

Do reflex comments on laboratory reports alter patient management?

| | |
|---------------|--|
| Item Type | Journal article |
| Authors | Wilkinson, B;Whitehead, SJ;George, E;Horton, S;Bellaby, J;Mohamed, S;Ford, C;Min, SS;Gama, R |
| Citation | Wilkinson, B., Whitehead, S.J., George, E. et al. (2020) Do reflex comments on laboratory reports alter patient management? Annals of Clinical Biochemistry, 57(4), pp. 312-315. |
| DOI | 10.1177/0004563220928355 |
| Publisher | SAGE Publications |
| Journal | Annals of Clinical Biochemistry |
| Download date | 2026-04-15 17:15:24 |
| License | https://creativecommons.org/licenses/by-nc-nd/4.0/ |
| Link to Item | http://hdl.handle.net/2436/623442 |

1
2
3 Do reflex comments on laboratory reports alter patient management?
4
5

6 Ben Wilkinson¹, Simon J Whitehead¹, Elaine George², Sally Horton², Judith
7 Bellaby², Sagal Mohamed², Clare Ford¹, San San Min¹, Rousseau Gama^{1,3}
8
9

10
11
12
13
14 ¹Blood Sciences, Black Country Pathology Services, The Royal Wolverhampton
15 NHS Trust, Wolverhampton, UK, ² West Midlands Familial
16 Hypercholesterolaemia Service , University Hospitals Birmingham NHS
17 Foundation Trust, Birmingham, UK and ³ School of Medicine and Clinical Practice,
18 Wolverhampton University, Wolverhampton, UK.
19
20
21
22
23
24
25
26

27 **Corresponding author:** Rousseau Gama
28 Black Country Pathology Services
29 The Royal Wolverhampton NHS Trust
30 Wolverhampton, WV10 0QP. UK
31 Email: rousseau.gama@nhs.net
32
33
34
35

36 **Keywords:** Reflex comments, interpretative comments, familial
37 hypercholesterolaemia
38
39

40 **DECLARATIONS**
41

42
43 **Conflicts of interests:** None
44

45
46 **Funding:** This project received no grant from any funding agency in the public,
47 commercial or not-for-profit sectors. The authors received no financial support
48 for the authorship and/or publication of this article.
49

50
51 **Ethical approval:** Service evaluation and therefore ethical approval not
52 required.
53
54

55 **Guarantor:** RG
56

57
58 **Contributorship:** BW researched the literature and wrote the first draft. EG
59 and RG conceived the idea of writing a report. All contributed data, critically
60

1
2
3 reviewed the manuscript and approved the final version of the manuscript. RG is
4 guarantor.
5
6

7 **Acknowledgements:** None
8
9

10 **Abstract**

11 **Introduction**

12
13
14
15
16
17
18 Laboratory comments appended on clinical biochemistry reports are common in
19 the UK. Although popular with clinicians and the public there is little evidence
20 that these comments influence the clinical management of patients.
21
22
23
24
25
26
27
28

29 **Methods**

30
31
32 We provided reflex automated laboratory comments on all primary care lipid
33 results including, if appropriate, recommendation of direct referral to the West
34 Midlands Familial Hypercholesterolaemia service (WMFHS). Over a two year
35 period, the number GP referrals from the Wolverhampton City Clinical
36 Commissioning Group (CCG) to the WMFHS were compared to four comparator
37 CCGs of similar population size, who were not provided with reflex laboratory
38 comments.
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54

55 **Results**

56
57
58
59
60

1
2
3 Over the study period, the WMFHS received more referrals from
4
5
6 Wolverhampton GPs (241) than any other comparator CCG (range 8-65) and
7
8
9 greater than the combined referrals (172) from all four comparator CCGs
10
11
12
13

14 **Conclusion**

15
16
17 Targeted reflex laboratory comments may influence the clinical management of
18
19
20 patients and may have a role in the identification of individuals with Familial
21
22
23 Hypercholesterolaemia.
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Introduction

Familial hypercholesterolaemia (FH), a disorder of lipoprotein metabolism characterised by raised circulating concentrations of LDL cholesterol, carries an increased risk of premature atherosclerotic cardiovascular disease (CVD).¹⁻³ Early detection and treatment of FH is important since lipid-lowering therapy is highly effective and gives the same life expectancy as the general population.⁴ Subsequent cascade testing to identify relatives of people with FH is also highly cost-effective. ⁴ People with FH, however, are commonly undiagnosed and are therefore untreated. ⁴

In March 2017, the West Midlands Regional Familial Hypercholesterolaemia Service (WMFHS), the first region wide screening service in the England, was launched with extensive primary care promotion by the WMFHS of the service similarly across all clinical commissioning groups (CCGs) within the West Midlands. From December 2017, we provided automated rule-based comments on all general practitioner (GP) lipid results specific for primary or secondary CVD prevention based on National Institute for Health and Care Excellence (NICE) clinical guidance (CG); NICE CG071 and NICE CG181 ^{5,6} and the WMFHS guidelines. These comments included, if appropriate, recommendations for direct GP referral to WMFHS service.

