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Diabetes and pancreatic cancer

24th January 2024, 09.00 – 11.45, Zoom Webinar

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Different Types of Diabetes
Type 3c Diabetes
Pancreatic Cancer and Diabetes

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Disclosures

Vicki Alabraba

- Speaker fees from: Dexcom, NovoNordisk, Eli Lilly, Sanofi, Menarini, AstraZeneca, Roche, SBK
- DSN Forum UK LTD Director

Laura McGeeney

- Secretary of the Nutrition Interest Group of the Pancreatic Society of GB and Ireland (NIGPS), the group receives unconditional grants from Viatris who make Creon

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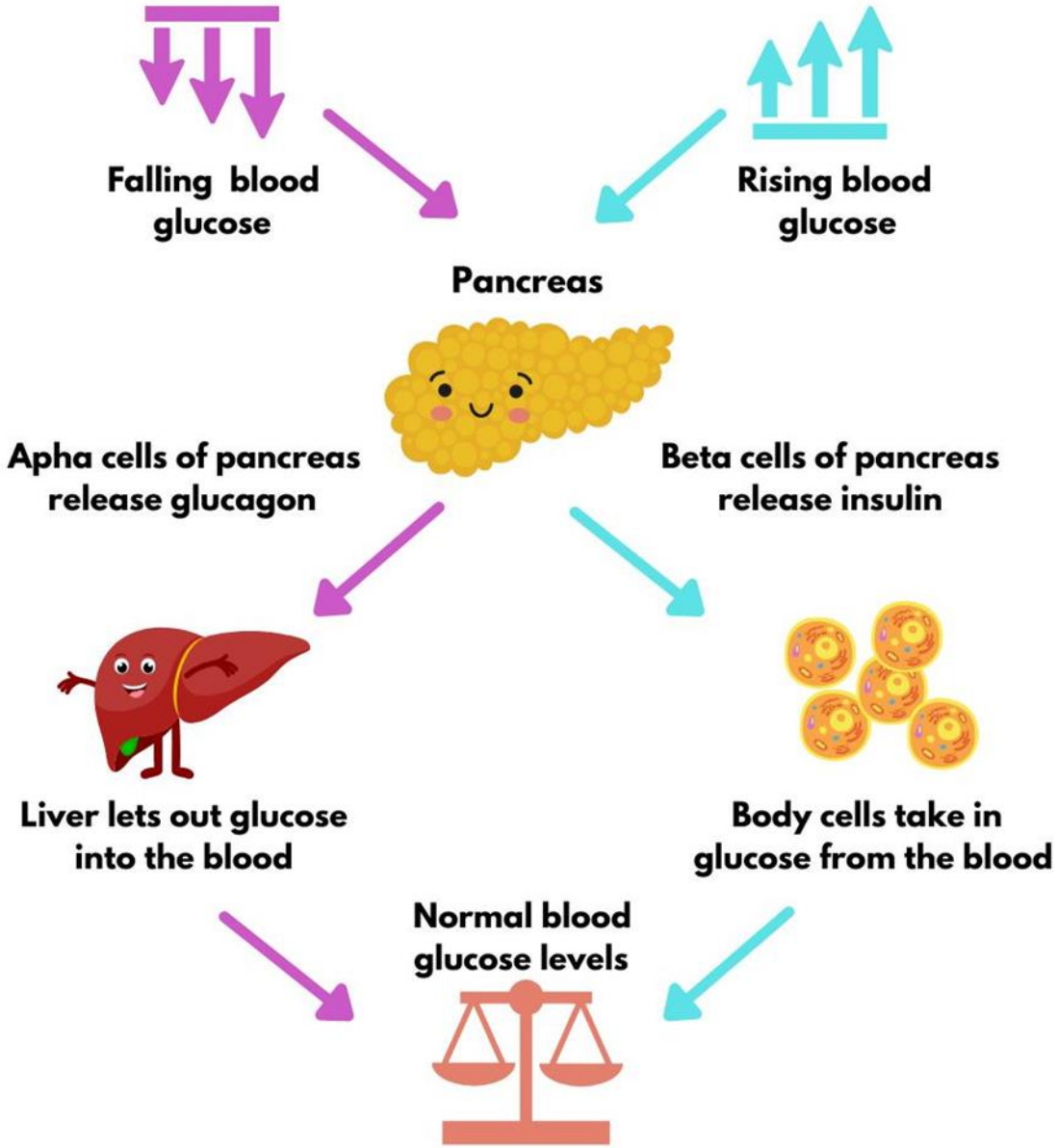

