Annex IX

DIRECT Research Questions

The Data Access Committee (DAC) will assess all requests for DIRECT data. This Annex describes the DIRECT aims, phenotypes and related research questions to enable the DAC to decide if a data access request falls within the remit of DIRECT (i.e. is in-scope) or not.

DIRECT aims and phenotypes

For avoidance of doubt the following definitions apply:

DIRECT aims
The DIRECT study aims to identify and validate biomarkers that are associated with two phenotypes: glycaemic deterioration in patients with pre-diabetes and diabetes, and therapeutic response to treatments of diabetes, including metformin, sulphonylureas, GLP-1R agonists, and obesity surgery.

DIRECT phenotypes
For the purposes of this document and other related DIRECT documents the phenotypes of glycaemic deterioration and therapeutic response outlined in the DIRECT aims, are considered to be the "DIRECT phenotypes".

Primary DIRECT research
Any research that utilises DIRECT data or resource where the research question involves a DIRECT phenotype in any form is considered to be a primary research output of DIRECT. This includes work that is required prior to analysis with the DIRECT phenotype that is carried out for the purpose of subsequent DIRECT analyses.

Examples

These are by way of example, and are not exclusive of any other research aim.

The following are examples that fall within scope for DIRECT research

WP2.1 & 2.2
1. Any analysis where the endpoint is deterioration of glycaemia
2. Analysis of diet, activity, lifestyle data as required for the full analysis – publication of this analysis would be a primary DIRECT publication

WP3
1. Any analysis where the endpoint is therapeutic response to metformin or sulphonylureas, or GLP-1, or obesity surgery
2. Analysis validating the GLP-1 and other incretin assays
3. Analysis of any intensive physiology collected as part of a study of response to GLP-1

WP2/4/5 and 3/4/5
1. Any analysis where genomics (genetic and non-genetic) are included in the analysis by phenotype

2. Any work where integration across –omic levels is required prior to the full phenotypic analysis, including where a publication arises that does not depend on the final phenotype.

WP6

1. Assay development and validation studies of biomarkers performed on DIRECT samples or arising from DIRECT work.

Examples of research that is out of scope for DIRECT research

1. MRI imaging. Analysis of genomics of renal cysts (!) (NB analysis of genomics of liver fat or pancreatic fat or other associations with liver and pancreatic fat fall within scope)

2. Genomics of quantitative traits that are not involved in the DIRECT phenoytpes: e.g. Haemoglobin; blood pressure