



Thames Audit Group

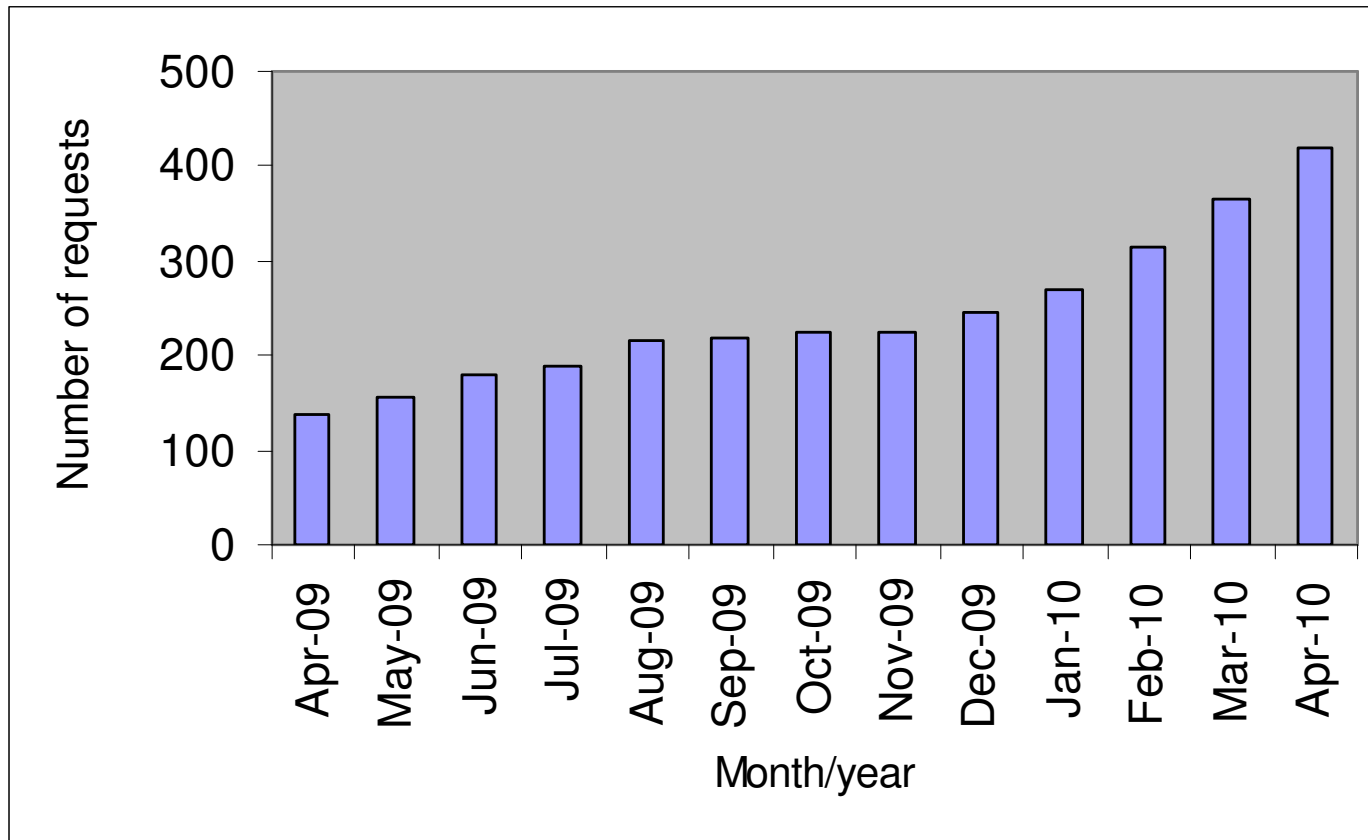
Audit of Serum 25 Hydroxy Vitamin D (25OH D) Requests and Results