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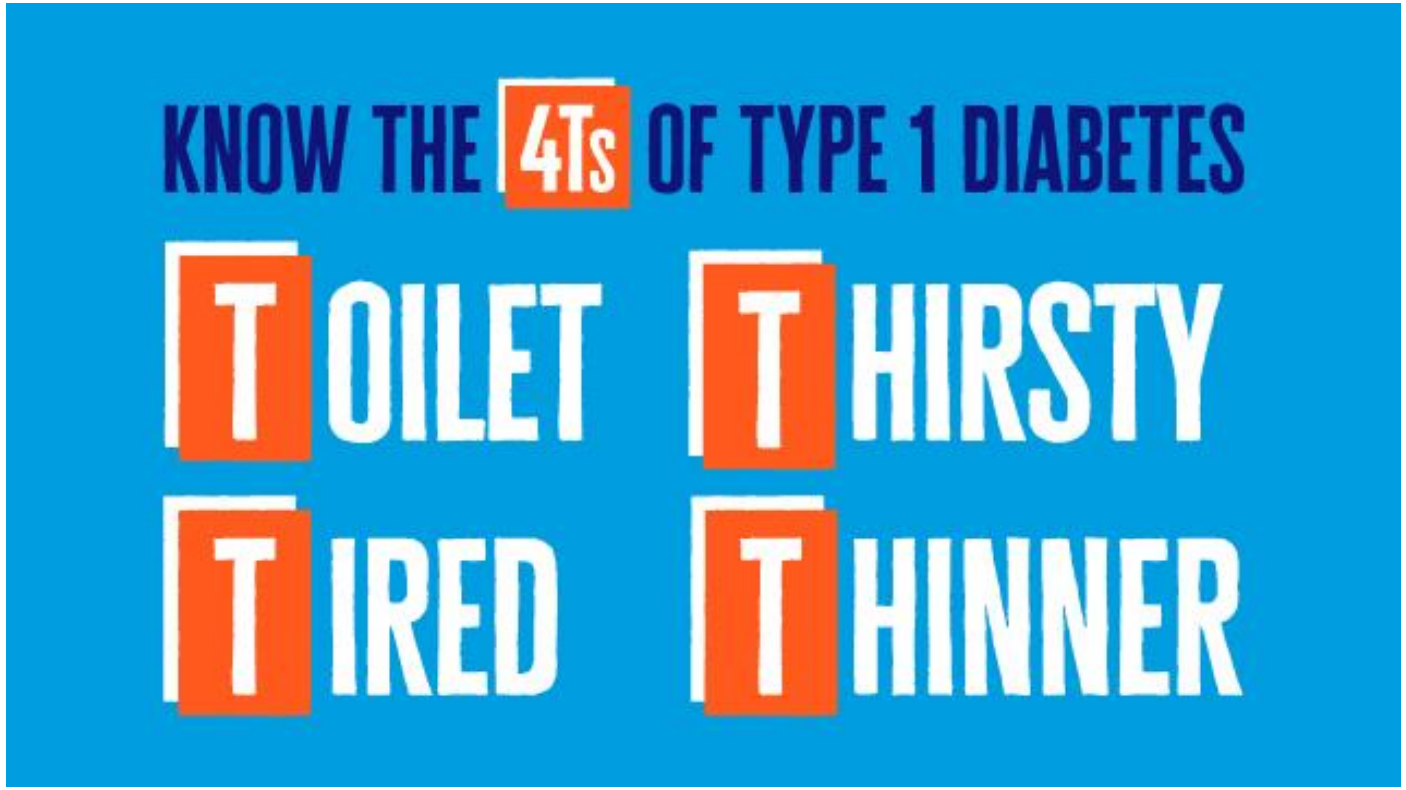
Type 1 Diabetes



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Type 1 diabetes	
Pathophysiology	Autoimmune pancreatic beta cell destruction
Age at diagnosis	Usually < 30 years but can occur at any age
Weight	Usually BMI < 25 but don't rule out based on BMI.
Family history	Uncommon (5-10%)
Auto antibodies	Positive
History autoimmune conditions	Often personal or family history (thyroid and/or coeliac)
C-peptide	Low - but can have residual function up to 5 years after diagnosis
DKA risk	High - ketones not always present at diagnosis or may be low level

Adapted from diagnosis and classification of diabetes in primary care 'Medscape Primary Care Hacks' by Kevin Fernando

