https://mailchi.mp/cd7ebd29a3b8/prime

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How to get involved:

We love to hear from anyone interested in insulin-related conditions!

➢ Send your questions, feedback or ideas to info@prime-study.eu
➢ Ask us for contributions to your newsletters or public events. We love to contribute!
➢ Attend one of our public events – watch our website, newsletter, and social media for updates

<table>
<thead>
<tr>
<th>Tentative schedule for public events</th>
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<tbody>
<tr>
<td>14 November 2021: World Diabetes Day</td>
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<tr>
<td>January 2022: PRIME General Assembly</td>
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<td>2025: End of PRIME project</td>
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