efpia

innovative medicines initiative

DIRECT
DIABETES RESEARCH ON PATIENT STRATIFICATION

Discovery of biomarkers for glycaemic deterioration before and after the onset of type 2 diabetes: *A showcase from the epidemiological studies within the IMI DIRECT Consortium*

Research Assistant → Project Manager & PhD Student → Postdoc → Postdoc Fellow
2011 2012 2016 2018

Robert Koivula

22 & 23 October 2018 • IMI Scientific Symposium • Brussels, Belgium

Overall Aim of DIRECT: Develop personalized medicine approaches in the prevention and treatment of type 2 diabetes

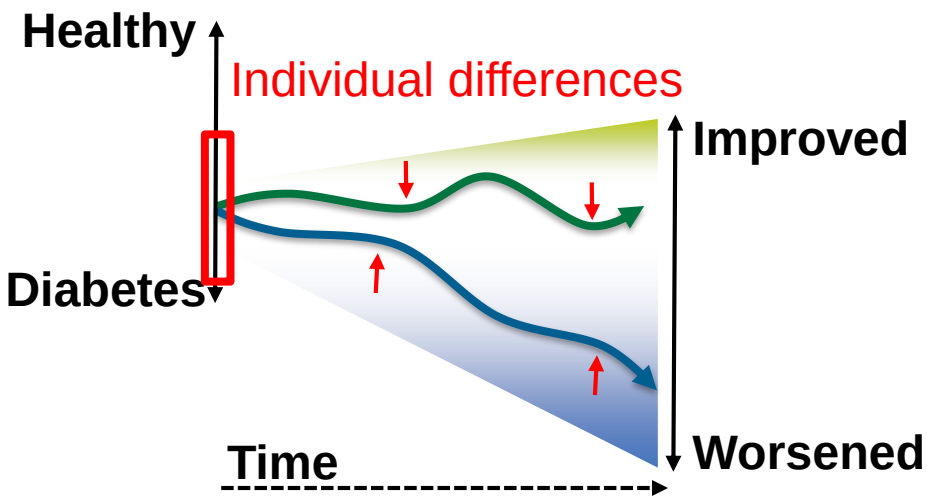
- **Glycaemic Deterioration | Therapeutic Response | Bariatric Surgery | Systems Biology | Omics**

  Leads: Ewan Pearson (Dundee)

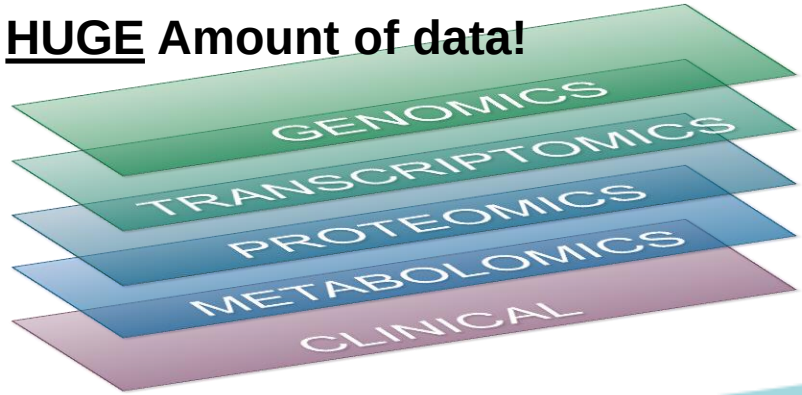
  & Hartmut Ruetten (Sanofi)
- I focus **<u>Glycaemic Deterioration WP</u>**

  Leads: Paul Franks (Lund) & Imre Pavo (Lilly)

  I helped Paul coordinate this WP
- 2 **new** European multicentre prospective cohorts
  - 'prediabetes': N ~ 2000
  - 'type 2 diabetes': N ~ 800
- **Multiple Timepoints** (0, 18, 36/48 months)
- **Deep phenotyping**: Clinical Measures, Blood and Urine Biochemistry, MRI, Accelerometry, Diet, Genomics, Transcriptomics, Proteomics, Metabolomics, Metagenomics …



<u>HUGE</u> Amount of data!



Koivula RW, Diabetologia, 2014 / Koivula RW, BiorXiv, 2018

IMI collaborations helped overcome many challenges

- Large number of samples and big data create opportunities to overcome big challenges!
  - Data: Central data repositories, central analysis clusters, satellite data processing centres
  - Samples: Central biobanks, central and satellite assaying labs
- 22 Academic Partners, 5 Industry Partners
- Meetings: Plenum, Managing Board, Analyst + countless smaller meetings and workshops, weekly tele/video conferences
- Requires funding (DIRECT ~45M Eur.) and organisation!
- **Hugely collaborative scientific environment, a lot of science being shared!**