Dr Laila Tibi

West Hertfordshire Hospitals NHS Trusts

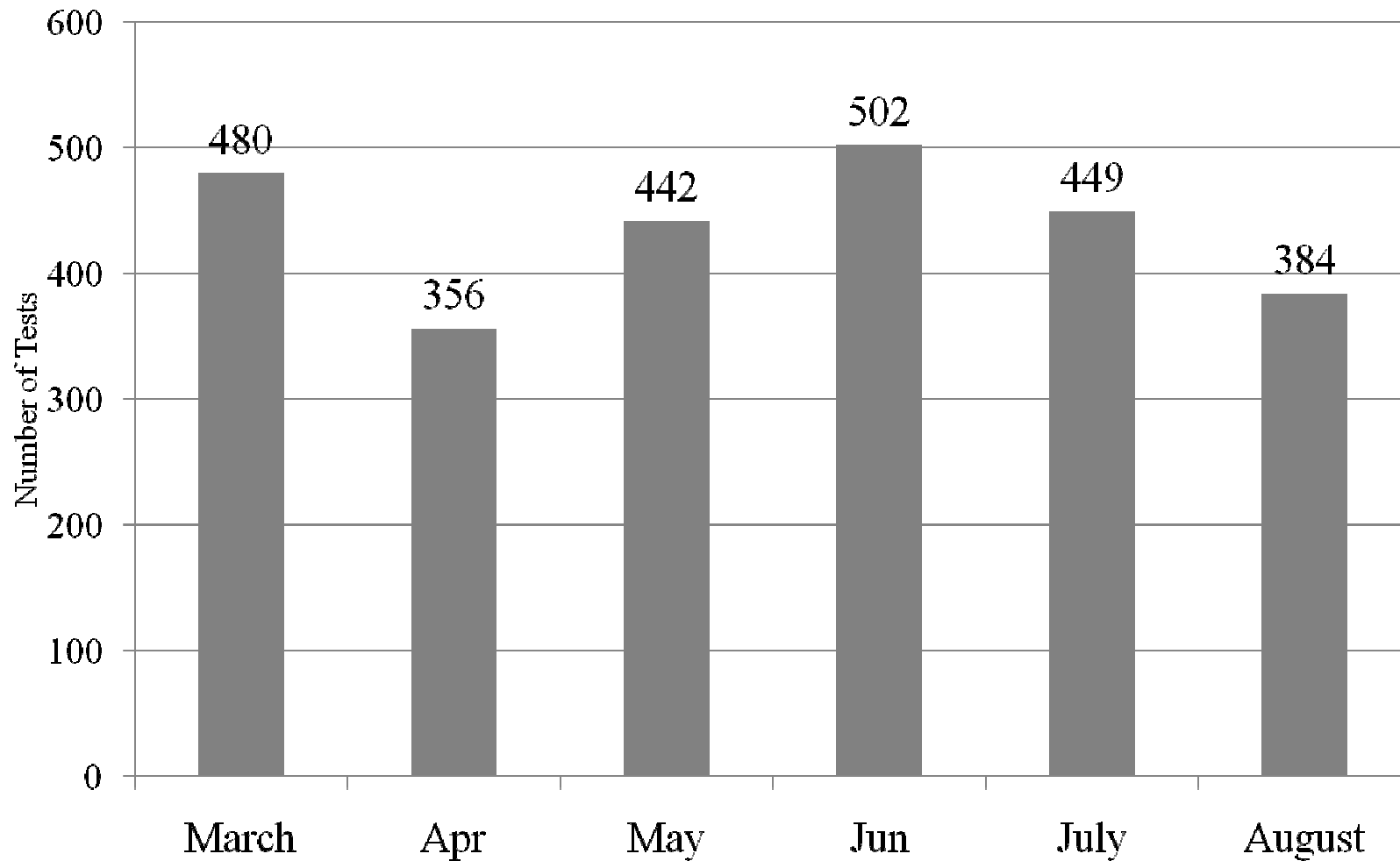
Requests for 25 OH D rapidly increasing

Monthly numbers of 25OH D requests 2009 – 2010
(West Hertfordshire Hospitals NHS Trust)