1
2
3 The addition of comments onto clinical biochemistry reports is widespread in
4
5
6 the UK, but there is scant evidence that they influence the patient
7
8
9 management.^{7,8} We, therefore, evaluated the impact of reflex comments,
10
11
12 based on lipid results, recommending direct GP referral to the WMFHS.
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Methods

Patients and Methods

Requesting and reporting of pathology tests by GPs, using our pathology services, is almost exclusively electronic. The electronic requesting of lipids requires the requester to complete two drop down boxes to determine if fasting or non-fasting and primary or secondary CVD prevention.

Serum cholesterol, HDL cholesterol and triglycerides were measured using methods and reagents supplied by Abbott diagnostics on the Abbott ARCHITECT c16000 analyser (Abbott Diagnostics, Abbott Park, IL, USA). The Friedewald equation was used to automatically calculate LDL-cholesterol in fasting serum samples when triglycerides levels were less than 4.5 mmol/L.⁹

Lipid comments were then appended on all primary care lipid results, including those recommending referral to WMFHS (Table 1). GPs following these recommendations then complete and email a referral FH proforma to the WMFHS. The referrals are reviewed by WMFHS specialist FH nurses, who assess eligibility for genetic testing largely based on the Welsh criteria.¹⁰ Eligible patients are invited to attend the WMFHS and are seen within their

1
2
3 respective primary care CCG. Patients undergo full assessment and FH genetic
4
5
6 analysis if indicated. Patients with a FH mutation are counselled and provided
7
8
9 information on FH and then referred directly into the local lipid clinic for
10
11
12 further management and follow-up. Cascade screening is undertaken by the
13
14
15 WMFHS. Patients without FH are counselled and discharged back to their GP
16
17
18 with advice to manage according to NICE CG181. ⁶ However patients with a
19
20
21 polygenic aetiology and high CVD risk/family history may also be directly
22
23
24 referred to a local lipid clinic for assessment.
25
26
27

28 **Data collection**

29
30
31 Data from 01/11/2017 to 31/10/2019 were collected from the WMFHS
32
33
34 database on referrals to the WMFHS from GP practices in the Wolverhampton
35
36
37 Clinical Commissioning Group (CCG) and from four comparator CCGs serving a
38
39
40 similar size population. The GPs from the comparator CCGs were not provided
41
42
43 with automated laboratory based reflex comments on lipid results.
44
45
46
47

48 Patients referred by Wolverhampton GPs were then identified and the receipt,
49
50
51 by the GP, of comments recommending referral to WMFHS was confirmed.
52
53
54
55
56
57
58
59
60

Results

The WMFHS received more referrals from Wolverhampton GPs than any other comparator CCG and greater than the combined primary care referrals from all four comparator CCGs (Table 2).

Wolverhampton GP referral to the WMFHS was preceded by laboratory reported reflex comments in all 241 patients. Of those referred, 27 failed to respond to several invitations to attend the WMFHS, five were new referrals waiting processing, 108 were ineligible for genotyping and nine are awaiting DNA results. Nineteen monogenetic mutations were identified in the remaining 92 patients who were genotyped.

Discussion

1
2
3
4
5
6
7 Although reflective and reflex comments on laboratory reports are widespread
8
9 7,8 and generally appreciated by clinicians and the public, 11-13 evidence for their
10
11 effectiveness is limited. 7,8 Reflective testing is a process whereby a laboratory
12
13 specialist adds additional tests or individualised interpretative comments or
14
15 both to aid the diagnosis and management of individual patients. 14-17 Reflex
16
17 testing, on the other hand, is a less time-consuming process based on automated
18
19 computerised rules to generate appropriate extra tests or interpretative
20
21 comments or both.
22
23
24
25
26
27
28
29

30 Previous case controlled studies report that reflective comments on laboratory
31
32 reports on hypercholesterolaemic patients advising specialist referral increase
33
34 the detection of familial hypercholesterolaemia. 14,15 Our report, however,
35
36 indicates that reflex interpretative comments may also influence clinical
37
38 practice, since direct referrals from the Wolverhampton GPs to the WMFHS
39
40 were 3.7 to 30 fold greater than comparator CCGs. Our study is particularly
41
42 notable since GPs have to obtain, complete and email a referral proforma to the
43
44 WMFHS; a significant effort.
45
46
47
48
49
50
51

52
53 It is possible that the difference in GP referrals across CCGs could be related
54
55 to wider social determinants, such as access to healthcare and socioeconomic
56
57 status, as well promotion of the WMFHS within each CCG. Wolverhampton,
58
59
60

1
2
3 however, has a high index of multiple deprivation and apart from the reflex
4
5
6 comments, the WMFHS was not advertised by any local initiative within the
7
8
9 Wolverhampton CCG.

