



Diagnosing Dyslipidaemia

AHSN NENC

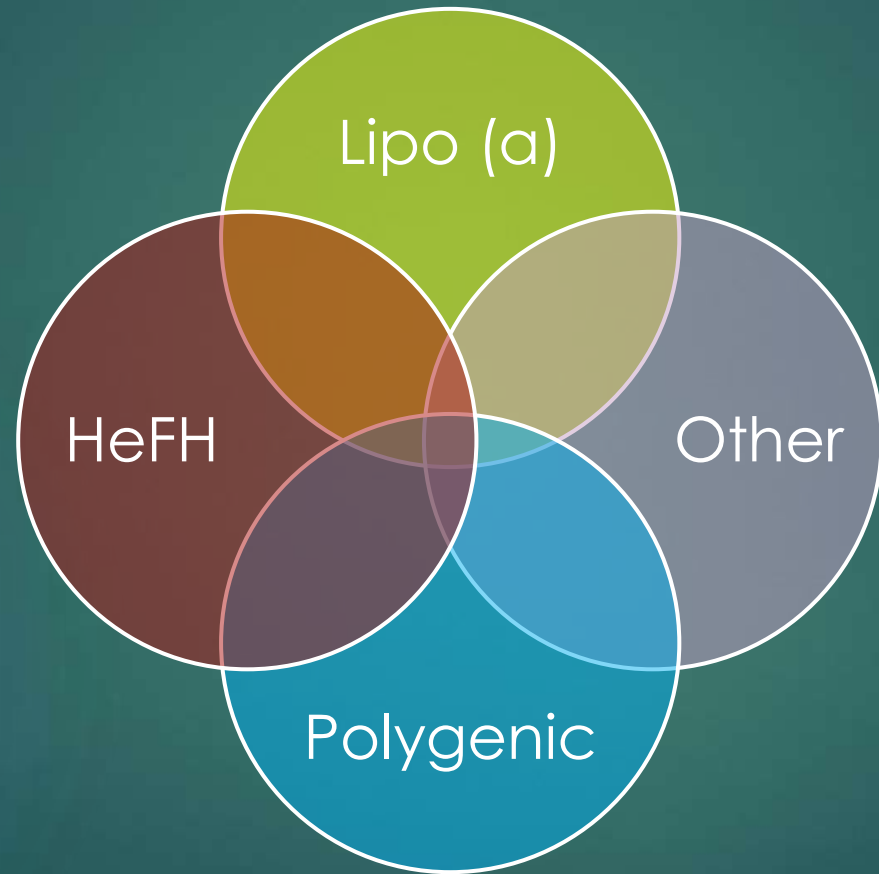
CVD Prevention Programme Launch Event

Wednesday 4th November 2020

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SOUTH TYNESIDE AND SUNDERLAND NHS FOUNDATION TRUST

It's not always as easy as you might think!



Case 1



A fairly typical referral.....

- ▶ 58 yr old woman – fit and well
- ▶ No family history of CVD
- ▶ Mother and sister both have hypercholesterolaemia
- ▶ Non fasted bloods
 - Total Chol = 7.4 HDL = 2.4
 - LDL = 4.5 TG = 1.1
 - HbA1c = 32 mmol/mol TSH = 1.13
- ▶ Q Risk score = 3.4%
- ▶ Does this patient need genetic testing for Familial Hypercholesterolaemia?
- ▶ Does this patient need to be on Lipid Lowering Therapy?

Simon Broome Criteria

	Criterion
1	Total cholesterol >7.5 mmol/L or LDL > 4.9 mmol/L in adults
2	Tendon xanthomata in patient, 1 st or 2 nd degree relative
3	Family history of premature MI (60 yrs in 1 st degree or 50 in 2 nd degree)
4	Family history of total cholesterol >7.5 mmol/L (1 st / 2 nd degree relative)

1 + 2 = Definite Familial Hypercholesterolaemia

1 + 3 or 4 = Possible Familial Hypercholesterolaemia

How High is High?

