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PRIMO CONVEGNO NAZIONALE DEL CENTRO DI MEDICINA DI PRECISIONE – HEAL ITALIA PER LE MALATTIE RARE

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Responsabile scientifico
Prof. **Gianluca Moroncini**

UnivPM – Ancona
Aula Montessori
Facoltà di Medicina
e Chirurgia

venerdì 28 febbraio
14:30 → 18:30
sabato 1 marzo
09:00 → 13:00

Progetto "Health Extended ALliance for Innovative Therapies, Advanced Lab-research, and Integrated Approaches of Precision Medicine (HEAL ITALIA) Codice PE00000019, CUP I33C22006900006 – finanziato dal PNRR M4C2 I1.3 – DD MUR 341 del 15/03/2022

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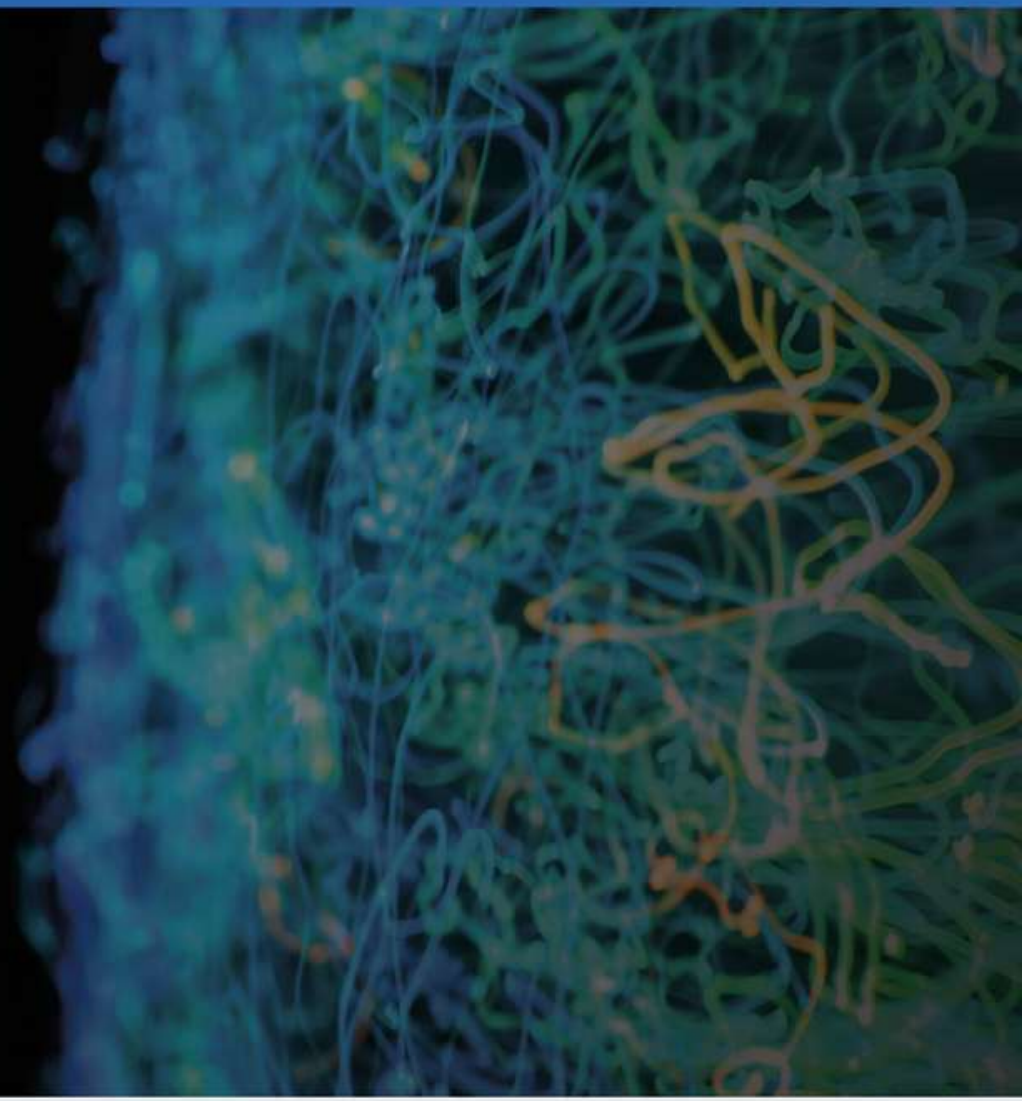
La medicina di precisione nella gestione clinica delle malattie rare



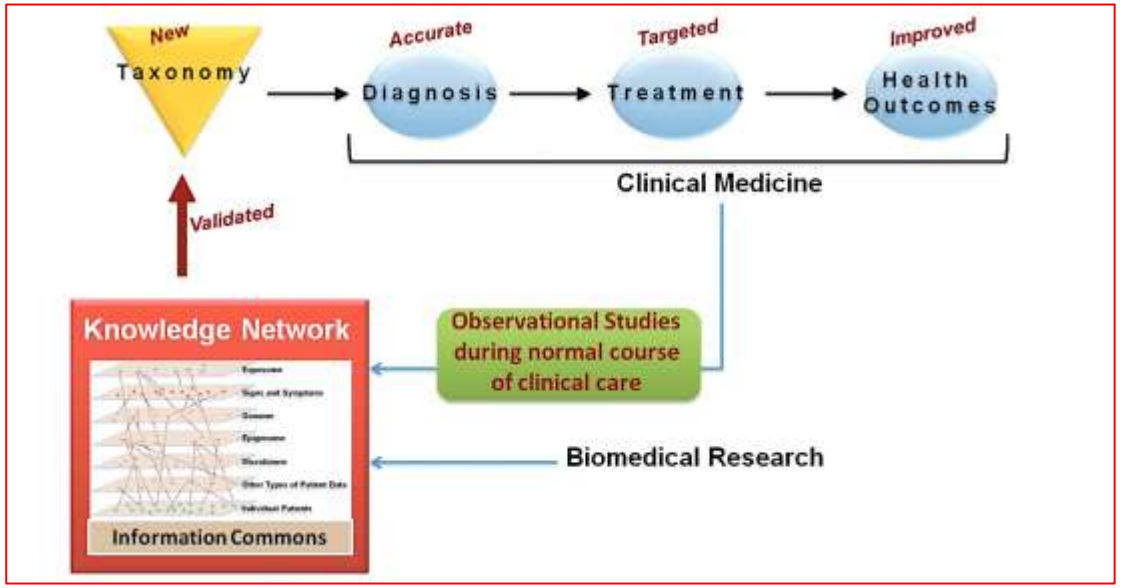
Piero Marchetti

Dip. Medicina Clinica e Sperimentale

Università di Pisa

….Un po’ di òvvia semantica (tanto per cominciare…)

- Medicina di precisione: *insieme di strategie di prevenzione, diagnosi e trattamento che tengono conto della variabilità individuale (Collins F, NEJM 2015)*



Exposome, Signs and symptoms, Genome, Epigenome, Transcriptome, Microbiome

Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease (2011)

NATIONAL ACADEMIES Sciences Engineering Medicine

Diabetes Care Volume 43, July 2020 1617

Precision Medicine in Diabetes: A Consensus Report From the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

Wendy K. Chung,[1,2] Karel Erion,[3] Jose C. Florez,[4,5,6,7,8] Andrew T. Hattersley,[9] Marie-France Hivert,[8,10] Christine G. Lee,[11] Mark I. McCarthy,[12,13] John J. Nolan,[14] Jill M. Norris,[15] Ewan R. Pearson,[16] Louis Philipson,[17,18] Allison T. McElvaine,[19] William T. Cefalu,[11] Stephen S. Rich,[20,21] and Paul W. Franks[22,23]

Diabetes Care 2020;43:1617–1635 | https://doi.org/10.2337/dci20-0022

Diabetes Care Volume 45, February 2022 261

ADA/EASD Precision Medicine in Diabetes Initiative: An International Perspective and Future Vision for Precision Medicine in Diabetes

John J. Nolan,[1] Anna R. Kahkoska,[2] Zhila Semnani-Azad,[3] Marie-France Hivert,[4] Linong Ji,[5] Viswanathan Mohan,[6] Robert H. Eckel,[7] Louis H. Philipson,[8] Stephen S. Rich,[9] Chandra Gruber,[10] and Paul W. Franks[11,12,13]