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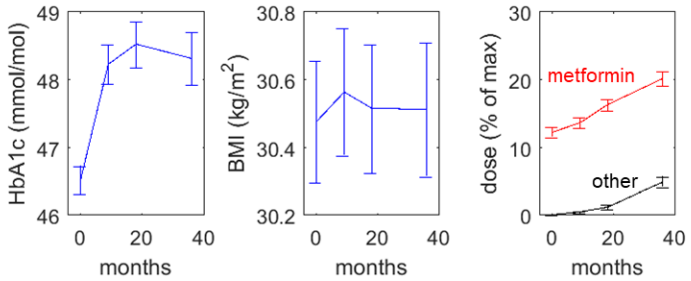
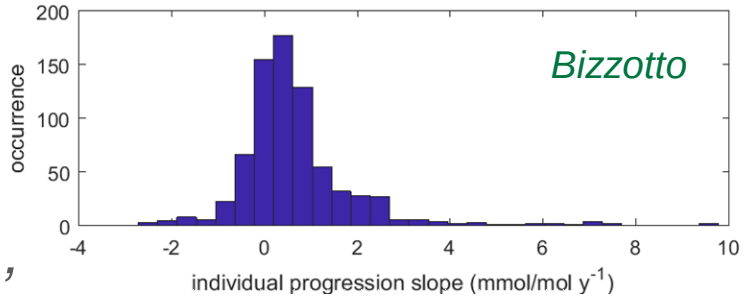
Showcase: Central project challenges

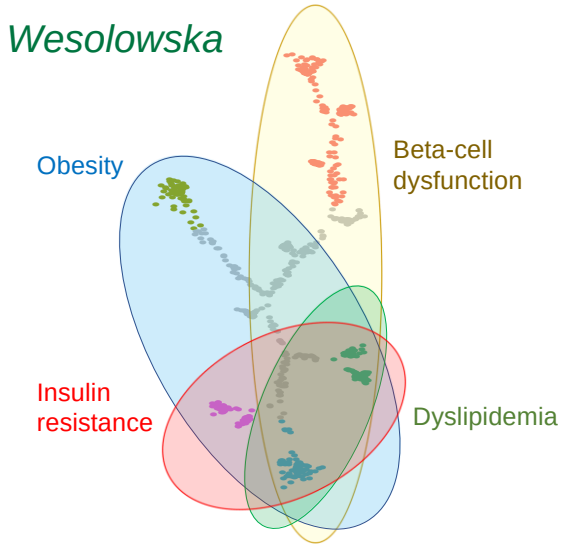
Glycaemic Deterioration Trajectories

- Complexities in modeling ‘trajectories’ in time series data for glycaemic deterioration
  - Treatment/lifestyle, methods, linearity
- Ability to quantify glycaemic deterioration
  - Central to all prospective analyses
  - Actually understanding T2D progression

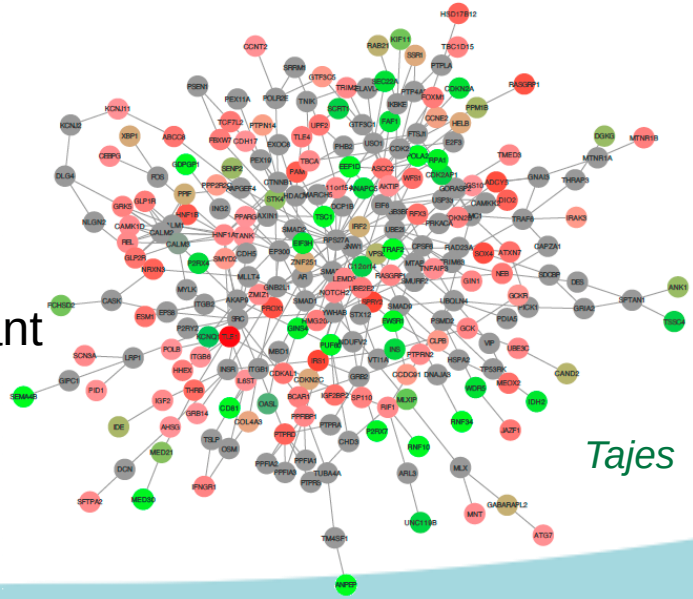




Sub-clustering Diabetes | Multi-Omic ‘Big Data’



- Subclusters of Diabetes / Prediabetes using clinical data
  - Pre-emptive personalised treatment
- Biological networks and participant clusters using multi-omic data
  - Novel aetiology insight
  - Pre-emptive personalised treatment



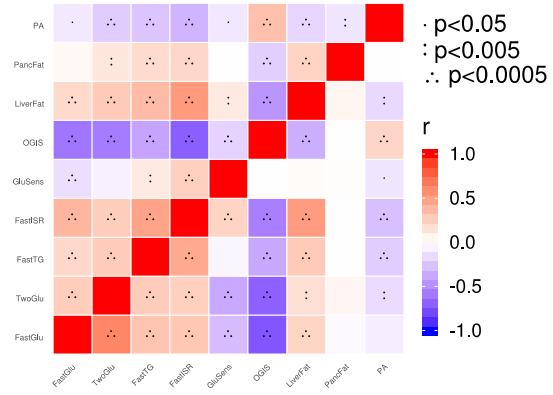
Unpublished results, with thanks to all IMI DIRECT partners!