25OH D Workload March – August 2011

(West Hertfordshire Hospitals NHS Trust)



Guidelines

National Guidelines eg from NICE not available as to:

When to measure 25OH D (Clinical Guidelines)

How best to measure 25OH D (Laboratory)

How best to report 25OH D

Guidelines available for specific patient groups eg
antenatal care (NICE clinical guideline 62)

Questionnaires

100 Questionnaires sent out to laboratories within Thames Audit Group

Received 21 completed questionnaires
(9 were from Teaching Hospital Trusts)

Poor response rate (21%)

Responses were from single Trusts composed of several laboratories especially in London area

Audit Sections

- **25OH D Requests**
- 25OH D Methods
- 25OH D Results

Question 1

Please tick category for your annual workload for 25OH D

Annual 25OH D workload	Number of Trust Laboratories	
	April 2009-2010	April 2010-2011
<500	2	0
500 - 1000	4	4
1000 - 5000	7	4
5000 - 10,000	4	4
>10,000	4	9*
* 6 of these Referral Laboratories		

Question 2

What percentage of 25OH D requests are from GPs, Hospital (in and out-patients), referrals from other laboratories?

	Number of Trust Laboratories		
Percentage of requests	GPs	Hospital	Referrals from other Laboratories
0 – 20	3	4	17
21 – 40	4	8	1
41 – 60	9	4	2
61 – 80	4	3	1
>80	0	1	0
	1 laboratory % not given		

Question 3

Do you vet 25OHD requests?

	Number of Trust Laboratories
Yes	10*
No	11

*Selectively vet. Agreement with some clinicians where send all requests eg patients with cystic fibrosis, galactosaemia, HIV, MS, osteogenesis imperfecta pre pamidronate

If Yes, when would you reject 25OH D requests?

Reject:

Obvious recent repeats (eg **within 3 months**)

If repeated **within 3 months** and requests with no clinical details

If repeated **within 3 months** or if several previous tests “replete” results

Requests **within 3 months** of previous request

Repeats **under 90 days** unless concern about validity of previous result

GP requests from patients :

on vit D replacement repeat **under 2 months**

Without clinical details such as osteoporosis, ?osteomalacia/rickets, ?toxicity

Trust inappropriate requests from in-patients and from unfunded out-patient clinics (eg new pain clinic)

If **calcium, phosphate, alk phos well within ref range** and lack of clinical details such as fracture, bone pain. If interval between requests **less than 6 months**

If **PTH, calcium, alk phos within normal range** unless from endo/renal/rheumatology or clinical details say on replacement

If **calcium, phosphate, alk phos within normal range** but done if <16 years, on anti-convulsants or diagnosed with TB

Question 4

Do you have local guidelines for 25OH D requests?

	Number of Trust Laboratories
Yes	4
No	17

Local Guidelines (Trust Laboratory 1)

- Is it necessary to always assay serum 25-hydroxyvitamin D concentrations?
 - Children – yes, all children with suspected vitamin D deficiency should have their levels assayed
 - Adults – not if classical signs and symptoms of Vitamin D deficiency AND with known risk factors AND with abnormal biochemistry (eg raised alk phos)
- All patients receiving therapy for vitamin D deficiency should be monitored as follows:
 - 1 month: plasma calcium concentration
 - 3 months: plasma-calcium, phosphate and PTH

Local Guidelines (Trust Laboratory 2)

Nutritional deficiency is better confirmed by 25-D measurement and is particularly indicated in the elderly, the institutionalised , Asians, malabsorption and patients on long term anticonvulsants

Minimum repeat measurement interval for 25D following replacement is 3 months. Interval dependent on baseline level of vitamin D and vitamin D dose

Local Guidelines (Trust Laboratory 3)

Adults

Symptomatic deficiency: osteomalacia (25 OH D <30 nmol/L)

Aim of treatment is to achieve 25 OHD levels of >80 nmol/L after 12 weeks. No routine monitoring is necessary for patients on long term maintenance doses of vitamin D up to 2000 IU/day

Asymptomatic deficiency – daily supplement of 800 – 2,000 IU/day. Review vitamin D and calcium at 12 weeks and continue maintenance dose long term. Monitoring not required

Local Guidelines (Trust Laboratory 4)

The testing of vitamin D deficiency has risen exponentially (in ----)and the costs of the new assays for 25(OH) are placing a burden on secondary care. -----has advised that this should stop as 80% of all those referred are proving to be in the range required for treatment/intervention.