Diabetes Care 2022;45:261–266 | https://doi.org/10.2337/dci21-2216

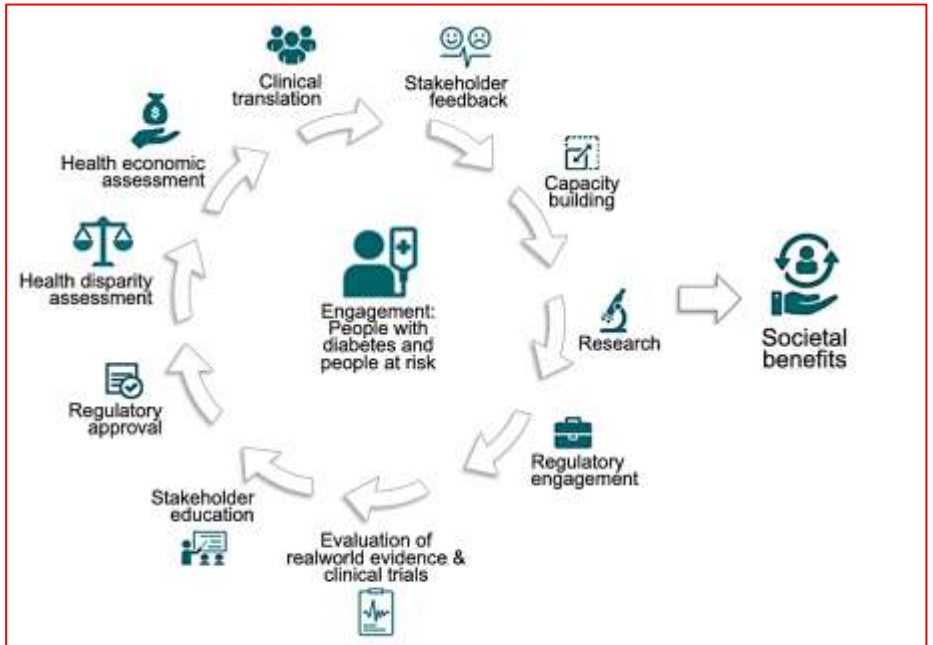
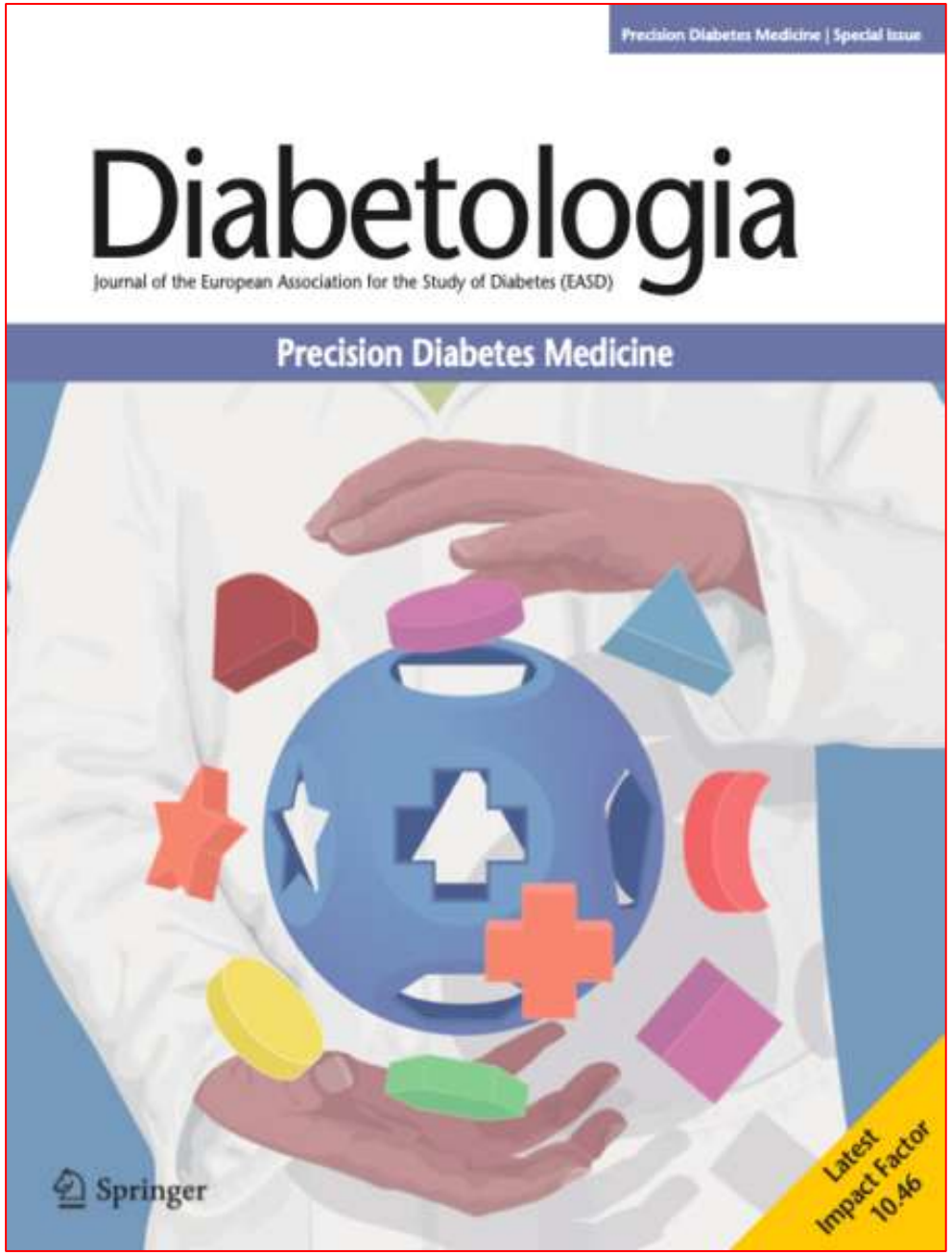
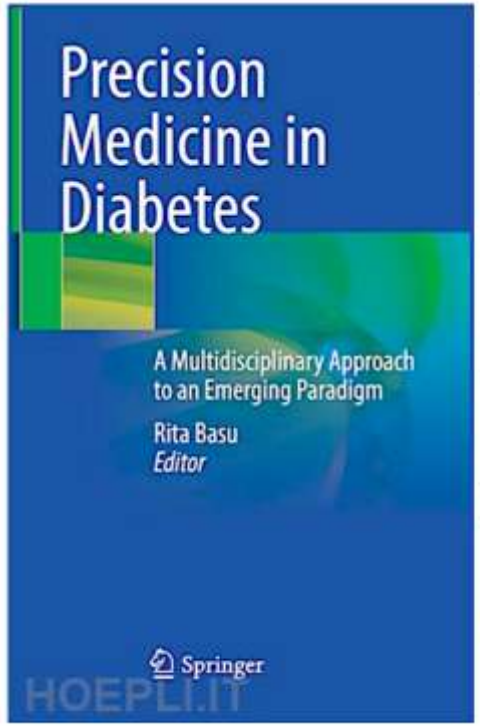


Figure 2—Key steps in the iterative process of implementing the PDMI into clinical practice.

Figure 1—Key milestones and timelines of the ADA/EASD PMDI. Adapted from Chung et al. (1). RFA, request for applications.





Precision Medicine in Diabetes

A Multidisciplinary Approach to an Emerging Paradigm

BASU RITA (CURATORE)

nature medicine

Consensus Statement

https://doi.org/10.1038/s41591-023-02502-5

Second international consensus report on gaps and opportunities for the clinical translation of precision diabetes medicine