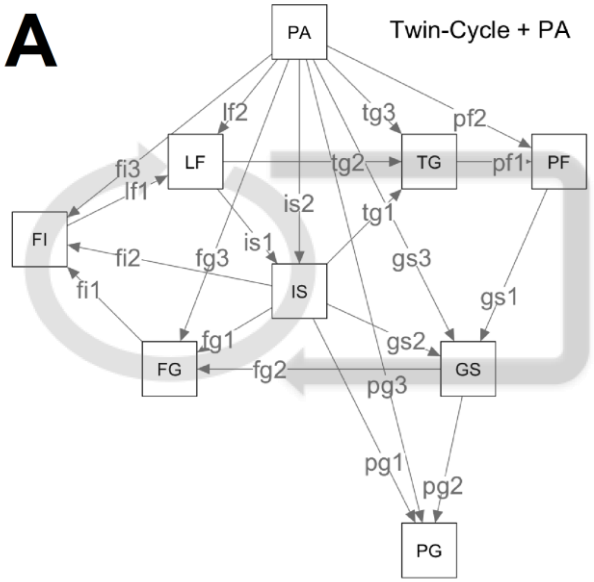
Showcase: One of my own projects

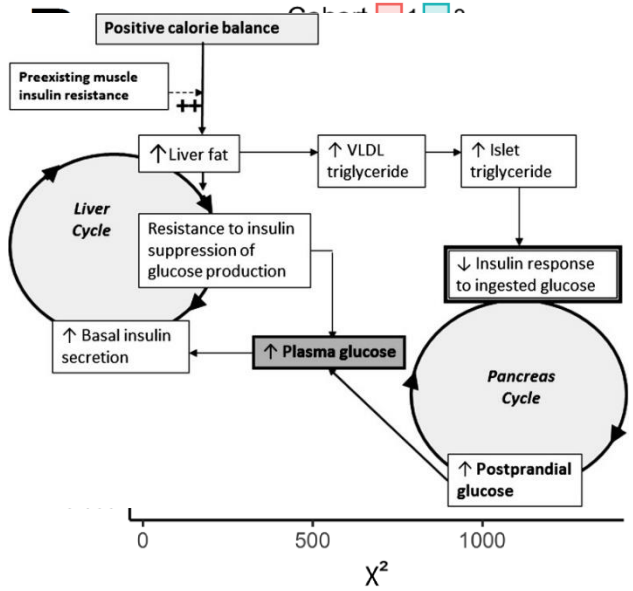
Testing complex existing network hypotheses

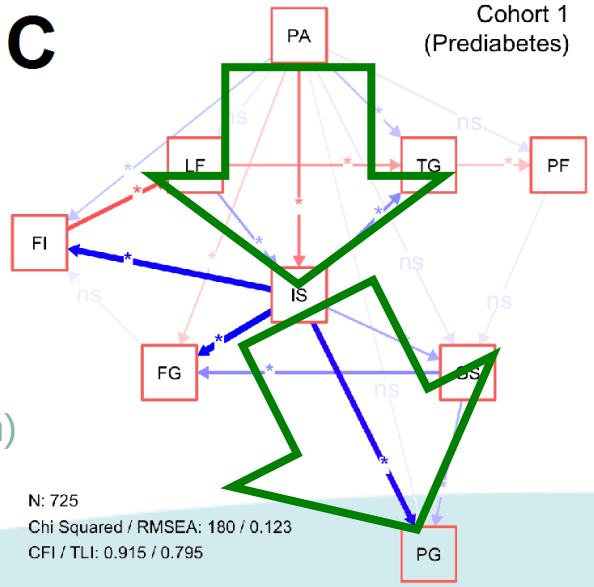
- Physical activity improves glycaemic control, why?
- Metabolic variables largely correlated so what's the mechanism?
  - Taylor Twin-Cycle hypothesis (Diabetes 2013)?

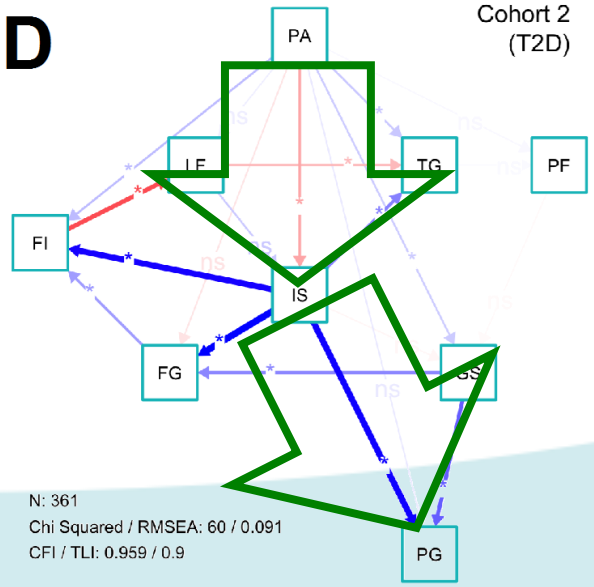
1. Twin-cycle fits (largely)
2. Insulin sensitivity mediates physical activity – glycaemia











Koivula RW, 2018 (in submission)