Cholesterol Centiles Calculator v0.01

NIHR | Newcastle In Vitro
Diagnostics Co-operative

Age
58

Non-HDL Cholesterol (mmol/L)
5.0

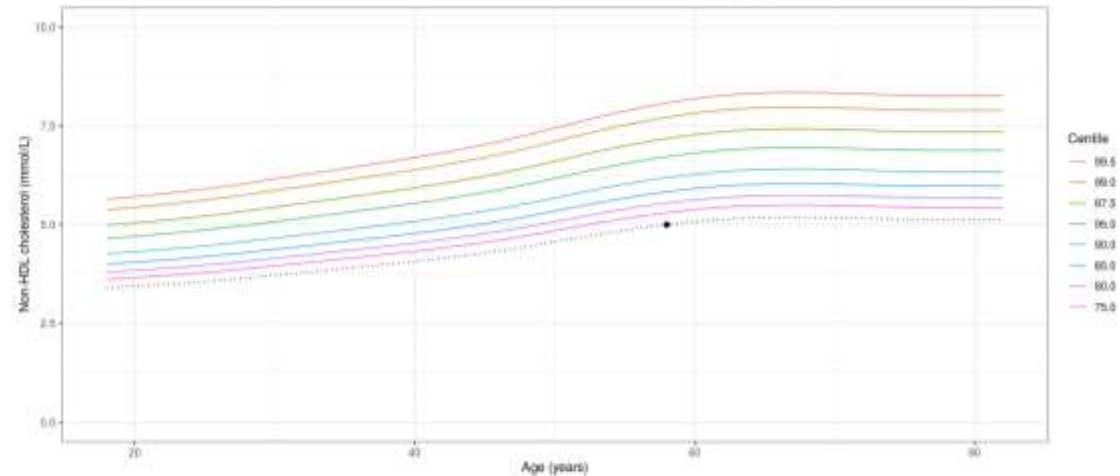
Total Cholesterol (mmol/L)
0

[Update Plot](#)

[Home](#) [Non-HDL Cholesterol](#) [Total Cholesterol](#)

[Male](#) [Female](#)