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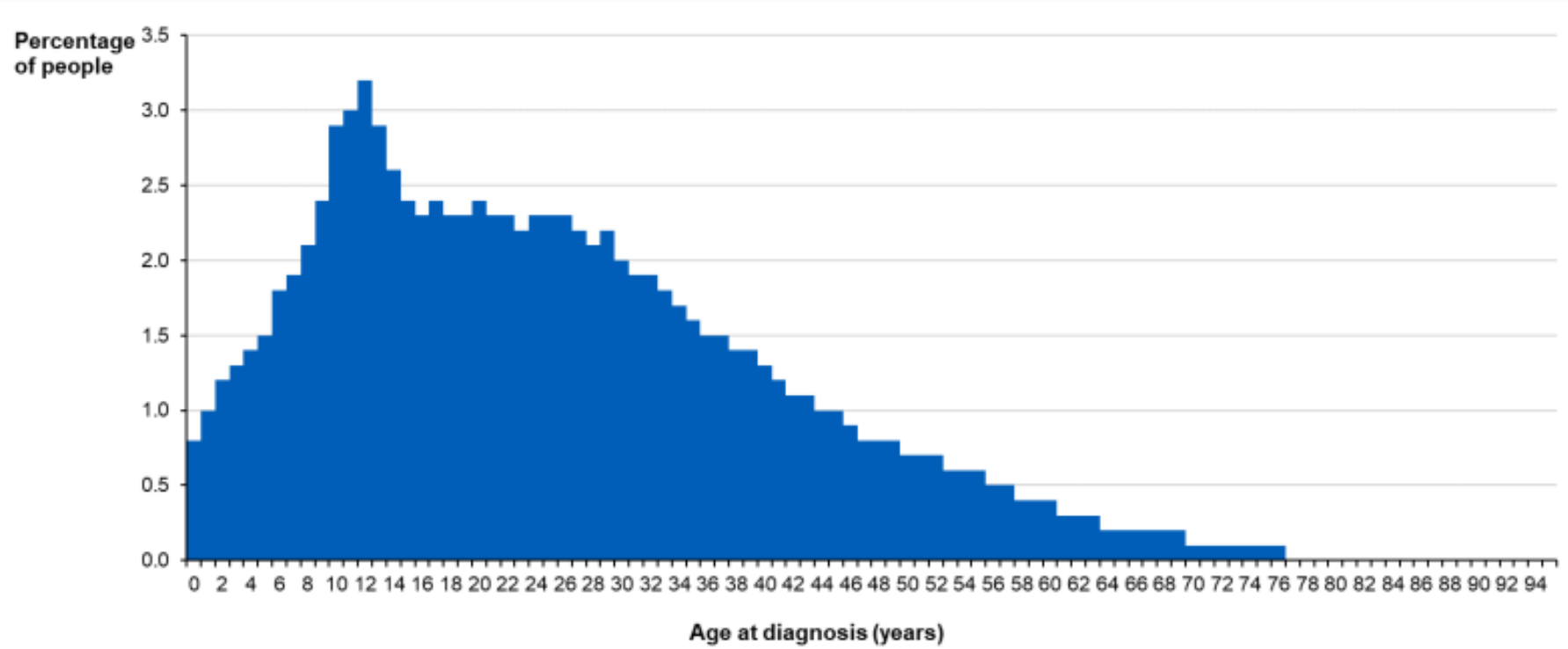
Type 1 Diabetes: Age at diabetes diagnosis

Figure 2: People with type 1 diabetes, by age of diagnosis*, England and Wales, 2019-20



Presentations of type 1 diabetes climb steeply through childhood and peak in adolescence. They continue to present at a steady high rate to around 30 years old where they decline gradually with low rates presenting from the mid-fifties. Approximately two-thirds are diagnosed by aged 30 years old and one third thereafter.

National Diabetes Audit 2019-2020

Diabetes/Pancreatic Autoantibodies

Diabetes Profile			
Islet Cell Antibody			
Anti-GAD Antibody		IU/mL	0 - 9
Anti-IA2 antibodies		IU/mL	0 - 9
Anti-ZNT8 antibodies		RU/mL	0 - 15

Miscellaneous antibodies :
GAD antibody is associated with type 1 diabetes mellitus. SB/SM

Endogenous insulin production can be assessed by measuring C-peptide in the blood or urine. However this is not routinely done at diagnosis and may be more valuable 3 years after diagnosis if the diagnosis is deemed as ‘unclear’.