10
11
12 Currently in England, only 7% of those with FH have been identified. NHS
13
14
15 England, therefore, plans to expand access to genetic testing for FH to identify
16
17
18 at least 25% of those with FH in the next five years through the NHS genomics
19
20
21 programme.⁴ It has been proposed that this will be achieved through NHS
22
23
24 Health Checks run by local authorities working with Public Health England (PHE),
25
26
27 community pharmacists and GP practices detecting high-risk conditions including
28
29
30 FH. PHE recommend systematic searching of primary care records to identify
31
32
33 those at highest risk of FH based on their lipid levels.¹⁸ The clinical laboratory,
34
35
36 however, is also ideally positioned to facilitate improved detection of FH as
37
38
39 demonstrated in this and other studies.^{14,15}

40
41
42 Based largely on the Welsh criteria,¹⁰ 45% of referrals were ineligible for
43
44
45 genotyping. Direct and more appropriate referral from our laboratory to
46
47
48 WMFHS is possible but this would require GPs to provide more clinical
49
50
51 information, when electronically completing lipid requests, to enable calculation
52
53
54 of the Welsh score and patient consent for genetic testing. GP representatives
55
56
57 felt that this would require considerable effort as clinical information is
58
59
60 difficult to access during the electronic requesting process especially as many

1
2
3 patients on whom lipids are requested would not meet criteria for consideration
4
5
6 of FH.
7
8

9
10 In conclusion, as far as we are aware, this is the first study indicating that
11
12 reflex comments on laboratory reports directly influence the clinical practice of
13
14 primary care physicians. This approach may have a role in the identification of
15
16 individuals with Familial Hypercholesterolaemia and warrants further
17
18
19
20
21 exploration.
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References

1. Navar-Boggan AM, Peterson ED, D'Agostino RB, et al. Hyperlipidemia in early adulthood increases long-term risk of coronary heart disease. *Circulation*. 2015;131: 451-8.
2. Nordestgaard BG, Chapman MJ, Humphries SE, et al. Familial hypercholesterolaemia is underdiagnosed and undertreated in the general population: guidance for clinicians to prevent coronary heart disease: Consensus Statement of the European Atherosclerosis Society. *Eur Heart J*. 2013; 34: 3478-90.
3. Barkas, F., Elisaf, M. and Milionis, H. Statins decrease the risk of stroke in individuals with heterozygous familial hypercholesterolemia: A systematic review and meta-analysis. *Atherosclerosis*. 2015; 243: 60-4.
4. The NHS Long Term Plan (2019). Available from <https://www.longtermplan.nhs.uk/>
5. National Institute for Health and Care Excellence. Familial hypercholesterolaemia: identification and management. [London]: NICE; 2008 [updated 2019 Aug]. Clinical guideline [CG71]. Available from: <https://www.nice.org.uk/guidance/cg71>

1
2
3 6. National Institute for Health and Care Excellence. Cardiovascular disease:
4 risk assessment and reduction, including lipid modification Clinical guideline
5
6
7

8 [CG181]. NICE 2014 [updated 2106 Sept]. Available from:

9
10
11 <https://www.nice.org.uk/guidance/cg181>
12
13

14
15 7. Kilpatrick ES, Freedman D. A national survey of interpretative reporting in
16 the UK. *Ann Clin Biochem.* 2011; 48: 317-20.
17
18

19
20
21 8. McKeeman GC, Hall SL, Freedman DB. Reflex and reflective testing practice
22 in Clinical Biochemistry in the United Kingdom - a national survey. *Ann Clin*
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

9. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of
low-density lipoprotein cholesterol in plasma, without use of the preparative
ultracentrifuge. *Clin. Chem.* 1972; 18: 499-502.