Received: 17 May 2023

Accepted: 14 July 2023

A list of authors and their affiliations appears at the end of the paper

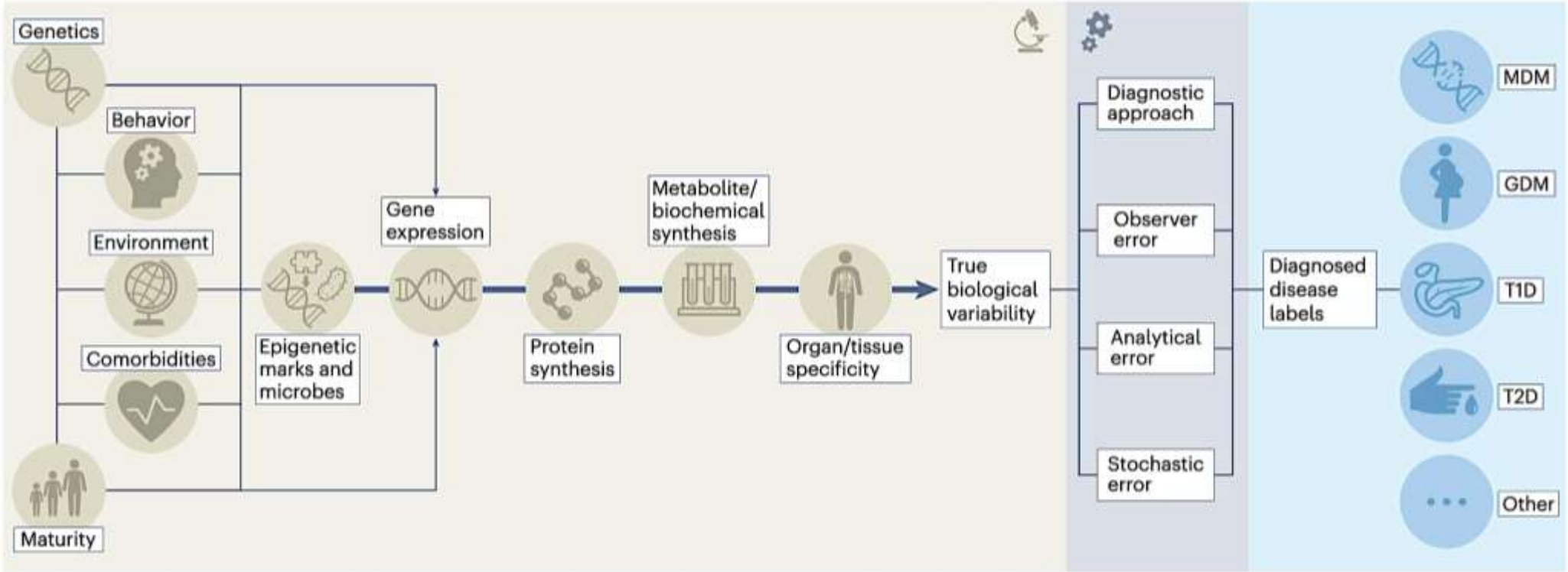
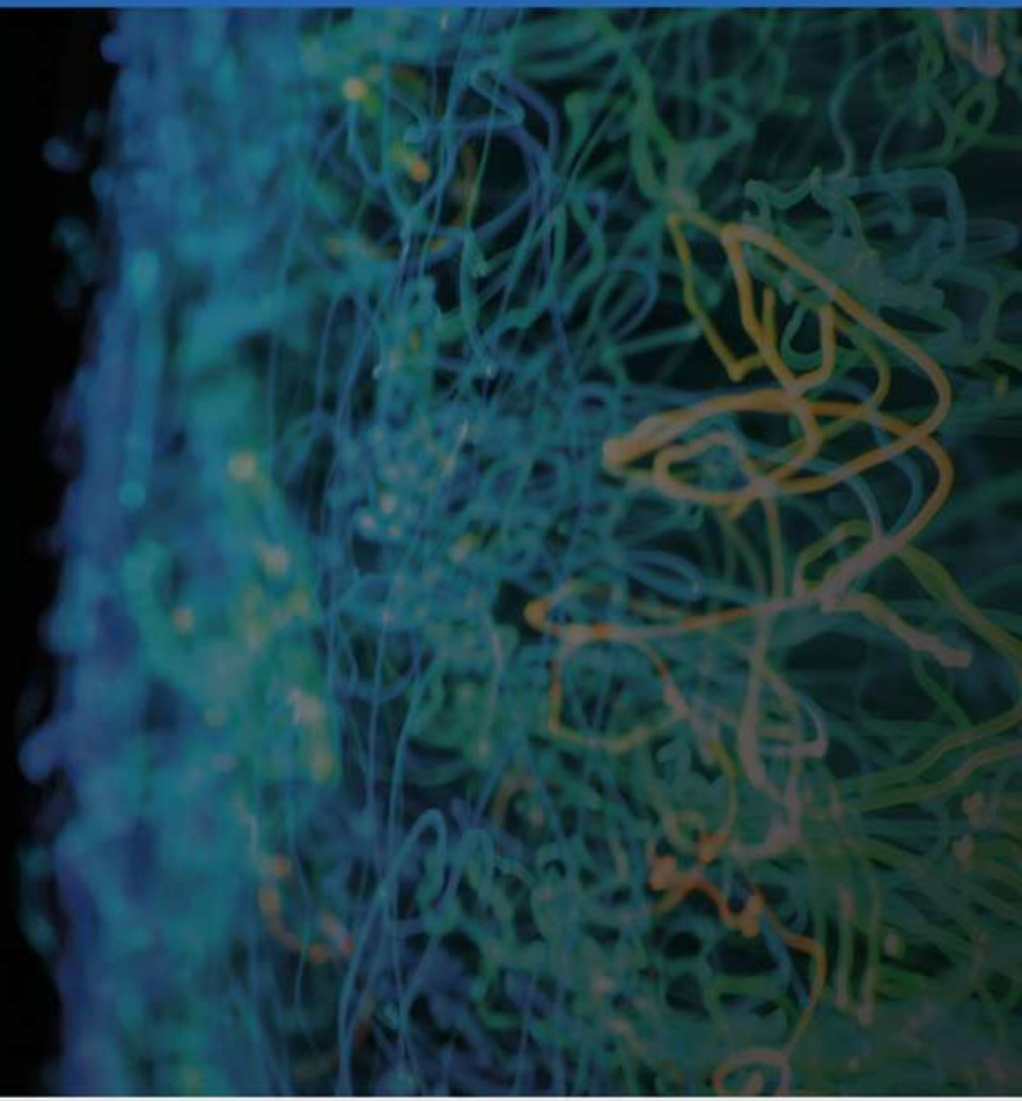


Fig. 1 | Sources of heterogeneity in diabetes. The success of precision diabetes medicine will be enhanced by successfully leveraging heterogeneity in diabetes. To do so will require parsing 'signal' from 'noise'; the figure illustrates the key sources of heterogeneity within each of these domains.

La medicina di precisione nella gestione clinica delle malattie rare



Piero Marchetti

PO Endocrinologia - Università di Pisa

….Un po’ di òvvia semantica (tanto per cominciare…)

- Medicina di precisione: *insieme di strategie di prevenzione, diagnosi e trattamento che tengono conto della variabilità individuale (Collins F, NEJM 2015)*
- Malattie rare: *patologie gravi, spesso invalidanti, che colpiscono un numero ridotto di persone, con una prevalenza inferiore al limite, stabilito a livello europeo, di 5 casi su 10.000 abitanti (∽10.000 riportate)*