American Diabetes Association

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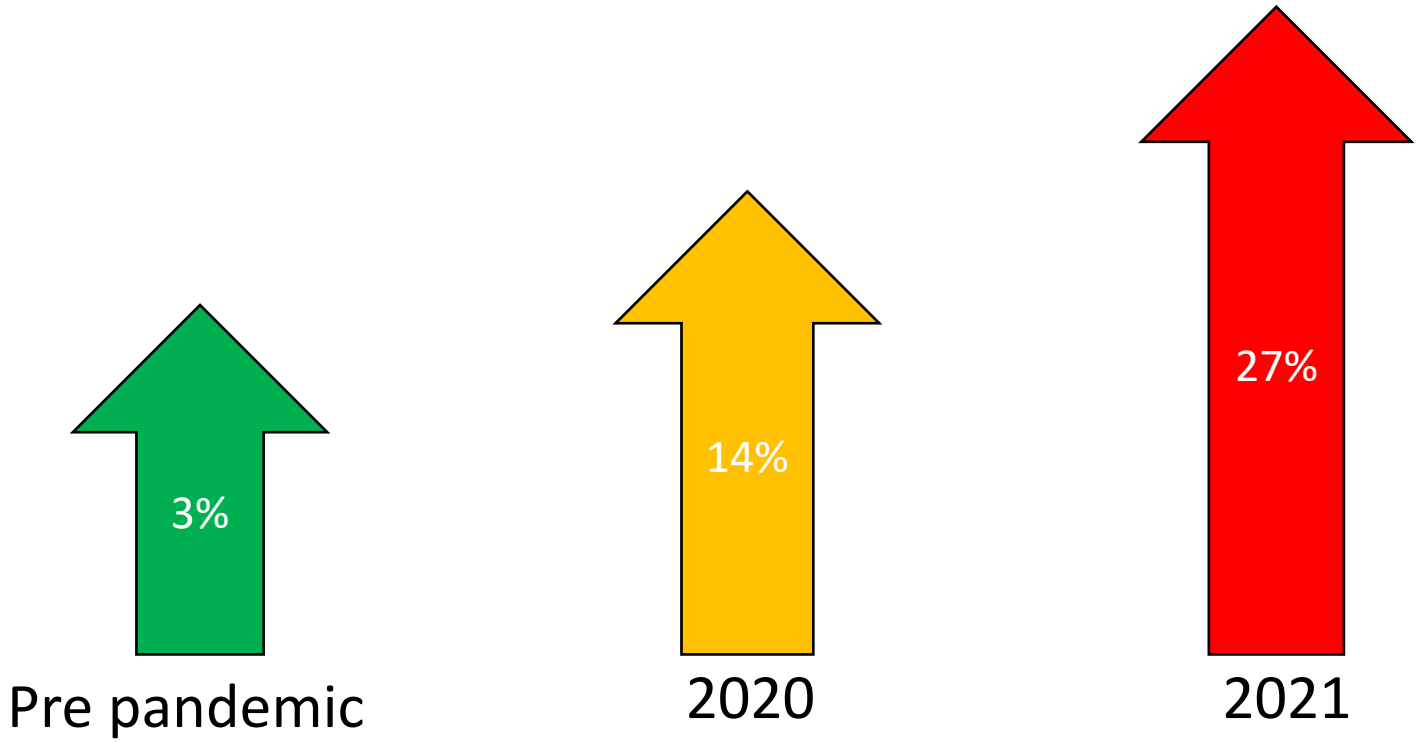
Increasing Global Rates of Type 1 Diabetes



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What about LADA?

LADA	
Pathophysiology	Gradual autoimmune pancreatic beta cell destruction
Age at diagnosis	Can occur at any age but may be older
Weight	Usually a lower BMI but don't rule out based on BMI alone
Family history	Variable
Auto antibodies	Positive
History autoimmune conditions	Variable
C-peptide	Normal initially – declines more rapidly than in type 2 diabetes
DKA risk	Low initially – as insulin deficiency progresses, the risk can increase

Adapted from diagnosis and classification of diabetes in primary care 'Medscape Primary Care Hacks' by Kevin Fernando

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TYPE 2 DIABETES KNOW YOUR RISK

Know Your Risk

Finding out your risk of type 2 diabetes only takes a few minutes. It could be the most important thing you do today.

Find out your risk

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Changing Landscape of Type 2 Diabetes

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Type 2 diabetes	
Pathophysiology	Insulin resistance with insulin deficiency over time
Age at diagnosis	Any age – young onset increasing prevalence
Weight	Usually overweight or obesity
Family history	Common (75-90%)
Auto antibodies	Negative
History autoimmune conditions	Variable
C-peptide	High or normal at diagnosis May decline in long standing T2D
DKA risk	Low – ketones not usually present at diagnosis

Adapted from diagnosis and classification of diabetes in primary care ‘Medscape Primary Care Hacks’ by Kevin Fernando

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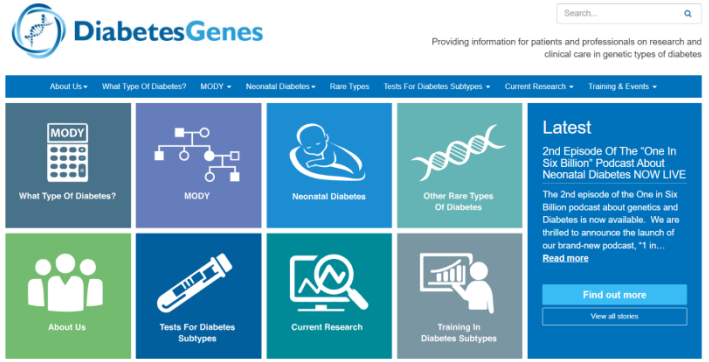
Monogenic Diabetes (MODY)



- Rare (1-2% of all diabetes)
- Mutations in a single gene
- Usually affects adults < 25 years
- Inherited from affected parent with the condition - Autosomal Dominant Inheritance.
- Children of an affected parent have a 50% chance of inheriting the affected gene and developing MODY.
- Several different types of MODY
- Can be treated with oral medication or insulin depending on the gene mutation and type of MODY

Exeter Diabetes App (diabetesgenes.org)

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Type 3c Diabetes

- Pancreatic dysfunction that produces both endocrine and exocrine impairment
- Endocrine – insulin (beta cells), glucagon (alpha cells), polypeptide (PP cells) and incretin hormone dysfunction.
- Exocrine – Maldigestion and malabsorbtion of nutrients leading to impaired digestion and utilisation.
- Pathogenesis is due to decreased (or deficiency) insulin production and glucagon response leading to impaired hepatic gluconeogenesis and unstable glucose levels and in sometimes problematic hypoglycaemia.