Centiles for non-HDL in the female population



Details entered
Sex: Female
Age: 58 years
Non-HDL: 5 mmol/L

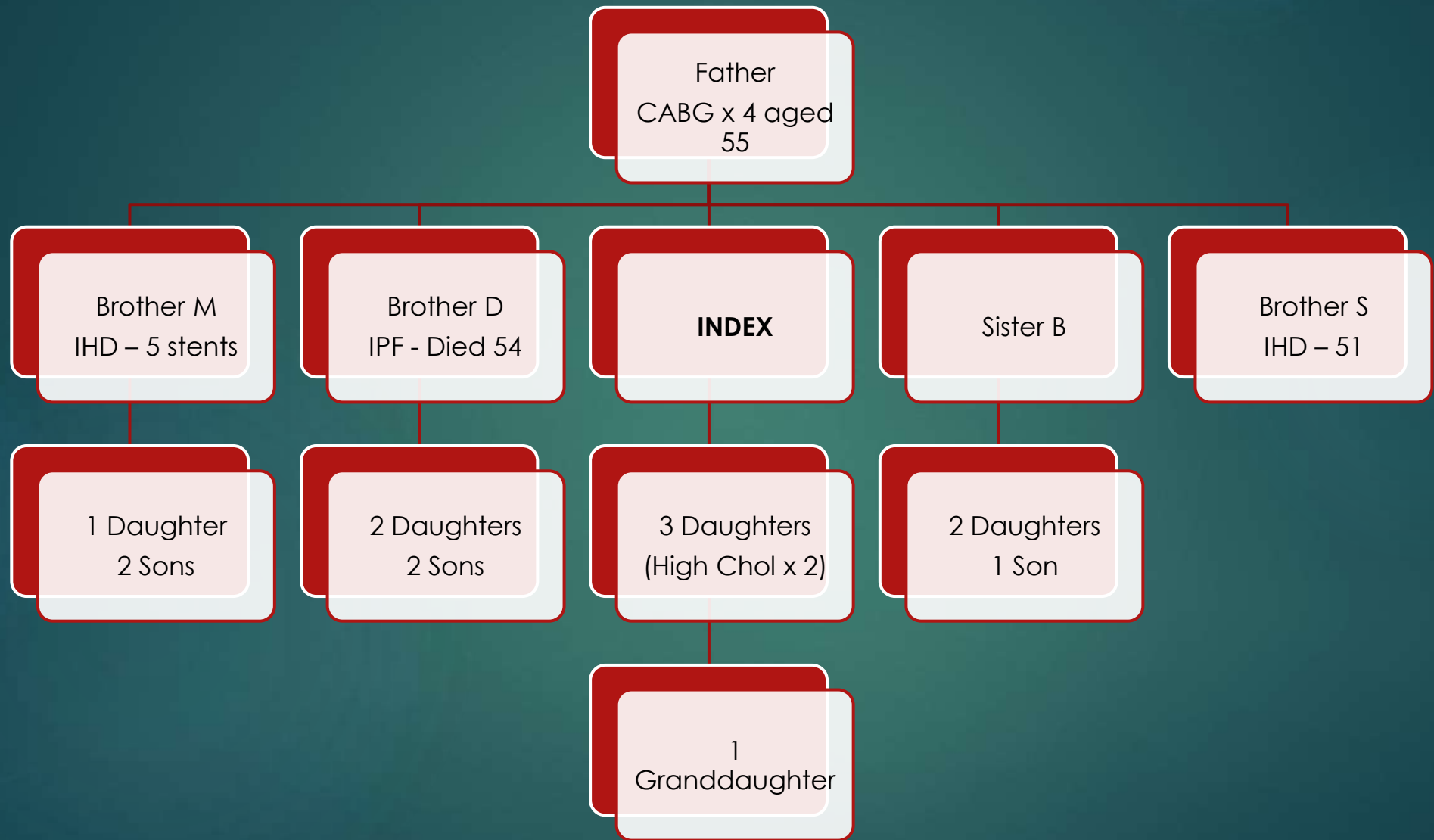
Based on the details entered, the patient is closest to centile 68.1.
This centile corresponds to a non-HDL of 5 mmol/L.

Case 2



Referral from Cardiology - ? For PCSK9i

- ▶ 54 yr old man
- ▶ Recent admission with NSTEMI
 - RCA PCI with insertion of 2 stents
- ▶ Previous ACS with PCI + stents FRH aged 48 yrs
- ▶ Suboptimal Lipid profile on Atorvastatin 80 mg + Ezetimibe 10 mg
 - Total Chol = 5.2 HDL = 1.2
 - LDL = 3.5 TG = 1.2
- ▶ Previous had cholesterol level in “double figures”
- ▶ Strong family history of premature IHD



Father
CABG x 4 aged
55

Brother M
IHD - 5 stents

Brother D
IPF - Died 54

INDEX

Sister B

Brother S
IHD - 51

1 Daughter
2 Sons

2 Daughters
2 Sons

3 Daughters
(High Chol x 2)

2 Daughters
1 Son

1
Granddaughter

Additional Information

- ▶ Non Smoker
- ▶ Previous Alcohol intake 10 units per week
- ▶ Previously cycling 20 miles 2-3 x a week
- ▶ Bilateral Achilles tendon Xanthoma
 - Massive Left TX
 - Large Right TX
- ▶ No Corneal Arcus or Xanthelasma
- ▶ Pre treatment lipid profile (via GP)
 - Total Chol = 12.1 - HDL = 1.31
 - LDL = 9.79 - TG = 2.2

