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Developing General Practice and Web-Based Toolkits for the Familial Hypercholesterolaemia (FH) Case Ascertainment Tool (FAMCAT)

Dr Stephen Weng
NIHR Research Fellow
NIHR School for Primary Care Research
University of Nottingham

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The National Institute for Health Research School for Primary Care Research (NIHR SPCR) is a partnership between the Universities of Bristol, Cambridge, Keele, Manchester, Newcastle, Nottingham, Oxford, Southampton and University College London.

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What is FH?

- Inherited autosomal dominant disease (*PCSK9, APOB, LDLR*)
- Low density lipoprotein (LDL) cholesterol in higher than normal from birth
- No cure but there is effective management and treatment

Substantial increase in premature CHD risk

How common is FH?

- Frequency from 1/500 to 1/200
- Similar frequency to juvenile onset diabetes

120,000 to 320,000 affected in the UK

How is FH treated?

- Referral to specialist secondary care services
- High intensity statins
- Lifestyle modification

50% reduction in LDL-C & 37% reduction in CHD mortality

FH – natural history

Age (years)	♂ % CHD	♀ % CHD
<30	5	0
30-39	22	2
40-49	48	7
50-59	80	51
60-69	100	75

Slack J. Risks of ischaemic heart-disease in familial hyperlipoproteinaemic states. *The Lancet* 1969; **294**(7635): 1380-2.

NICE National Institute for Health and Care Excellence

Identification and management of familial hypercholesterolaemia

Issued: August 2008

NICE clinical guideline 71
guidance.nice.org.uk/cg71

Dx for possible FH:

- Total cholesterol > 7.5 mmol/L (LDL-C 4.9 mmol/L) **& at least one of the following:**

- **Family history of myocardial infarction** < 50 years in second-degree relative OR < 60 years in first-degree relative

OR

- **Family history of raised total cholesterol > 7.5 mmol/L** (LDL-C 4.9 mmol/L) in adult first or second- degree relative OR > 6.7 mmol/L in child, brother or sister aged < 16 years

Familial Hypercholesterolaemia Case Ascertainment Tool

- Clinical Practice Research Datalink (CPRD) – 2.9 million patients with cholesterol recorded (including 5050 confirmed FH cases)
- Developed risk Prediction Algorithm determines probability a patient has FH
- Nine diagnostic indicators (including cholesterol, family history, secondary causes, age, gender, triglycerides, statins prescribing)

MODEL COMPARISONS	AUC c-statistic (95% Confidence Interval)
Primary Analysis	
Model 1: TC > 7.5 mmol/L or LDL cholesterol > 4.9 mmol/L	0.556 (0.527 – 0.587)
[1]Model 2: NICE/Simon-Broome Criteria	0.749 (0.735 – 0.763)
[2]Model 3: Dutch Lipid Clinic Criteria	0.737 (0.723 – 0.752)
Model 4: FAMCAT	0.860 (0.848 – 0.871)

Weng SF, Kai J, Andrew Neil H, Humphries SE, Qureshi N. Improving identification of familial hypercholesterolaemia in primary care: Derivation and validation of the familial hypercholesterolaemia case ascertainment tool (FAMCAT). *Atherosclerosis* 2015; 238(2): 336-43.

Translation of FAMCAT to UK General Practice: *FH Case-Finder*

Requirements:

- Direct extraction of General Practice patient data based on NHS Read Codes/SNOMED CT
- Algorithm ranking of probability of FH from most probable to least probable
- Mail-merge from patient level data
- Auditing feature for feedback to GPs on patients assessed and screened
- Display family history recording
- Display prescribing of statins

CHART Summary Sheet

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FHC CASEFINDER LIBRARY

Practice Population	5330
Of whom are aged 16 to 120	4630
Of whom have had a cholesterol recording at any time	1269

BREAK DOWN OF ABOVE PATIENTS INTO RISK GROUPS	Diagnosed	Very High Risk	High Risk	Population Risk
	2	11	97	1159
Of whom were diagnosed in last 12 months	0			
Of whom have been screened in last 12 months	0	0	0	0
Of whom have not been screened in last 12 months	2	11	97	1159

PATIENTS SCREENED IN LAST 12 MONTHS	Diagnosed	Very High Risk	High Risk	Population Risk
Number of patients screened/assessed/in last 12 months	0	0	0	0
Screening Methods				
Of whom were assessed by Dutch Criteria in last 12 months	0	0	0	0
Of whom were assessed by Simon Broome in last 12 months	0	0	0	0
Of whom had Hyperlipidaemia screen in last 12 months	0	0	0	0
Referred to Specialist or Consultant				
Of whom were referred to a Specialist/Consultant in last 12 months	0	0	0	0