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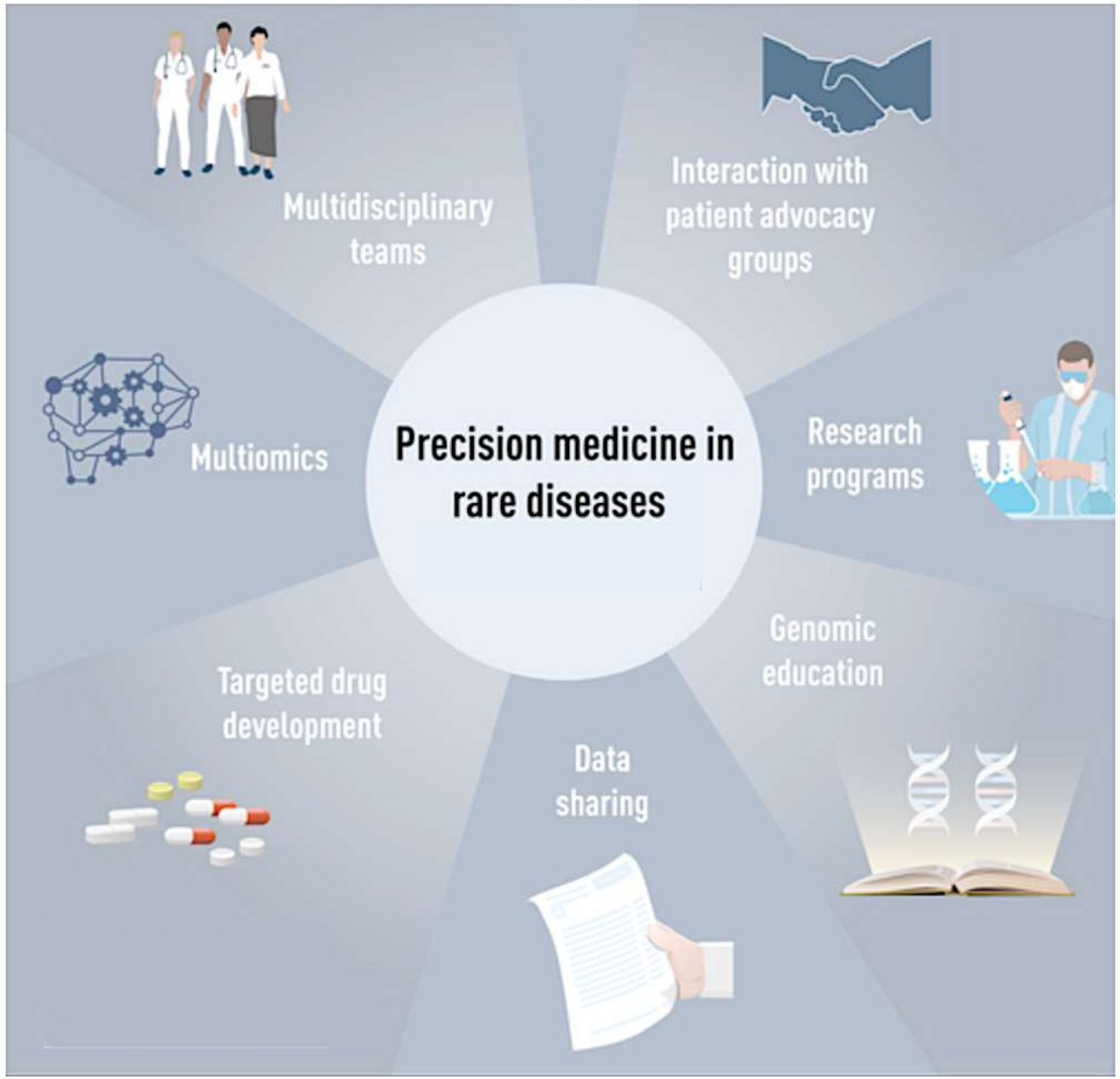
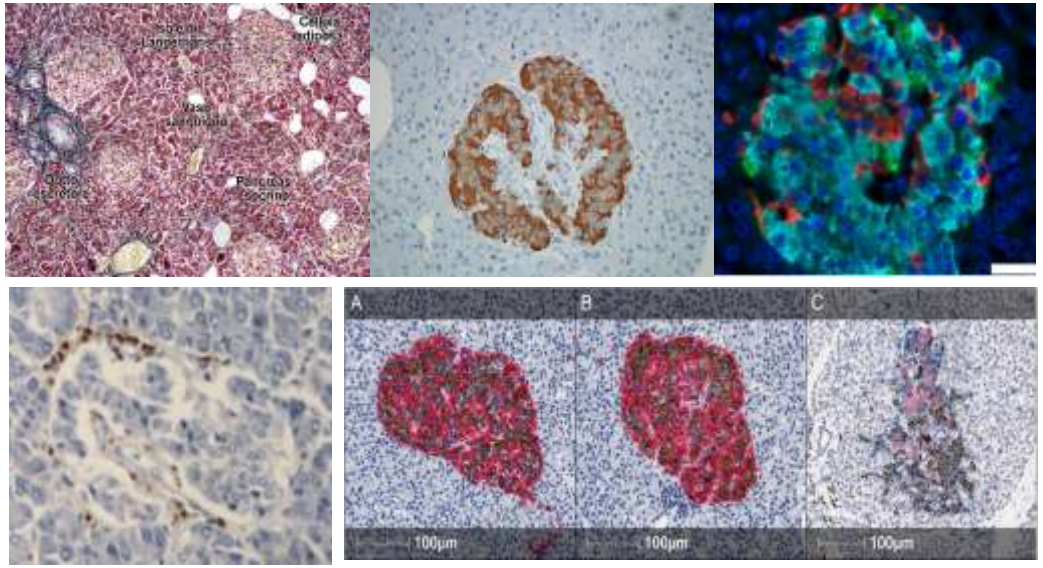


Adapted from Tesi B et al, J Intern Med 2023

Conflitto di interesse!



Sono un diabetologo!!!