Further Investigations

- ▶ Lipoprotein (a) = 78 nmol/L
- ▶ Apolipoprotein B100 = 0.98 g/L
 - Apo B : Total Chol = 0.213
 - Non HDL : Apo B = 3.27
- ▶ DLCNS = 17 (out of a maximum of 18)
- ▶ Negative SGT
- ▶ Polygenic SNPs = 1.098 (9th Decile)
- ▶ Automatic FGT
- ▶ LDLR ^ c.2061dupC p.(Asn688Glnfs*29)

Dutch Lipid Clinic Network Score - DLCNS

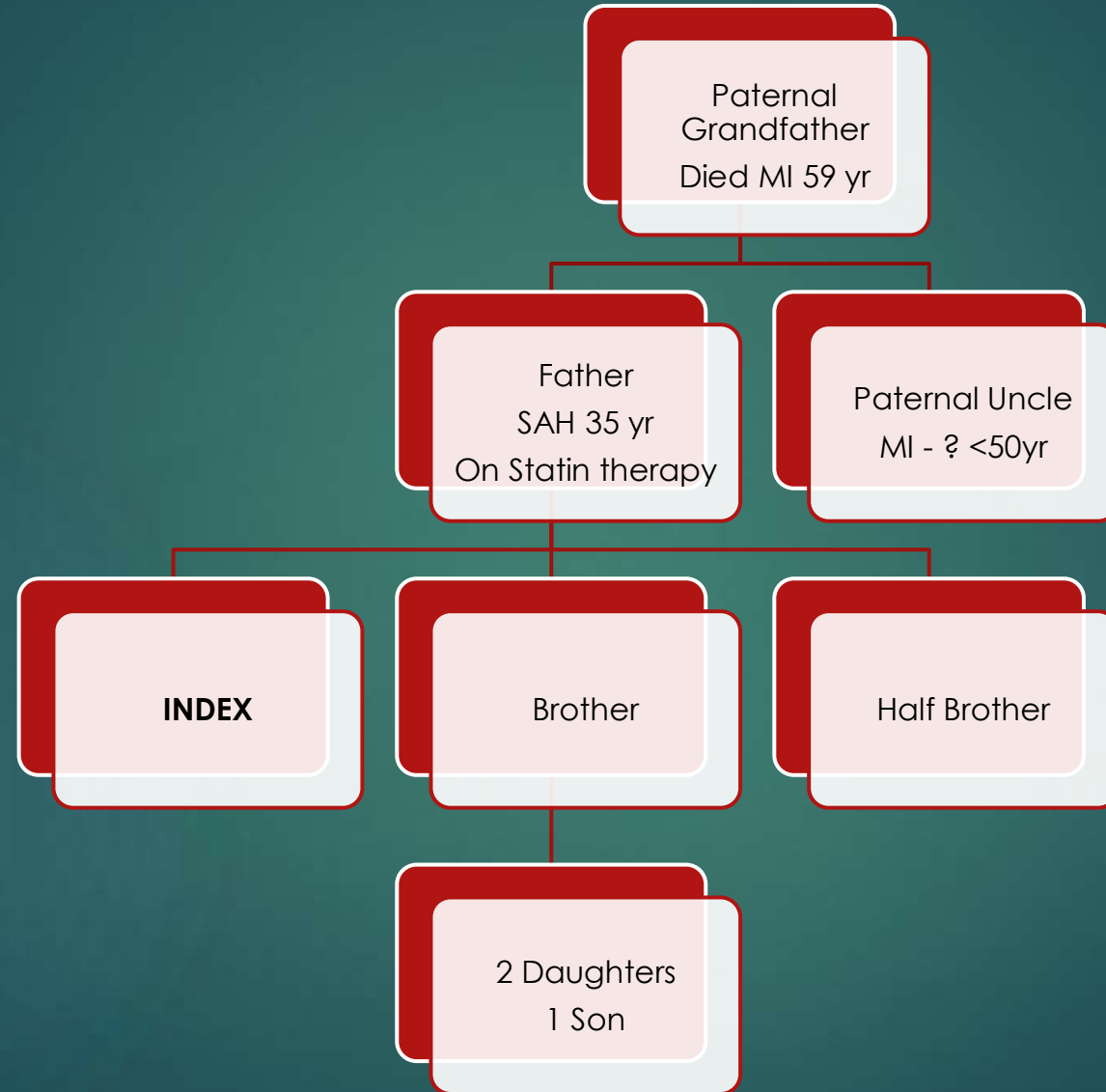
- ▶ 1. Family History
 - 1^o Relative with CHD / Premature CVD 1
 - 1^o Relative with untreated LDL-C >5.5 mmol/L 1
 - 1^o Relative with Xanthoma or Corneal Arcus 2
 - 1^o Relative <18 yr LDL-C > 3.9 mmol/L 2
- ▶ 2. Personal History
 - Premature CHD (♂ < 55 yr ; ♀ < 60 yr) 2
 - Premature CVD (PVD / CeVD) 1
- ▶ 3. Physical Examination
 - Tendon Xanthoma 6
 - Premature Corneal Arcus (< 45 yr) 4
- ▶ 4. Fasted untreated LDL-C (with TG <2.3 mmol/L)
 - >8.6 mmol/L 8
 - 6.5 – 8.5 mmol/L 5
 - 4.9 – 6.4 mmol/L 3
 - <4.9 mmol/L 1