10. Haralambos K, Whatley SD, Edwards R, et al. Clinical experience of scoring
criteria for Familial Hypercholesterolaemia (FH) genetic testing in Wales.
Atherosclerosis. 2015; 240: 190-6

11. Barlow IM. Are biochemistry interpretative comments helpful? Results of a
general practitioner and nurse practitioner survey. *Ann Clin Biochem* 2008; 45:
88-90

- 1
2
3 12. Barlow IM. Do interpretative comments influence patient management and
4 do our users approve of the laboratory 'adding on' requests? A follow-up General
5 Practitioner and Nurse Practitioner survey. *Ann Clin Biochem* 2009; 46: 85-6
6
7
8
9
10
11
12 13. Darby D, Kelly A. Reflective testing - what do our service users think? *Ann*
13 *Clin Biochem* 2006; 43: 361-8
14
15
16
17
18
19 14. Bell AB, Bender R, Hooper AJ et al. Impact of interpretative commenting on
20 lipid profiles in people at high risk of familial hypercholesterolaemia. *Clinica*
21 *Chimica Acta*. 2013; 422: 21-5
22
23
24
25
26
27
28 15. Bender R, Edwards G, MacMahon J et al. Interpretative comments
29 specifically suggesting specialist referral increase the detection of familial
30 hypercholesterolaemia. *Pathology*. 2016; 48: 463-6
31
32
33
34
35
36
37 16. Paterson JR, Paterson R. Reflective testing: how useful is the practice of
38 adding on tests by laboratory clinicians? *J Clin Pathol* 2004; 57: 273-5.
39
40
41
42
43 17. Verboeket-van de Venne WP, Oosterhuis WP, Keuren JF, Kleinveld HA.
44 Reflective testing in the Netherlands: usefulness to improve the diagnostic and
45 therapeutic process in general practice. *Ann Clin Biochem* 2009; 46: 346-7.
46
47
48
49
50
51
52 18. Public Health England (2018) Familial Hypercholesterolaemia Implementing a
53 systems approach to detection and management. Available from:
54 [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/at](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/744441/familial-hypercholesterolaemia-implementing-a-systems-approach-to-detection-and-management.pdf)
55
56
57
58
59
60

1
2
3 [tachment_data/file/731873/familial_hypercholesterolaemia_implementation_g](#)
4
5
6 [uide.pdf](#)
7
8

9
10 19. Ministry of Housing, Communities, Local Government (2019) English indices
11
12 of deprivation 2019. In: GOV.UK. Available from:

13
14
15 <https://www.gov.uk/government/statistics/english-indices-of-deprivation-2019>.
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1: Reflex comments advising referral to the West Midlands Familial Hypercholesterolaemia Service

(Primary Prevention)

TC \geq 7.5 mmol/L & Trigs \leq 5.0 mmol/L

Exclude secondary causes of hyperlipidaemia

If not previously done, refer to the West Midlands Familial

Hypercholesterolaemia Service for genetic testing and advice by e-mailing a completed electronic form to Westmidlands.fhnurses@nhs.net who can also provide the electronic form.

If gene +ve Familial Hypercholesterolaemia: Refer to lipid clinic.

If not Familial Hypercholesterolaemia then:

Manage according cardiovascular risk using QRISK2.

Do not use QRISK2 and consider statins in patients aged $>$ 84y, with CKD and with type 1 diabetes.

Target: Greater than 40% reduction in non-HDL cholesterol (NICE CG 181)

(Secondary Prevention)

TC \geq 7.5 mmol/L & Trigs \leq 5.0 mmol/L

Exclude and treat secondary causes of hyperlipidaemia

If not previously done, refer to the West Midlands Familial

Hypercholesterolaemia Service for genetic testing and advice by e-mailing a completed electronic form to Westmidlands.fhnurses@nhs.net who can also provide the electronic form.

If gene +ve Familial Hypercholesterolaemia: Refer to lipid clinic.

Target: Greater than 40% reduction in non-HDL cholesterol or non-HDL cholesterol $<$ 2.5 mmol/L whichever is the lower.

Refer to lipid clinic for PCSK9 inhibitors if LDL cholesterol $>$ 3.5 mmol/L despite maximal tolerated statin and ezetimibe therapy.

Table 2 Number of referrals to WMFHS from Wolverhampton CCG and four comparator CCGs between 01/11/2017 to 31/10/2019

| CCG | Number of referrals | Population Size | IMD Rank ¹⁹ |
|-------------------|----------------------------|------------------------|-------------------------------|
| Wolverhampton CCG | 241 | 262,000 | 16 |
| Comparator CCG | 50 | 270,000 | 117 |
| Comparator CCG | 65 | 279,000 | 84 |
| Comparator CCG | 8 | 300,000 | 15 |
| Comparator CCG | 49 | 274,000 | 25 |

CCG is Clinical Commissioning Group

IMD is Index of Multiple Deprivation (Rank 1 is the most deprived of 191 English CCGs)