International Diabetes Federation

537 million

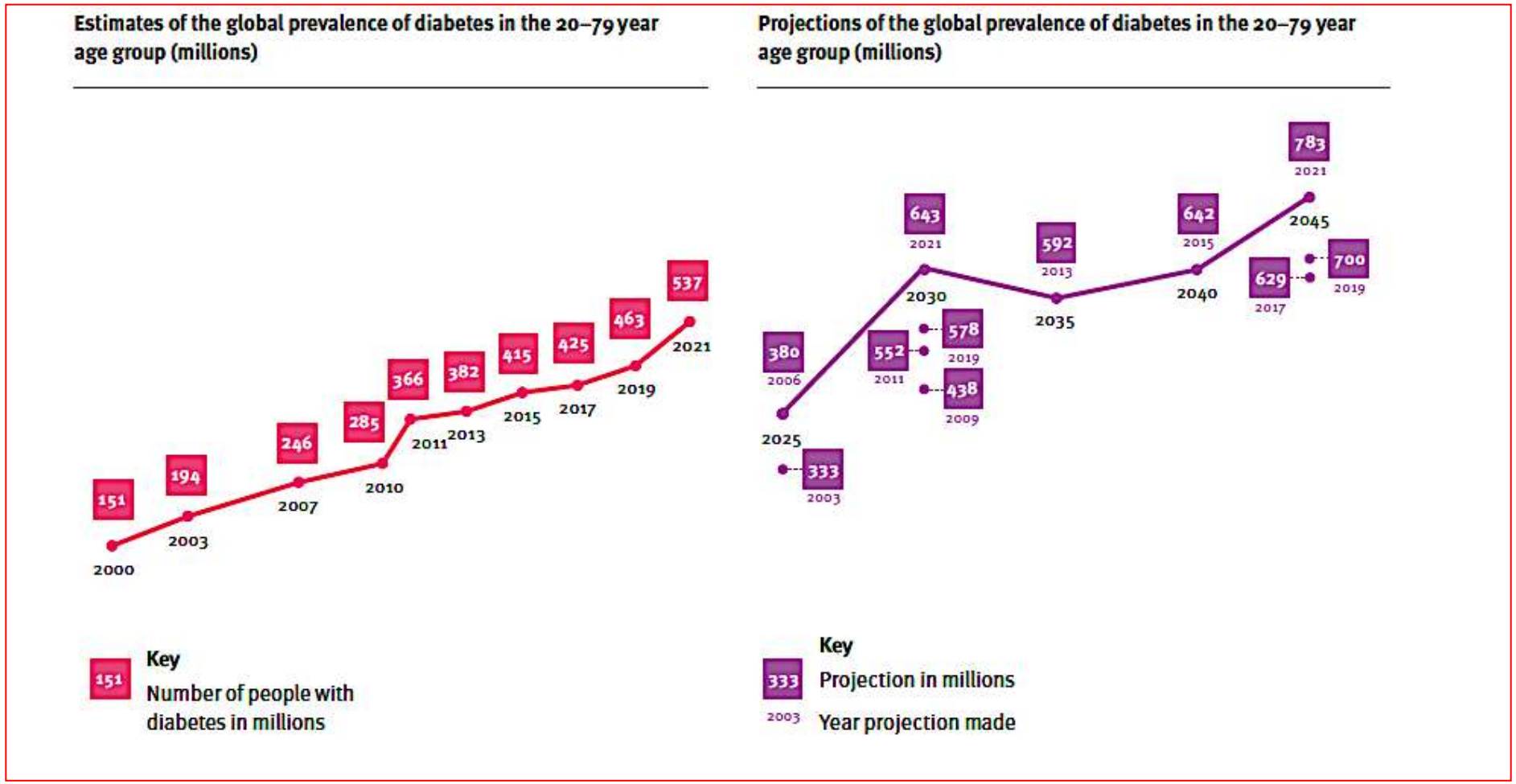
people worldwide have diabetes

IDF Diabetes Atlas

10TH edition

2021

IDF prevalence of diabetes



IDF highlights

1 in 10
Adults (20-79 years) has diabetes
537 million people

1 in 18
Adults (20-79 years) has impaired fasting glucose
319 million people

3 in 4
People with diabetes live in low and middle-income countries

1 in 2
Adults is undiagnosed
240 million people

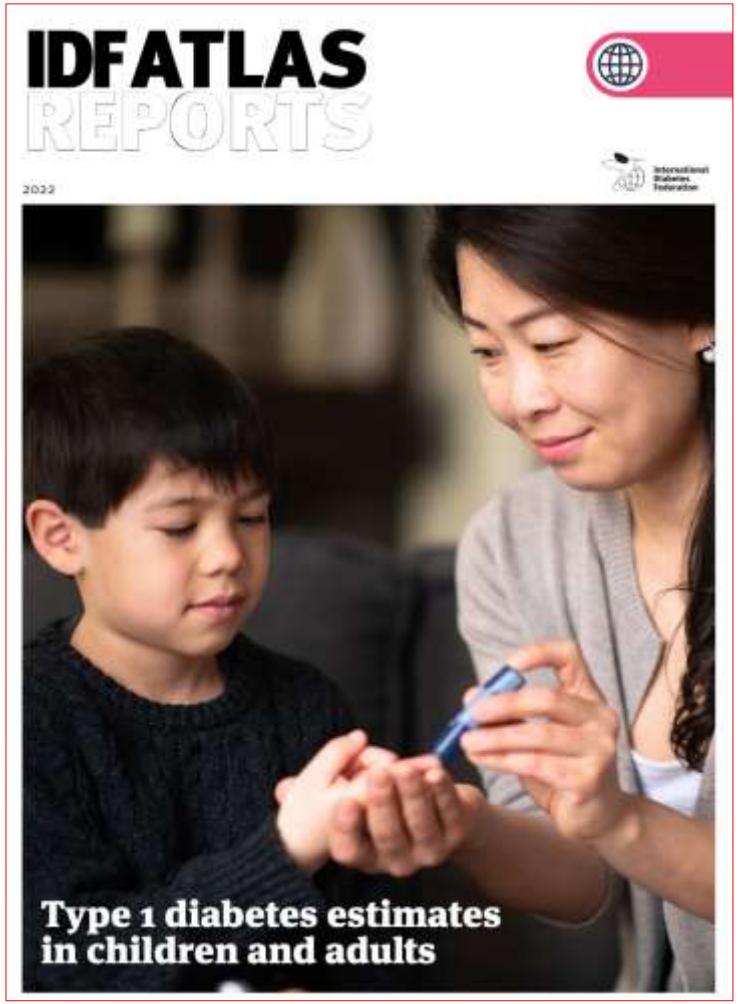
1 in 6
Live births (21 million) affected by hyperglycaemia in pregnancy, 80% have mothers with GDM

9%
Of global health expenditure spent on diabetes (USD 966 billion)

1 in 9
Adults (20-79 years) has impaired glucose tolerance
541 million people

1.2 million
Children and adolescents below 20 years have type 1 diabetes

6.7 million
Deaths attributed to diabetes



Key messages

- In 2022, there were 8.75 million people living with type 1 diabetes globally
- 1.52 million of these people were under 20 years old

In 2022, there were 530,000 new cases of T1D diagnosed at all ages, with 201,000 of these less than 20 years of age.

This number is predicted to increase to 13.5-17.4 M people living with T1D by 2040

Gregory GA et al, Lancet Diabetes Endocrinol 2022

Number of individuals with diabetes in each country, by age (2022)

Country	Age <20 years	Age 20 - 59 years	Age >=60 years	Total
Italy	12,119	106,873	67,709	186,701

Classification of diabetes mellitus

Category	Key features
Type 1	Immune-mediated beta cell death (type 1a) Conspicous/absolute insulin deficiency Includes LADA (latent autommune diabetes of adulthood) Includes idiopatic type 1 diabetes (type 1b)
Type 2	Combination of beta cell dysfunction and death Varying degrees of insulin resistance
Other specific types	Vastly heterogenous Includes monogenic forms
Gestational diabetes	Onset during pregnancy

Adapted from Marchetti P et al, Transplantation of the Pancreas, Gruessner&Gruessner Eds, Springer, 2023

Other specific types

A. Genetic defects of β-cell function
   1. Chromosome 12, HNF-1α (MODY3)
   2. Chromosome 7, glucokinase (MODY2)
   3. Chromosome 20, HNF-4α (MODY1)
   4. Chromosome 13, insulin promoter factor-1 (IPF-1; MODY4)
   5. Chromosome 17, HNF-1β (MODY5)
   6. Chromosome 2, *NeuroD1* (MODY6)
   7. Mitochondrial DNA
   8. Others

B. Genetic defects in insulin action
   1. Type A insulin resistance
   2. Leprechaunism
   3. Rabson-Mendenhall syndrome
   4. Lipoatrophic diabetes
   5. Others

C. Diseases of the exocrine pancreas
   1. Pancreatitis
   2. Trauma/pancreatectomy
   3. Neoplasia
   4. Cystic fibrosis
   5. Hemochromatosis
   6. Fibrocalculous pancreatopathy
   7. Others

D. Endocrinopathies
   1. Acromegaly
   2. Cushing's syndrome
   3. Glucagonoma
   4. Pheochromocytoma
   5. Hyperthyroidism
   6. Somatostatinoma
   7. Aldosteronoma
   8. Others

E. Drug or chemical induced
   1. Vacor
   2. Pentamidine
   3. Nicotinic acid
   4. Glucocorticoids
   5. Thyroid hormone
   6. Diazoxide
   7. β-adrenergic agonists
   8. Thiazides
   9. Dilantin
   10. γ-Interferon
   11. Others

F. Infections
   1. Congenital rubella
   2. Cytomegalovirus
   3. Others

G. Uncommon forms of immune-mediated diabetes
   1. "Stiff-man" syndrome
   2. Anti-insulin receptor antibodies
   3. Others

H. Other genetic syndromes sometimes associated with diabetes
   1. Down syndrome
   2. Klinefelter syndrome
   3. Turner syndrome
   4. Wolfram syndrome
   5. Friedreich ataxia
   6. Huntington chorea
   7. Laurence-Moon-Biedl syndrome
   8. Myotonic dystrophy
   9. Porphyria
   10. Prader-Willi syndrome
   11. Others