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STANDARDS OF CARE | DECEMBER 16 2021

2. Classification and Diagnosis of Diabetes: *Standards of Medical Care in Diabetes—2022* FREE

American Diabetes Association Professional Practice Committee

Classification

Diabetes can be classified into the following general categories:

1. Type 1 diabetes (due to autoimmune β-cell destruction, usually leading to absolute insulin deficiency, including latent autoimmune diabetes of adulthood)
2. Type 2 diabetes (due to a progressive loss of adequate β-cell insulin secretion frequently on the background of insulin resistance)
3. Specific types of diabetes due to other causes, e.g., monogenic diabetes syndromes (such as neonatal diabetes and maturity-onset diabetes of the young), diseases of the exocrine pancreas (such as cystic fibrosis and pancreatitis), and drug- or chemical-induced diabetes (such as with glucocorticoid use, in the treatment of HIV/AIDS, or after organ transplantation)
4. Gestational diabetes mellitus (diabetes diagnosed in the second or third trimester of pregnancy that was not clearly overt diabetes prior to gestation)

Pancreatic Diabetes or Diabetes in the Context of Disease of the Exocrine Pancreas

Pancreatic diabetes includes both structural and functional loss of glucose-normalizing insulin secretion in the context of exocrine pancreatic dysfunction and is commonly misdiagnosed as type 2 diabetes. Hyperglycemia due to general pancreatic dysfunction has been called “type 3c diabetes” and, more recently, diabetes in the context of disease of the exocrine pancreas has been termed pancreoprivic diabetes (1). The diverse set of etiologies includes pancreatitis (acute and chronic), trauma or pancreatectomy, neoplasia, cystic fibrosis (addressed elsewhere in this chapter), hemochromatosis, fibrocalculous pancreatopathy, rare genetic disorders (188), and idiopathic forms (1); as such, pancreatic diabetes is the preferred umbrella terminology. Pancreatitis, even a single bout, can lead to postpancreatitis diabetes mellitus (PPDM). Both acute and chronic pancreatitis can lead to PPDM, and the risk is highest with recurrent bouts. A distinguishing feature is concurrent pancreatic exocrine insufficiency (according to the monoclonal fecal elastase 1 test or direct function tests), pathological pancreatic imaging (endoscopic ultrasound, MRI, computed tomography), and absence of type 1 diabetes–associated autoimmunity (189–194). There is loss of both insulin and glucagon secretion and often higher-than-expected insulin requirements. Risk for microvascular complications appears to be similar to other forms of diabetes. In the context of pancreatectomy, islet autotransplantation can be done to retain insulin secretion (195,196). In some cases, autotransplant can lead to insulin independence. In others, it may decrease insulin requirements (197).

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Poll

- What causes are associated with type 3c diabetes?

- Pancreatitis
- Pancreatic cancer
- Pancreatic surgery
- Pancreatic trauma
- Cystic fibrosis
- Haemocromotsis

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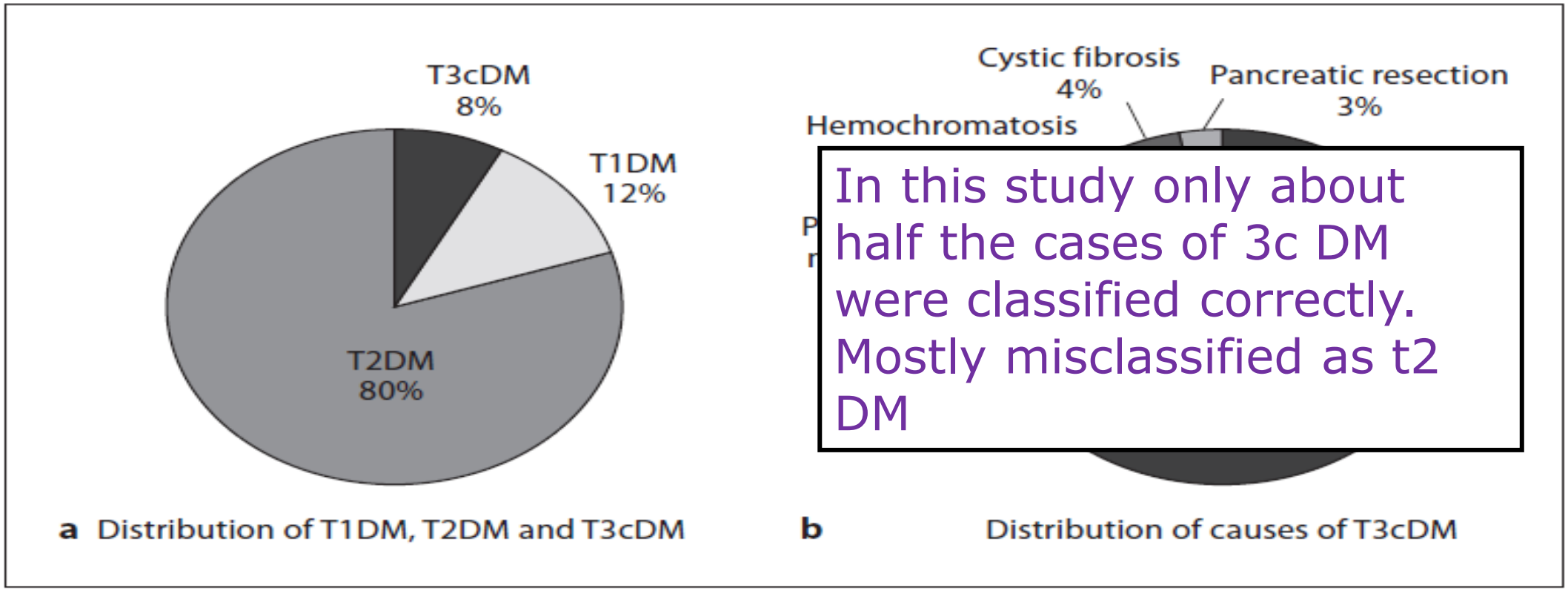
Prevalence