FAMILY HISTORY CODES - Recorded since July 2016	Diagnosed	Very High Risk	High Risk	Population Risk
All patients	2	11	97	1159
Of whom have a Negative Family History	0	0	0	0
Of whom have a Positive Family History	0	0	0	0
Of whom have a Unknown Family History	2	11	97	1159
Of whom have a Contradictory Family History	0	0	0	0

LIPID LOWERING DRUGS IN LAST 6 MONTHS	Diagnosed	Very High Risk	High Risk	Population Risk
All patients	2	11	97	1159
Of whom have a contraindication to statins	0	0	0	2
Of whom are on high potency statins	0	0	0	0
Of whom are on medium potency statins	0	0	0	0
Of whom are on low potency statins	0	0	0	0
Of whom are on another lipid lowering drug	0	0	0	0
Of whom have no statin contraindication and are not on any of the above	2	11	97	1157

Patient Level Data: *Named (Identifiable version at practice); Pseudo-anonymised for researchers/CCGs*

MIQUEST response file FHCRREPA.CSV was created on 28/06/16 using Refdate 31/08/16

FHC_CASEFINDER FHCRREPA: FHC Risk Score - Pseudonymised

Reference	Age	Sx	Registered_Date	Latest TC Ever Code	Latest TC Ever Date	Latest TC Ever Value1	Latest LDL Ever Code	Latest LDL Ever Date	Latest LDL Ever Value1	Item to use	Latest High Potency LLD with a TC in 3M after Date	Latest Med Potency LLD with a TC in 3M after Date	Latest Low Potency LLD with a TC in 3M after Date	Latest Other LLD with a TC in 3M after Date	Latest High Potency LLD with a LDL in 3M after Date	Latest Med Potency LLD with a LDL in 3M after Date	Latest Low Potency LLD with a LDL in 3M after Date	Latest Other LLD with a LDL in 3M after Date	Latest Family History of FH Code	Latest Family History of FH Date	Latest Family History of MI Code	Latest Family History of MI Date	Latest Family History of Raised Cholesterol Code	Latest Family History of Raised Cholesterol Date	RELATIVE RISK	Risk Category	Latest FHC Diagnosis Code	Latest FHC Diagnosis Date
00QR	33	F	06/06/11	44P..	17/11/10	8.84				TC	12/09/10														94.42266	Very High Risk		
01DC	65	F	17/10/94	44P..	24/08/11	8.58				TC	21/08/11										12C5.	21/10/91			46.14808	Very High Risk		
00hM	67	F	23/07/05	44P..		7.79				TC															27.19165	Very High Risk		
01L5	55	M	16/03/09	44P..	02/04/11	8.46				TC	09/01/11			13/03/09											25.02609	Diagnosed	C3200	10/04
01HG	73	F	16/03/09	44P..	22/08/11	8.01				TC	21/08/11	20/03/10									12C3.	28/03/99			23.42786	Very High Risk		
01YA	54	F	16/03/09	44P..	28/04/11	8.15				TC	28/04/11														22.89522	Very High Risk		
026h	56	F	06/06/11	44P..	24/08/11	7.18				TC	22/07/11										12C2.	05/03/99			12.69222	Very High Risk		
00uP	67	M	16/03/09	44P..	26/01/11	7.97				TC		19/01/11													9.602442	Very High Risk		
01Lv	48	F	16/03/09	44P..	20/06/11	7.61				TC															8.004763	Very High Risk		
01Ux	52	F	16/03/09	44P..	27/03/11	7.57				TC															6.580149	Very High Risk		
01hS	65	F	16/03/09	44P..	02/02/11	7.64				TC											12C2.	08/02/99			6.215609	Very High Risk		
015U	53	F	17/09/09	44P..	14/06/10	7.71				TC															6.050047	Very High Risk		
zzsd	35	M	25/08/10	44P..	12/11/08	7.99				TC															5.924334	High Risk		
01QB	49	F	16/03/09	44P..	14/08/11	7.92				TC															5.72631	High Risk		
018L	58	F	23/08/09	44P..		6.57				TC															5.233504	High Risk		
026n	70	F	06/06/11	44P..	30/06/11	7.66				TC											12C2.	15/05/00			5.038383	High Risk		
zzob	71	F	19/04/11	44P..	25/04/11	7.54				TC											12C5.	22/04/11			4.797475	High Risk		
028D	61	F	06/06/11	44P..	23/08/09	6.65	44PD.	23/08/09	4.95	LDL															4.569691	High Risk		
zzun	80	F	06/06/10	44P..	22/02/11	6.88				TC	21/02/11										12C5.	22/05/10			4.47317	High Risk		