MODY

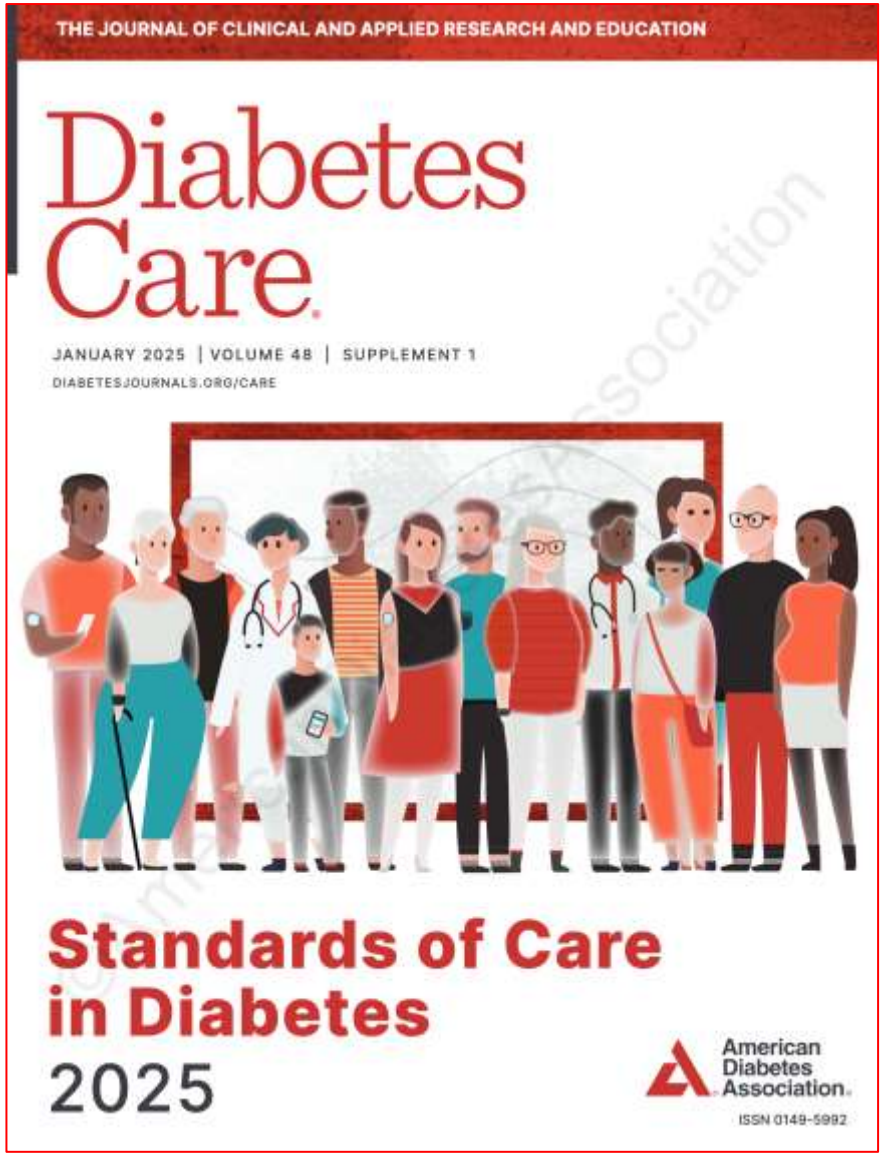


Table 2.6—Most common causes of monogenic diabetes

	Gene	Inheritance	Clinical features
MODY	*HNF1A*	AD	HNF1A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; lowered renal threshold for glucosuria; large rise in 2-h PG level on OGTT (>90 mg/dL [>5 mmol/L]); sensitive to sulfonylureas
	HNF4A	AD	HNF4A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; may have large birth weight and transient neonatal hypoglycemia; sensitive to sulfonylureas
	HNF1B	AD	HNF1B-MODY: developmental renal disease (typically cystic); genitourinary abnormalities; atrophy of the pancreas; hyperuricemia; gout
	GCK	AD	GCK-MODY: higher glucose threshold (set point) for glucose-stimulated insulin secretion, causing stable, nonprogressive elevated fasting blood glucose; typically does not require treatment; microvascular complications are rare; small rise in 2-h PG level on OGTT (<54 mg/dL [<3 mmol/L])
Neonatal diabetes	*KCNJ11*	AD	Permanent or transient: IUGR; possible developmental delay and seizures; responsive to sulfonylureas
	INS	AD	Permanent: IUGR; insulin requiring
	ABCC8	AD	Permanent or transient: IUGR; rarely developmental delay; responsive to sulfonylureas
	6q24 (*PLAGL1*, *HYMA1*)	AD for paternal duplications	Transient: IUGR; macroglossia; umbilical hernia; mechanisms include UPD6, paternal duplication, or maternal methylation defect; may be treatable with medications other than insulin
	GATA6	AD	Permanent: pancreatic hypoplasia; cardiac malformations; pancreatic exocrine insufficiency; insulin requiring
	EIF2AK3	AR	Permanent: Wolcott-Rallison syndrome: epiphyseal dysplasia; pancreatic exocrine insufficiency; insulin requiring
	EIF2B1	AD	Permanent diabetes: can be associated with fluctuating liver function (157)
	FOXP3	X-linked	Permanent: immunodysregulation, polyendocrinopathy, enteropathy X-linked (IPEX) syndrome: autoimmune diabetes, autoimmune thyroid disease, exfoliative dermatitis; insulin requiring

www.orpha.net

MODY is the most common form of monogenic diabetes. Prevalence is estimated to be about **1/10,000 in adults and 1/23,000 in children**.

Monogenic Diabetes in Youth With Presumed Type 2 Diabetes: Results From the Progress in Diabetes Genetics in Youth (ProDiGY) Collaboration

Diabetes Care 2021;44:2312–2319 | https://doi.org/10.2337/dc21-0491

Jennifer N. Todd,[1,2,3,4] Jeffrey W. Kleinberger,[5] Haichen Zhang,[5] Shylaja Srinivasan,[6] Sherida E. Tollefsen,[7] Lynne L. Levitsky,[8] Lorraine E. Levitt Katz,[9] Jeanie B. Tryggestad,[10] Fida Bacha,[11] Giuseppina Imperatore,[12] Jean M. Lawrence,[13] Catherine Pihoker,[14] Jasmin Divers,[15] Jason Flannick,[2,3] Dana Dabelea,[16] Jose C. Florez,[3,4,17,18] and Toni I. Pollin[5]

OBJECTIVE

Maturity-onset diabetes of the young (MODY) is frequently misdiagnosed as type 1 or type 2 diabetes. Correct diagnosis may result in a change in clinical treatment and impacts prediction of complications and familial risk. In this study, we aimed to assess the prevalence of MODY in multiethnic youth under age 20 years with a clinical diagnosis of type 2 diabetes.

RESEARCH DESIGN AND METHODS

We evaluated whole-exome sequence data of youth with a clinical diagnosis of type 2 diabetes. We considered participants to have MODY if they carried a MODY gene variant classified as likely pathogenic (LP) or pathogenic (P) according to current guidelines.

RESULTS

Of 3,333 participants, 93 (2.8%) carried an LP/P variant in *HNF4A* (16 participants), *GCK* (23), *HNF1A* (44), *PDX1* (5), *INS* (4), and *CEL* (1). Compared with those with no LP/P variants, youth with MODY had a younger age at diagnosis (12.9 ± 2.5 vs. 13.6 ± 2.3 years, $P = 0.002$) and lower fasting C-peptide levels (3.0 ± 1.7 vs. 4.7 ± 3.5 ng/mL, $P < 0.0001$). Youth with MODY were less likely to have hypertension (6.9% vs. 19.5%, $P = 0.007$) and had higher HDL cholesterol (43.8 vs. 39.7 mg/dL, $P = 0.006$).

CONCLUSIONS

By comprehensively sequencing the coding regions of all MODY genes, we identified MODY in 2.8% of youth with clinically diagnosed type 2 diabetes; importantly, in 89% ($n = 83$) the specific diagnosis would have changed clinical management. No clinical criterion reliably separated the two groups. New tools are needed to find ideal criteria for selection of individuals for genetic testing.

Neonatal diabetes

Neonatal diabetes mellitus (NDM) is defined as diabetes with onset before 6 months of age. The population frequency of NDM has been estimated at 1 in 300,000 to 1 in 400,000 (1 in 90,000 in some studies). Many of these cases are transient but nearly half of them develop permanent neonatal diabetes mellitus (PNDM).

Table 2.6—Most common causes of monogenic diabetes

	Gene	Inheritance	Clinical features
MODY	*HNF1A*	AD	HNF1A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; lowered renal threshold for glucosuria; large rise in 2-h PG level on OGTT (>90 mg/dL [>5 mmol/L]); sensitive to sulfonylureas
	HNF4A	AD	HNF4A-MODY: progressive insulin secretory defect with presentation in adolescence or early adulthood; may have large birth weight and transient neonatal hypoglycemia; sensitive to sulfonylureas
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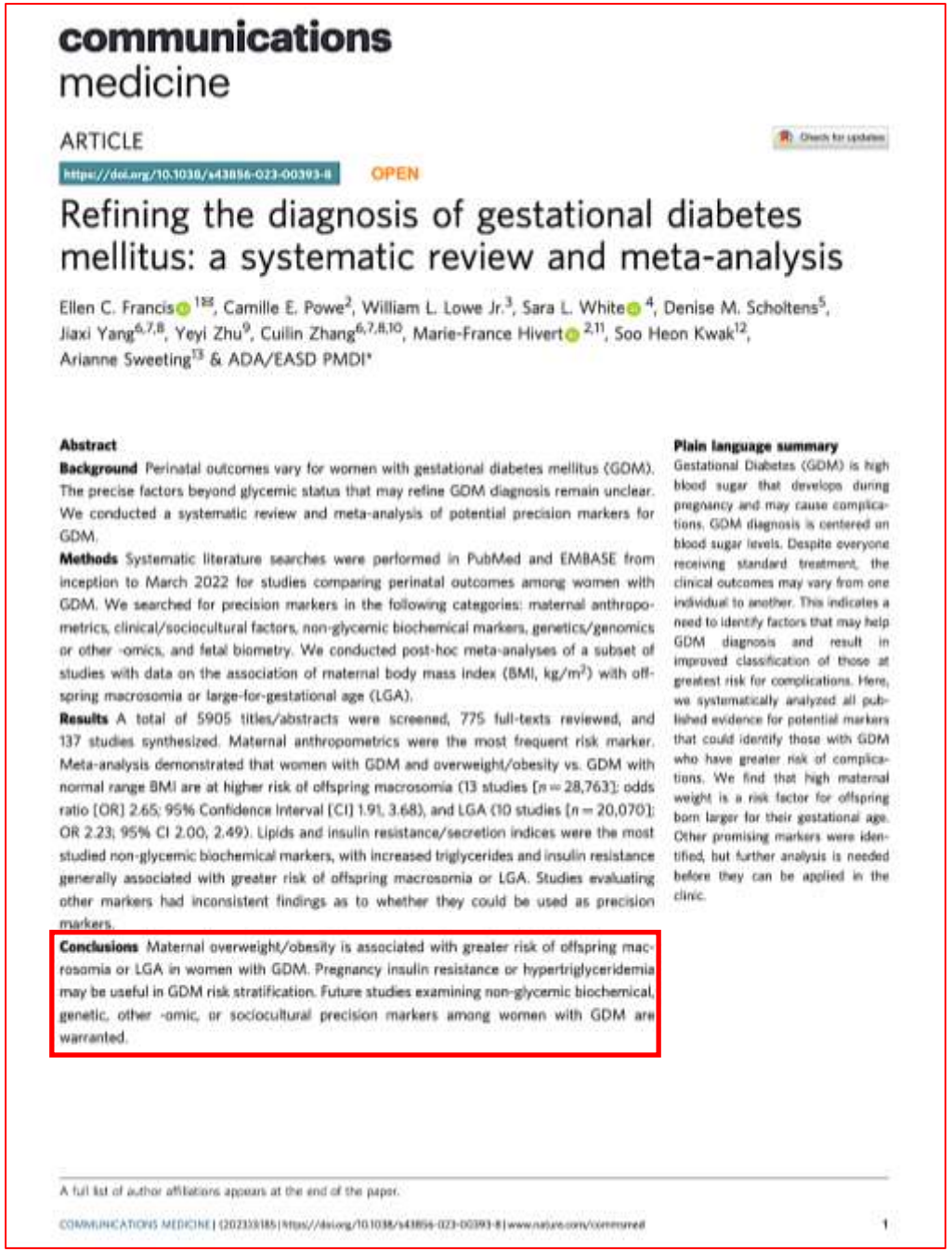
Type 2	Combination of beta cell dysfunction and death Varying degrees of insulin resistance
Other specific types	Vastly heterogenous Includes monogenic forms
Gestational diabetes	Onset during pregnancy