In this study only about half the cases of 3c DM were classified correctly. Mostly misclassified as t2 DM

Pancreatology

Review

Pancreatology 2011;11:279–294
DOI: 10.1159/000329188

Published online: July 9, 2011

Pancreatogenic Diabetes: Special Considerations for Management

YunFeng Cui[a, b] Dana K. Andersen[a]

Based on Hardt *et al*, Diab Care. Feb 2008. 31: 1,922 hospitalised DM patients

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Type 3c diabetes	
Pathophysiology	Insulin deficiency due to damage/trauma/cancer/surgery Often PEI present, e.g. diarrhoea and steatorrhoea, abdominal discomfort, flatulence and bloating. Check stool sample for faecal elastase-1. Low levels suggestive of PEI
Age at diagnosis	Any age
Weight	Variable
Family history	Variable
Auto antibodies	Negative
History autoimmune conditions	Variable
C-peptide	Low but will depend on the extent of insulin deficiency
DKA risk	Low

Adapted from diagnosis and classification of diabetes in primary care ‘Medscape Primary Care Hacks’ by Kevin Fernando

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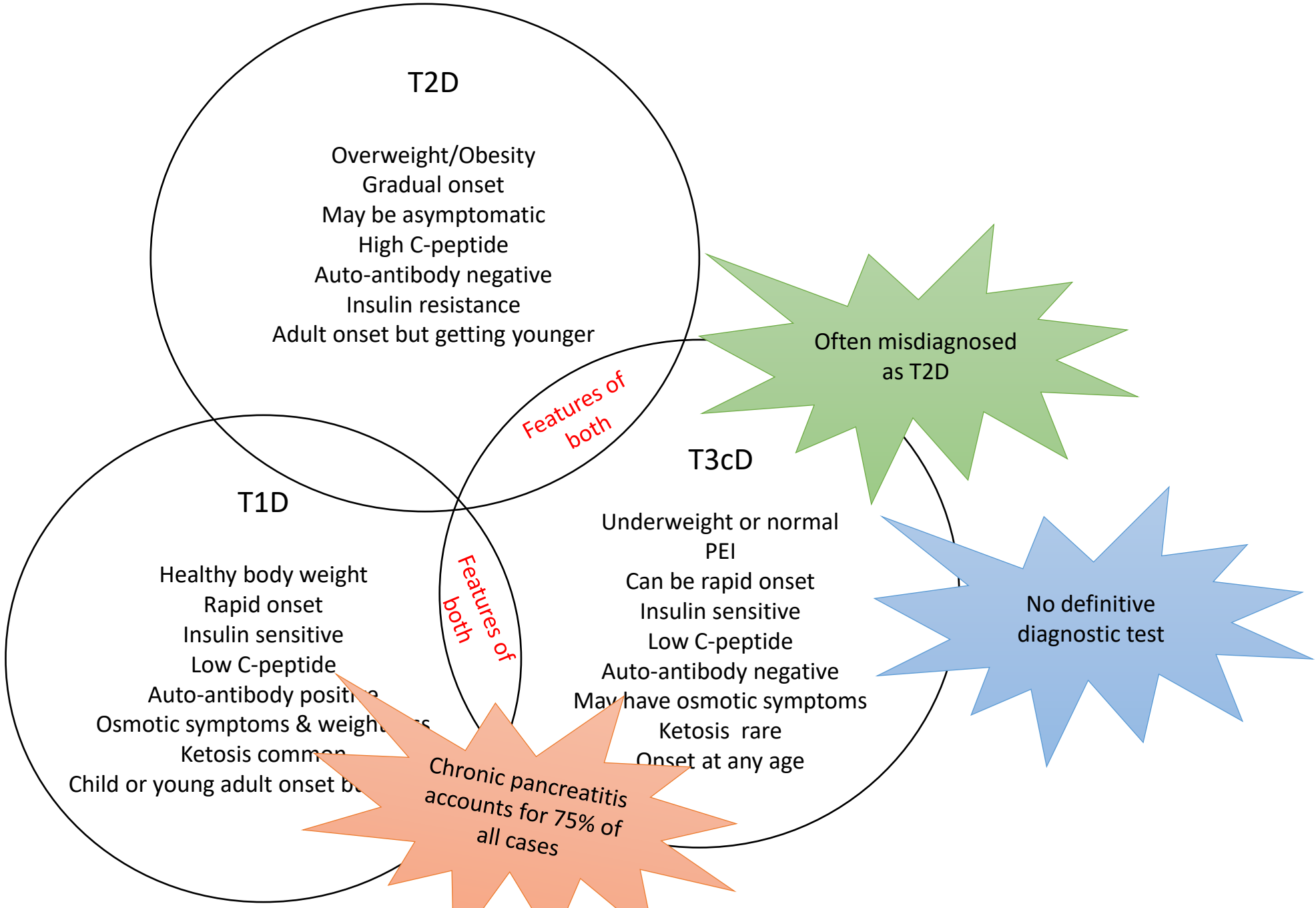