Pilot Data Extraction from Four General Practices

Practice	Total Patients	Adults > 16 years	Adults > 16 years & TC/LDL Recorded	High Probability FH
1 (East Midlands)	8,499	6,587	3,009	154
2 (East Midlands)	5,965	4,829	2,268	113
3 (East Midlands)	12,885	10,710	6,222	237
4 (North London)	6,581	5,526	3,082	271
Total	33,930	27,652	14,581	775

Proportion of GP Population Requires Assessment: 775/33,930 = 2.3%

Ranking system in tool will prioritise patients with highest probability of FH

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In Development: Mobile Application

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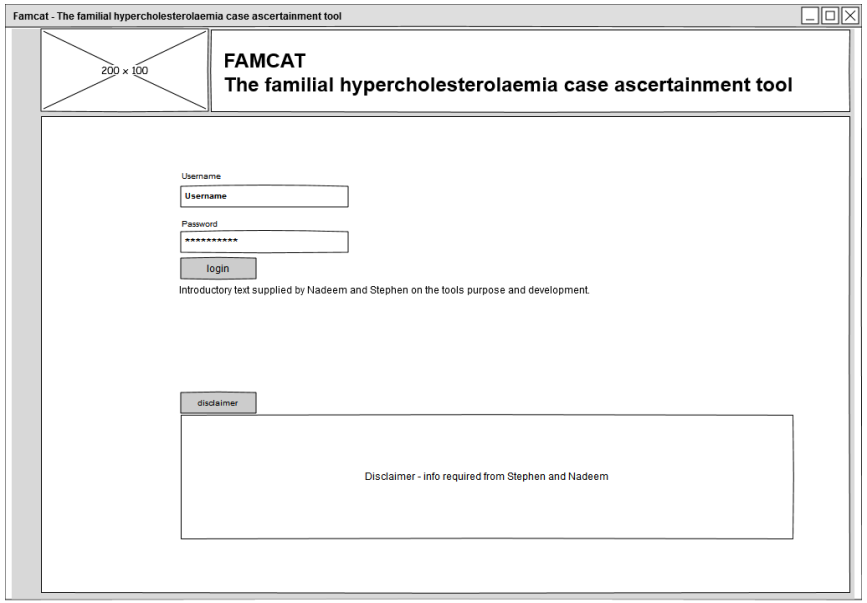