Case 3



GP Referral

- ▶ 28 yr old woman referred in 2014
- ▶ Recently seen in TIA Clinic – diagnosed with Complex Migraine
- ▶ Initial non fasting bloods
 - Total Chol = 8.6
 - LDL = 6.4
 - Gluc = 5.6 mmol/L
 - HDL = 1.2
 - TG = 2.2
 - TSH = 1.79
- ▶ Rpt fasting bloods
 - Total Chol = 7.8
 - LDL = 6.1
 - HDL = 1.2
 - TG = 1.0
- ▶ Smoker – 12 cpd
- ▶ Alcohol every other weekend (>30 units)
- ▶ Diet suboptimal (fruit/veg/fish) but regular exercise
- ▶ Previously on COCP but now on POP



Additional Information

- ▶ No corneal arcus
- ▶ Some thickening of left Achilles tendon – no definite xanthoma
- ▶ Rpt Fasting bloods
 - Total Chol = 7.7
 - LDL = 6.0
 - Gluc = 4.5 mmol/L
 - HDL = 1.2
 - TG = 1.2
 - TSH = 1.07
- ▶ Non HDL = 5.5 mmol/L
- ▶ Lipo (a) = 670 mg/L
- ▶ Apo B 100 = 1.7 g/L
- ▶ DLCNS = 4