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Poll

- How can you diagnose type 3c diabetes?

- HbA1c
- Fasting plasma glucose
- Random plasma glucose
- All of the above

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Diagnosis

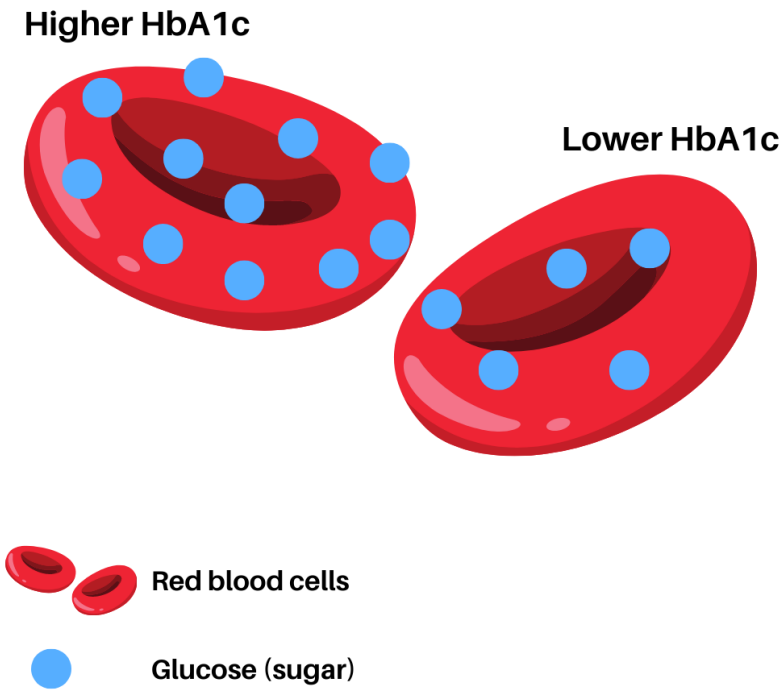
- Diabetes symptoms (e.g. polyuria, polydipsia and unexplained weight loss for Type 1) plus:
  - Random venous plasma glucose ≥ 11.1 mmol/l or
  - Fasting plasma glucose ≥ 7.0 mmol/l or
  - Two hour plasma glucose ≥ 11.1 mmol/l two hours after 75g anhydrous glucose in an oral glucose tolerance test (OGTT).

- If asymptomatic, diagnosis can't be made on a single result. A repeat test (preferably the same test) on another day is needed.

WHO (2021)

HbA1c for Diagnosis

- HbA1c of ≥48mmol/mol (6.5%) is diagnostic
- If asymptomatic the HbA1c should be repeated (within 2 weeks).
- If the 2nd sample is <48mmol/mol (6.5%) treat as 'high risk' of diabetes (pre-diabetes). Repeat HbA1c in 6 months or sooner if symptoms develop.
- <48mmol/mol (6.5%) does not exclude diabetes diagnosed using glucose tests.



WHO (2021)

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When HBA1c is not Appropriate

- ALL children and young people
- Suspected type 1 diabetes
- Symptoms of diabetes for less than 2 months
- Patients at high risk who are acutely ill (e.g. those requiring hospital admission)
- Acute pancreatic damage, including pancreatic surgery
- Pregnancy
- Presence of genetic, haematologic and illness-related factors that influence HbA1c and its measurement

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Proposed Diagnosis for T3c

World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.3748/wjg.v19.i42.7276

World J Gastroenterol 2013 November 14; 19(42): 7276-7281
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

TOPIC HIGHLIGHT

Asbjørn Mohr Drewes, MD, PhD, DMSc, Professor, *Series Editor*

Diagnosis and treatment of diabetes mellitus in chronic pancreatitis

Table 2 Proposed diagnostic criteria for type 3c diabetes mellitus

Major criteria (must be present)
Presence of exocrine pancreatic insufficiency (monoclonal fecal elastase-1 test or direct function tests)
Pathological pancreatic imaging (endoscopic ultrasound, MRI, CT)
Absence of type 1 diabetes mellitus associated autoimmune markers
Minor criteria
Absent pancreatic polypeptide secretion
Impaired incretin secretion (*e.g.*, GLP-1)
No excessive insulin resistance (*e.g.*, HOMA-IR)
Impaired beta cell function (*e.g.*, HOMA-B, C-Peptide/glucose-ratio)
Low serum levels of lipid soluble vitamins (A, D, E and K)

MRI: Magnetic resonance imaging; CT: Computed tomography; GLP-1: Glucagon-like peptide-1; HOMA-IR: Homeostasis model assessment of insulin resistance; HOMA-B: Homeostasis model assessment of beta-cell.