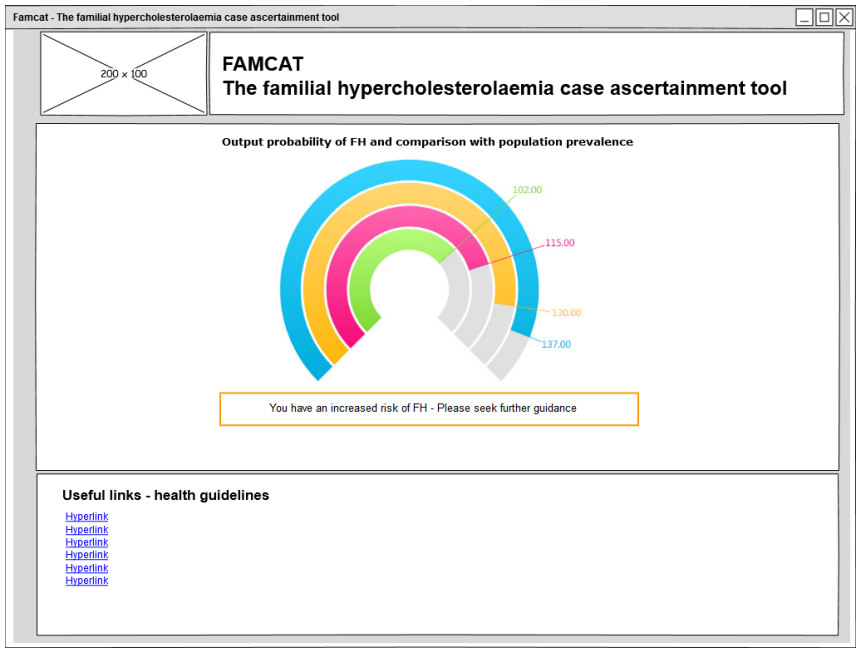

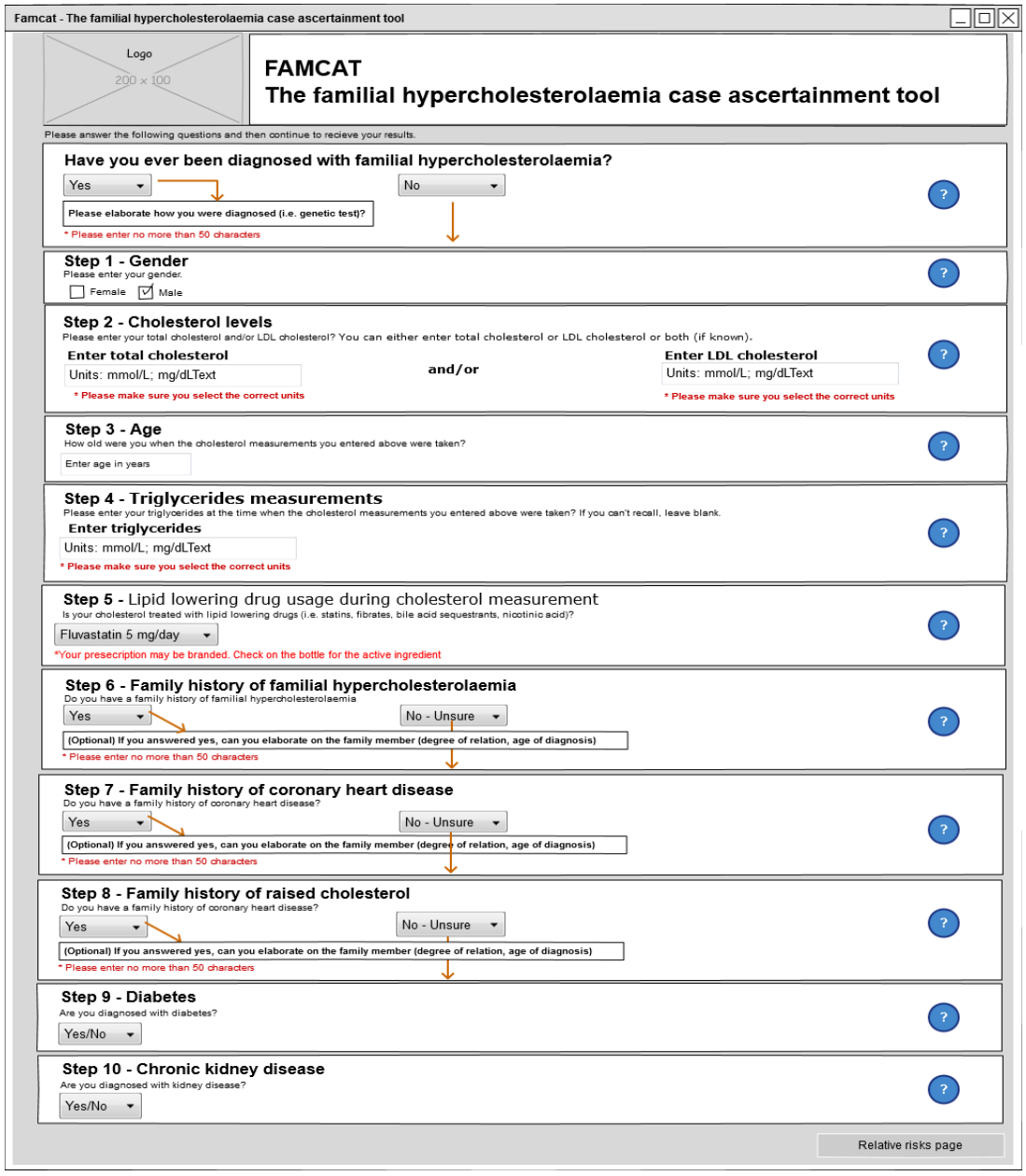

To Summarise:

- Shown that FAMCAT can accurate predict FH better than previous diagnostic criteria
- Developed an implementation to practice pathway and toolkit for general practice
- Developed web-based tool for non-UK audiences
- Successfully extracted data using the toolkit in four practices (3 East Midlands, 1 North London)

Going Forward:

- Assess the clinical utility of the FAMCAT prospectively in multi-centre study
- Assess diagnostic accuracy using a gold standard genetic diagnosis: next generation sequencing
- Full trial against usual care: cluster RCT design
- Full economic evaluation of FAMCAT to determine cost-effectiveness

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Interested in FH? Contact FAMCAT Study Team

stephen.weng@nottingham.ac.uk

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