High Index of suspicion

Age
28

Non-HDL Cholesterol (mmol/L)
6.5

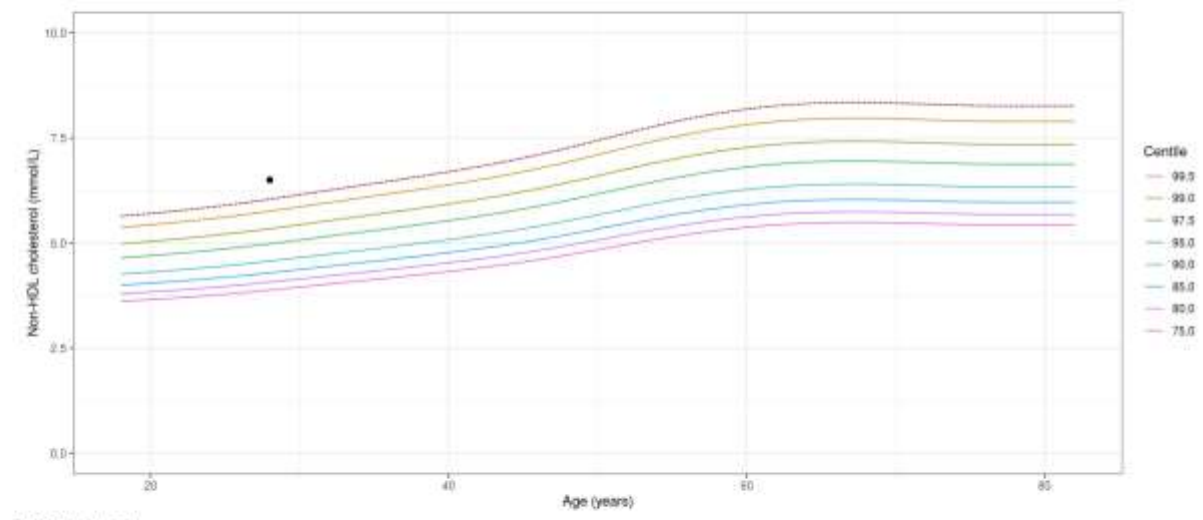
Total Cholesterol (mmol/L)
0

Update Plot

Home **Non-HDL Cholesterol** Total Cholesterol

Male Female

Centiles for non-HDL in the female population



Details entered
Sex: **Female**
Age: 28 years
Non-HDL: 6.5 mmol/L

Based on the details entered, **the patient is closest to centile 99.5.**
This centile corresponds to a non-HDL of 6.04 mmol/L.

Sutton's Law

- ▶ Wrote to Paternal Uncle to request permission to review medical records
- ▶ Paper records destroyed March 2014; able to access electronic records
- ▶ Previous Cholesterol = 8.0 mmol/L 1996 (aged 37 yrs)
- ▶ Bloods 1997
 - Chol = 7.6 mmol/L TG = 2.81 mmol/L
- ▶ Acute MI aged 44 yr
 - Chol = 7.2 mmol/L
- ▶ Rpt Bloods off therapy
 - Total Chol = 6.9 - HDL = 0.8
 - LDL = 5.0 - TG = 2.5
- ▶ Lipo (a) = 207 nmol/L
- ▶ DLCNS = 6 (if you ignore the TG – worth a punt!)
- ▶ LDLR c.1897C>T p.(Arg633Cys)

Lipoprotein (a)

- ▶ Modified form of LDL
- ▶ Highly atherogenic
- ▶ Major independent risk factor for CVD and AoS
 - > 90 nmol/L = increased risk
 - > 200 nmol/L = high risk
 - > 400 nmol/L = very high risk
- ▶ Highly inheritable
- ▶ Structurally similar to plasminogen – ?
prothrombotic effect
- ▶ No specific therapy currently
- ▶ Address modifiable risk factors

Case 4



Information from SystmOne

- ▶ 64 yr old male
- ▶ IHD – MI aged 49 yr; further MI 50 yr; impaired LVF
- ▶ PVD aged 52 yr
- ▶ No Lipid results pre statin therapy
- ▶ On Simvastatin 40 mg (2004 - 49yrs)
 - Total Chol = 6.4 HDL = 0.96
 - LDL = 4.5 TG = 1.99
- ▶ On Simvastatin 80mg (2012 – aged 56yrs)
 - Total Chol = 7.2 HDL = 1.1
 - LDL = 5.2 TG = 2.05
- ▶ Current smoker
- ▶ “Sister passed away from heart attack”

Attended FH Nurse Clinic at GP Surgery

- ▶ Provisional DLCNS = 5
- ▶ Bilateral superior corneal arcus - ? Present for how long?
- ▶ No Tendon Xanthoma
- ▶ No family history of premature CVD – Simon Broome negative

- ▶ Sample sent due to high index of suspicion – patient consented
- ▶ SGT Positive – c.10580 G>A p.(Arg3527Gln)
- ▶ Lipo (a) = 124 nmol/L

- ▶ Referred to Consultant Lipidologist Feb 2020

Case 5



GP Query through Advice and Guidance

- ▶ 39 yr old Fireman – fit and well
- ▶ Mixed dyslipidaemia on non fasted bloods
 - Total Chol = 8.7 HDL = 1.2
 - LDL = 3.9 TG = 3.9
- ▶ TSH = 1.56; HbA1c = 36 mmol/mol
- ▶ Father known to have hypercholesterolaemia
- ▶ Paternal Grandfather had MI aged 59 - died in his 80s
- ▶ Mother – fit and well
- ▶ 1 sister and 1 daughter
- ▶ Could this be FH?