Duggan *et al* (2017) suggest checking at least once:

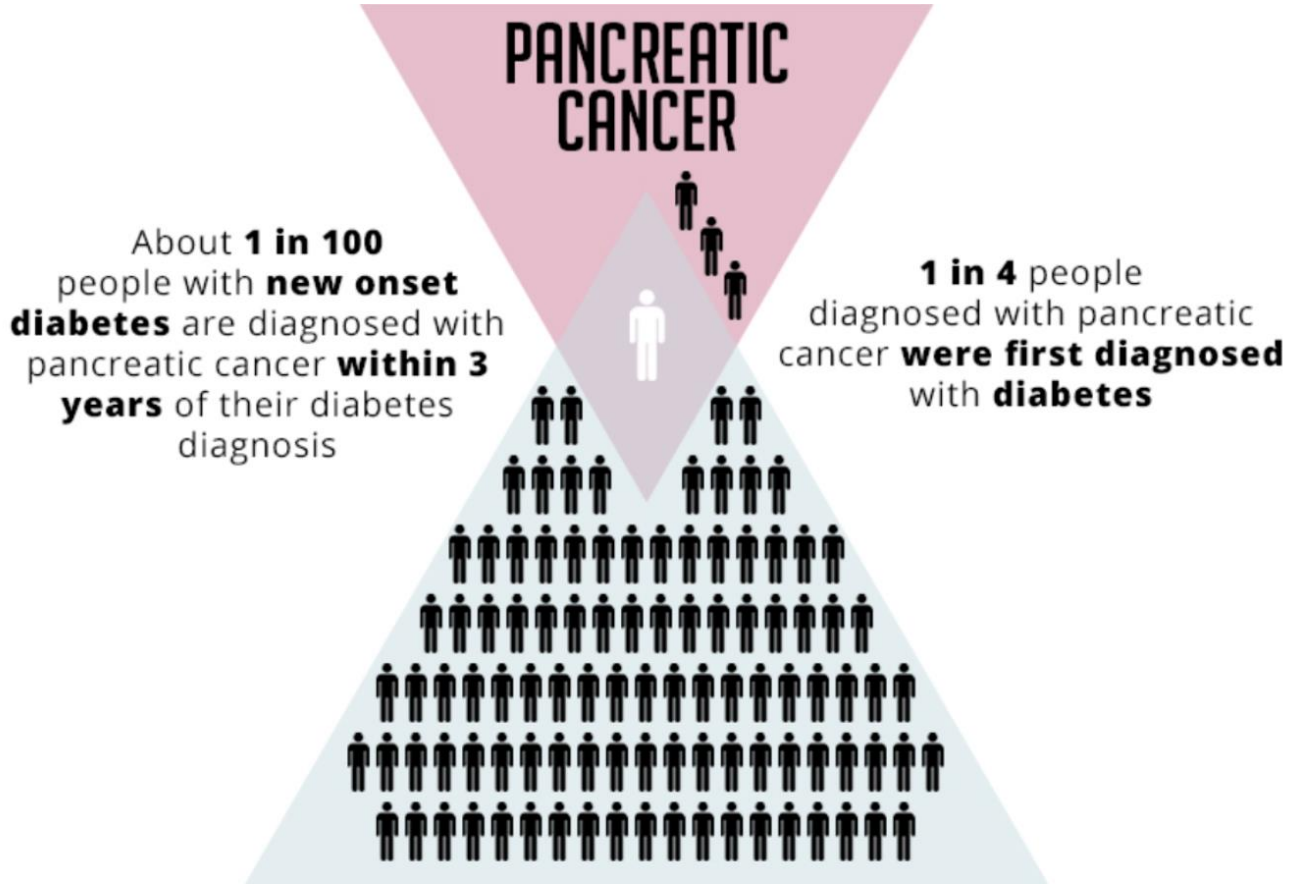
Diabetes autoantibodies

C-peptide:glucose ratio (measures beta cell function)

HOMA-IR (measures insulin resistance)

Pancreatic exocrine function and imaging

Diabetes and Pancreatic Cancer



NICE NG17 Guidance

For people aged 60 and over presenting with weight loss and new-onset diabetes, follow recommendations on assessing for pancreatic cancer in the section on pancreatic cancer in the NICE guideline on suspected cancer: recognition and referral. **[2022]**

National Cancer Institute