10-15% of pregnancies
2024: 374,000 births in Italy



communications medicine

ARTICLE

https://doi.org/10.1038/s43856-023-00393-8 OPEN

Refining the diagnosis of gestational diabetes mellitus: a systematic review and meta-analysis

Ellen C. Francis[1✉], Camille E. Powe[2], William L. Lowe Jr.[3], Sara L. White[4], Denise M. Scholtens[5], Jiaxi Yang[6,7,8], Yeyi Zhu[9], Cuilin Zhang[6,7,8,10], Marie-France Hivert[2,11], Soo Heon Kwak[12], Arianne Sweeting[13] & ADA/EASD PMDI*

Abstract

Background Perinatal outcomes vary for women with gestational diabetes mellitus (GDM). The precise factors beyond glycemic status that may refine GDM diagnosis remain unclear. We conducted a systematic review and meta-analysis of potential precision markers for GDM.

Methods Systematic literature searches were performed in PubMed and EMBASE from inception to March 2022 for studies comparing perinatal outcomes among women with GDM. We searched for precision markers in the following categories: maternal anthropometrics, clinical/sociocultural factors, non-glycemic biochemical markers, genetics/genomics or other -omics, and fetal biometry. We conducted post-hoc meta-analyses of a subset of studies with data on the association of maternal body mass index (BMI, kg/m^2) with offspring macrosomia or large-for-gestational age (LGA).

Results A total of 5905 titles/abstracts were screened, 775 full-texts reviewed, and 137 studies synthesized. Maternal anthropometrics were the most frequent risk marker. Meta-analysis demonstrated that women with GDM and overweight/obesity vs. GDM with normal range BMI are at higher risk of offspring macrosomia (13 studies [$n = 28,763$]; odds ratio [OR] 2.65; 95% Confidence Interval [CI] 1.91, 3.68), and LGA (10 studies [$n = 20,070$]; OR 2.23; 95% CI 2.00, 2.49). Lipids and insulin resistance/secretion indices were the most studied non-glycemic biochemical markers, with increased triglycerides and insulin resistance generally associated with greater risk of offspring macrosomia or LGA. Studies evaluating other markers had inconsistent findings as to whether they could be used as precision markers.

Conclusions Maternal overweight/obesity is associated with greater risk of offspring macrosomia or LGA in women with GDM. Pregnancy insulin resistance or hypertriglyceridemia may be useful in GDM risk stratification. Future studies examining non-glycemic biochemical, genetic, other -omic, or sociocultural precision markers among women with GDM are warranted.

Plain language summary

Gestational Diabetes (GDM) is high blood sugar that develops during pregnancy and may cause complications. GDM diagnosis is centered on blood sugar levels. Despite everyone receiving standard treatment, the clinical outcomes may vary from one individual to another. This indicates a need to identify factors that may help GDM diagnosis and result in improved classification of those at greatest risk for complications. Here, we systematically analyzed all published evidence for potential markers that could identify those with GDM who have greater risk of complications. We find that high maternal weight is a risk factor for offspring born larger for their gestational age. Other promising markers were identified, but further analysis is needed before they can be applied in the clinic.

A full list of author affiliations appears at the end of the paper.

DIABETICMedicine

DOI: 10.1111/j.1464-5491.2008.02622.x

Original Article: Genetics

Pregnancy outcome in patients with raised blood glucose due to a heterozygous glucokinase gene mutation

G. Spyer*, K. M. Macleod*, M. Shepherd*†, S. Ellard* and A. T. Hattersley*

*Institute of Biomedical Sciences and †Institute of Health and Social Care, Peninsula Medical School, Exeter, UK

Accepted 28 October 2008

Abstract

Aim To assess determinants of fetal growth in the offspring of pregnant women with hyperglycaemia due to a heterozygous glucokinase (GCK) gene mutation.

Methods Details of gestational age at delivery, fetal birth weight and maternal antenatal treatment were collected from patients and retrospective case note review of 82 offspring born to 42 women with GCK gene mutations and 31 offspring born to 13 unaffected normoglycaemic women with an affected partner. Fetal genotype was determined using direct sequencing from either a mouth swab or a blood sample.

Results In mothers with GCK mutations, non-mutation-carrying offspring were heavier than mutation-carrying offspring (corrected birth weight 3.9 ± 0.6 vs. 3.2 ± 0.8 kg; $P < 0.001$) and more likely to be macrosomic (> 4.0 kg; 39% vs. 7%, $P = 0.001$). There was no difference in corrected birth weight between offspring of insulin- and diet-treated women (3.7 ± 0.7 vs. 3.8 ± 0.6 kg; $P = 0.1$), although insulin-treated mothers delivered earlier (37.5 ± 1.7 vs. 38.9 ± 2.3 weeks; $P < 0.001$) due to increased obstetric intervention.

Conclusions Offspring of women with GCK mutations are at increased risk of macrosomia and its obstetric consequences. Fetal birth weight is predominantly altered by fetal genotype and not treatment of maternal hyperglycaemia with insulin. This probably reflects the large effect of a fetal GCK mutation on fetal insulin secretion and the difficulty in reducing the regulated maternal glycaemia caused by a glucose sensing defect in people with GCK mutations.

Diabet. Med. 26, 14–18 (2009)

› Nat Genet. 1998 Jul;19(3):268-70. doi: 10.1038/953.

Mutations in the glucokinase gene of the fetus result in reduced birth weight

A T Hattersley [1], F Beards, E Ballantyne, M Appleton, R Harvey, S Ellard

Affiliations + expand

PMID: 9662401 DOI: 10.1038/953

Abstract

Low birth weight and fetal thinness have been associated with non-insulin dependent diabetes mellitus (NIDDM) and insulin resistance in childhood and adulthood. It has been proposed that this association results from fetal programming in response to the intrauterine environment. An alternative explanation is that the same genetic influences alter both intrauterine growth and adult glucose tolerance. Fetal insulin secretion in response to maternal glycaemia plays a key role in fetal growth, and adult insulin secretion is a primary determinant of glucose tolerance. We hypothesized that a defect in the sensing of glucose by the pancreas, caused by a heterozygous mutation in the glucokinase gene, could reduce fetal growth and birth weight in addition to causing hyperglycaemia after birth. In 58 offspring, where one parent has a glucokinase mutation, the inheritance of a glucokinase mutation by the fetus resulted in a mean reduction of birth weight of 533 g (P=0.002). In 19 of 21 sibpairs discordant for the presence of a glucokinase mutation, the child with the mutation had a lower birth weight, with a mean difference of 521 g (P=0.0002). Maternal hyperglycaemia due to a glucokinase mutation resulted in a mean increase in birth weight of 601 g (P=0.001). The effects of maternal and fetal glucokinase mutations on birth weight were additive. We propose that these changes in birth weight reflect changes in fetal insulin secretion which are influenced directly by the fetal genotype and indirectly, through maternal hyperglycaemia, by the maternal genotype. This observation suggests that variation in fetal growth could be used in the assessment of the role of genes which modify either insulin secretion or insulin action.