Things to consider

- ▶ Tendency towards Mixed Dyslipidaemia
 - ? Due to non fasted sample?
 - Secondary causes ? Diabetes
 - ? Thyroid
 - ? Alcohol
 - ? Medications
- ▶ Family history of IHD
 - Not in 1st degree relative <60 yr or 2nd degree relative <50 yr
 - ? Lipoprotein (a)
- ▶ Family history of Hypercholesterolaemia
 - Male; common to be on statin
 - Female; common > 50 yrs
- ▶ Need to get more information

Further Investigations

- ▶ GP repeat fasted bloods
 - Total Chol = 7.9 HDL = 1.1
 - LDL = 5.4 TG = 3.1
 - Apo B100 = 0.72
 - Apo B : Total Chol = 0.09 Non HDL : Apo B100 = 9.44
 - Lipo (a) = <20 nmol/L
- ▶ Beta Quant consistent with Remnant (Type III) Hyperlipidaemia
- ▶ VLDL Cholesterol : TG ratio = 0.95
- ▶ Apo E isotyping confirmed that Homozygous for Apo E2

Familial Dysbetalipoproteinaemia

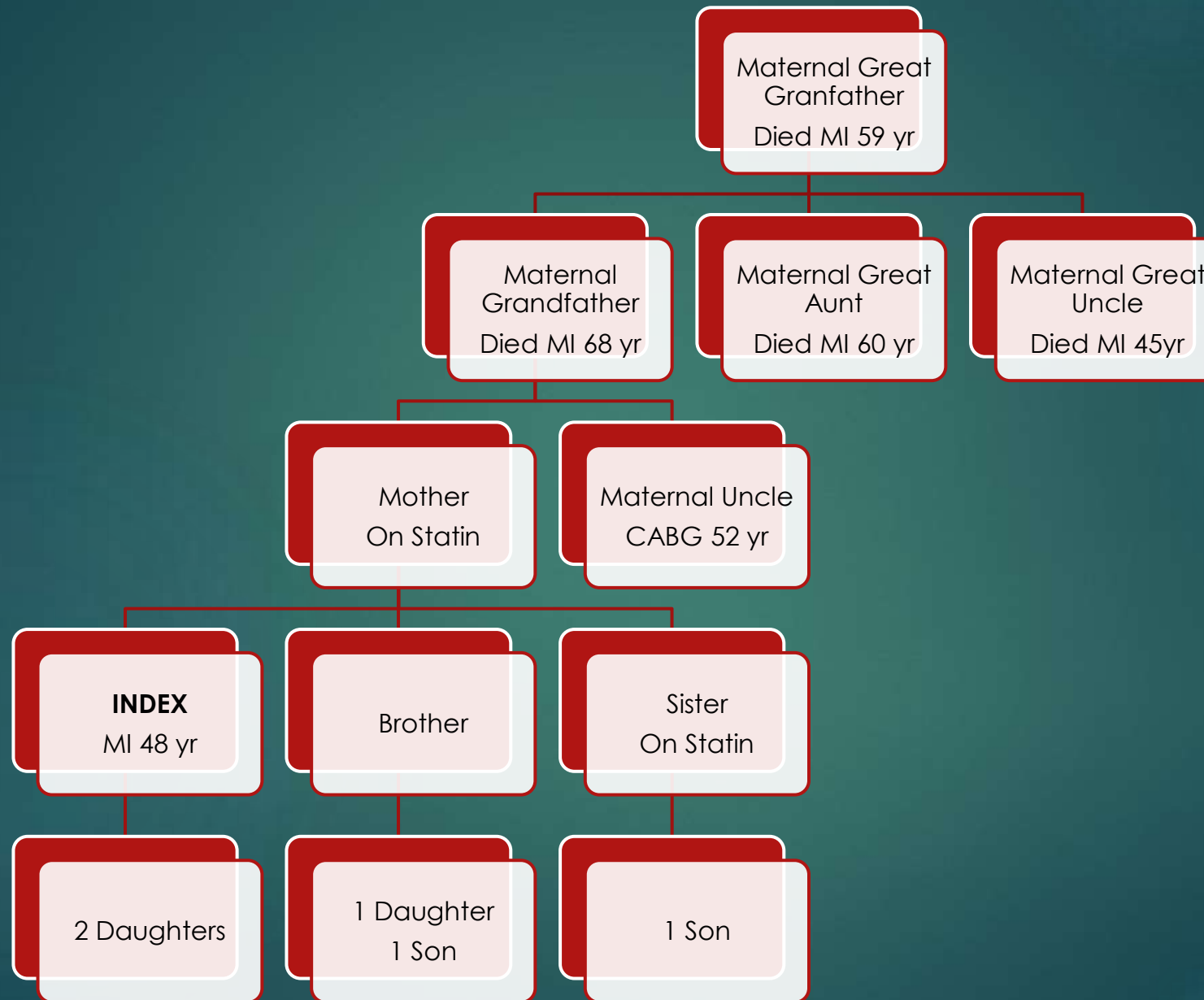
- ▶ Type III, Remnant Dyslipidaemia or Broad Beta Disease
- ▶ ApoB100 : Total Chol < 0.15
NonHDL : ApoB100 >5
- ▶ Autosomal Recessive – E2/E2 Isoform
Rare Autosomal Dominant Forms
- ▶ Reduced clearance of remnant IDL leads to increased atherosclerosis causing IHD and PVD
- ▶ Characteristic feature of yellowish xanthoma striata palmaris
- ▶ Xanthoma may also form at elbows, knees, knuckles, arms legs, buttocks and in Achilles tendon

Case 6



Cardiac Optimization MDT

- ▶ 49 yr old man; ex-smoker (10 cpd for ~ 20 years)
- ▶ Non STEMI Jan 2020 aged 48 yrs
- ▶ Admission bloods
 - Total Chol = 7.0
 - LDL-C = 4.9
 - HDL- C = 1.2
 - TG = 2.0
- ▶ Commenced on Atorvastatin 80 mg OD
- ▶ Documentation noted family history of IHD – no further details
- ▶ Plan
 - Repeat Lipid profile and make sure optimized
 - Check Lipo (a) given history of premature CVD
 - Need to review family history - ? FH



“I have a letter from my mother.....”

- ▶ Referred to Lipid Clinic in 2014 – aged 66yr
- ▶ Previous Cholesterol = 8.9 mmol/L in 2001 (aged 54 yr)
- ▶ DLCNS = 10
- ▶ FH Genetic testing Nov 2015
- ▶ Negative SGT / FGT / MLPA
- ▶ Polygenic SNP = 1.128 (9th Decile)
- ▶ Lipoprotein (a) = 2145 mg/L / 398 nmol/L
 - rs10455872 positive
- ▶ Son with Lipo (a) = 285 nmol/L
- ▶ Family members to be screened for Lipo(a) via Lipid Clinic

Take Home Messages

- ▶ Lots of patients fulfill Simon Broome – not all will have FH mutation
- ▶ Those likely to be eligible for FH genetic testing
 - Personal history of premature MI
 - LDL > 6.5 mmol/L
- ▶ Identify relatives who may be index eligible for genetic testing
- ▶ Index of suspicion
 - NICE criteria
 - Chol > 7.5 mmol/L < 30 yrs
 - Chol > 9.0 mmol/L > 30 yrs
 - Non HDL centile
 - Strong family history of IHD with normal Lipo (a)
- ▶ Be aware of aggregation factors
- ▶ Sometimes hunches pay off
- ▶ Check Apo B 100 with fasted lipid profile if mixed dyslipidaemia prior to commencing therapy

Any Questions?