Classification of diabetes mellitus

Category	Key features
Type 1	Immune-mediated beta cell death (type 1a) Conspicous/absolute insulin deficiency Includes LADA (latent autommune diabetes of adulthood) Includes idiopatic type 1 diabetes (type 1b)
Type 2	Combination of beta cell dysfunction and death Varying degrees of insulin resistance
Other specific types	Vastly heterogenous Includes monogenic forms
Gestational diabetes	Onset during pregnancy

Adapted from Marchetti P et al, Transplantation of the Pancreas, Gruessner&Gruessner Eds, Springer, 2023

The Lancet Diabetes & Endocrinology
Volume 13, Issue 2, February 2025, Pages 149-164

Review

Dissection of type 2 diabetes: a genetic perspective

Amélie Bonnefond PhD [a b], Prof Jose C Florez MD [c d e], Prof Ruth J F Loos PhD [f g], Prof Philippe Froguel MD [a b]

The polygenic background of type 2 diabetes predominantly affects pancreatic islets

Since the beginning of GWAS for type 2 diabetes in 2007, geneticists quickly noticed that the signals identified by these studies primarily affected insulin secretion in pancreatic islets rather than insulin resistance, as evidenced by the provocative title of the review by Richard Watanabe published in 2010: The genetics of insulin resistance: Where's Waldo? 118, 119 As mentioned earlier in this Review, the pathophysiological advances following GWAS have been slow because most SNPs identified …

Monogenic diabetes

In the 1980s, a hypothesis emerged suggesting that type 2 diabetes might be an autosomal dominant disorder caused by the dysfunction of a single dominantly transmitted mutated gene. This gene would exhibit variable penetrance, influenced by factors such as obesity and ageing.[7] In line with this hypothesis, a first gene—glucokinase (*GCK*)—causing monogenic diabetes following dominant inheritance was found in 1992. This discovery resulted from a combination of linkage analyses directed at a tandem …

Effect of the environment on type 2 diabetes via epigenetics

Type 2 diabetes is a multifactorial disease in which age and environmental factors play key roles in its development, acting upon a genetic predisposition. These environmental risk factors do not modify the constitutive genome (even if they might favour somatic mutations in different tissues including blood),158, 159 but instead they modulate the way genes and especially their regulatory non-coding region's function, mainly with epigenetic modifications. The epigenome consists of various …

Monogenic diabetes can present with a phenotype similar to that of polygenic type 2 diabetes

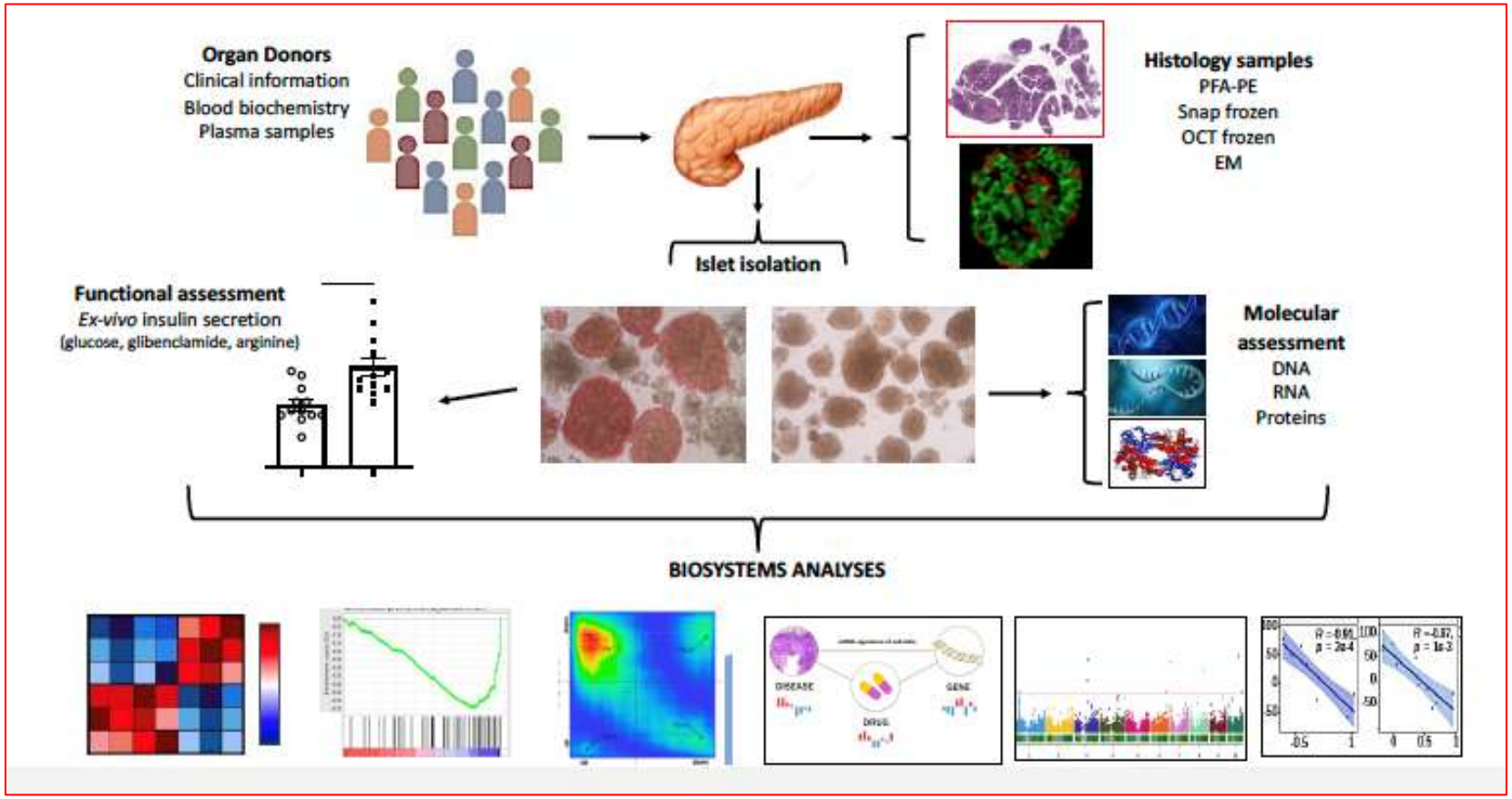
It is well known that the biology and pathophysiology of common diseases cannot simply be reduced to rigid categories, and that the involved molecular mechanisms and pathways are inherently complex and interconnected. This applies to diabetes and its genetics.

First, there is a phenotypic continuum between monogenic diabetes and polygenic diabetes. Monogenic diabetes does not necessarily imply early-onset diabetes associated with a normal weight, and polygenic diabetes does not imply late-onset …

From today to tomorrow: unveiling type 2 diabetes precision medicine insights from genetic studies

Personalised genomic medicine is a reality for patients with diabetes who have monogenic conditions and guidelines are helping physicians to provide optimal diabetes care.[68] The situation for type 2 diabetes is less advanced. Clinicians have long recognised that type 2 diabetes is a heterogeneous condition[172] due to a diagnostic approach based on the final common pathway of hyperglycaemia, such that any diabetes that is not monogenic, autoimmune, syndromic, or due to pancreatic injury is …

Our islet working flow



Condition	Number	Histology	Genomic DNA	Islet DNA	Islet RNA	Islet proteins	Plasma samples	Ex-vivo function
ND	628	619	512	279	357	145	580	538
T2D	144	137	111	49	74	36	120	121

Conclusions

- Precision medicine is fundamental for accurate prediction, prevention, diagnosis, prognosis and therapy of rare diseases
- Fostering knowledge is key, and integrated networks mandatory
- With increasing awareness, the horizon of rare diseases is expanding, and diabetes is growingly becoming part of it

Finanziato dall'Unione europea NextGenerationEU

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UnivPM – Ancona
Aula Montessori
Facoltà di Medicina
e Chirurgia

venerdì 28 febbraio
14:30 → 18:30
sabato 1 marzo
09:00 → 13:00

Progetto "Health Extended ALliance for Innovative Therapies, Advanced Lab-research, and Integrated Approaches of Precision Medicine (HEAL ITALIA) Codice PE00000019, CUP I33C22006900006 – finanziato dal PNRR M4C2 I1.3 – DD MUR 341 del 15/03/2022

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