The exception for testing adults for Vitamin D deficiency are as shown in the accompanying advice to GPs

- History of fragility fracture (>50 yrs);
- Falls in > 65 yrs
- Starting bone specific therapy such as bisphosphonates/strontium/PTH
- Patients on enzyme inducing anti-epileptic drugs

Question 5

Do you recommend time interval prior to repeat 25OH D after vitamin D replacement?

	Number of Trust Laboratories
Yes	14
No	7

If yes, please tick category for time interval

Time interval (months)	Number of Trust Laboratories
0 – 1	0
1 – 3	4
3 - 6	9
6 - 12	1

Audit Sections

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Question 6

Do you measure 25OH D in your laboratory?

	Number of Trust Laboratories
In Laboratory	11
Referred	10

Methods for Trust Laboratories that measure 25OH D

Method Group	Number of Laboratories	Analyser/Kit
Immunoassay	7*	Diasorin (n = 3) IDS (n = 2) Roche Cobas (n = 1) Abbott Architect (n = 1)
LC-MS/MS HPLC	5*	Waters (n = 3) ABSciex 5500 (n = 1) BioRad HPLC (n = 1)

*1 laboratory uses Immunoassay and LC-MS/MS

Question 7

Do you send 25OH D to a Referral Laboratory?

Referral Laboratory	Method	Number of Laboratories
Homerton	LC-MS/MS	3
The Royal London	LC-MS/MS	2
Barts	LC-MS/MS	1
Charing Cross	LC-MS/MS	1
Northwick Park	LC-MS/MS	1
UCLH	LC-MS/MS	1
Frimley Park	Immunoassay	1
Total Number		10

Question 8

If you are currently sending 25OH D to a Referral Laboratory are you considering measuring in your laboratory within the next year?

	Number of Trust Laboratories
Yes	6
No	4

Question 9

Between batch precision (CV %)
Laboratories measuring 25OH D

25OH D (nmol/L)	Immunoassay	HPLC LC-MS/MS	All methods
Deficient (approx 20)	3 - 13	4 - 13	3 – 13
Insufficient (approx 50)	2.5 – 14.5	4 – 9.2	2.5 – 14.5
Sufficient (approx 100)	2.5 – 7.7	4 – 7.8	2.5 – 7.8
Toxic (approx 200)	3.4 – 6.8	0.4 - 5	0.4 – 6.8

Question 10

What calibration standard does your method use?
Laboratories measuring 25OH D

Method group	Calibration standard
Immunoassay	Kit standards
HPLC LC-MS/MS	Commercial standard Traceable to NIST

Question 11

Does your method **measure** 25OH D2, 25OH D3, Total 25OH D?
Does your method detect C3 epimer?

Method	Measure	Detect C3 epimer
Immunoassay	Total 25OH D	2 Yes 3 Don't know
LC-MS/MS HPLC	25OH D2, 25OH D3	4 Yes (1 co-elutes) 1 Don't know

Question 12

Do you belong to EQA scheme for 25OH D?

	Number of Trust Laboratories
Yes (DEQAS)*	11
* 1 trying Randox EQA Scheme	
No (but these send to Referral Laboratories)	10

Audit Sections

- 25OH D Requests
- 25OH D Methods
- **25OH D Results**

Question 13

Do you **report**: Total 25OH D
25OH D2 and 25OH D3 separately
25OH D2, 25OH D3 and Total 25OH D

Report	Number of Trust	Methods
Total 25OH D	7	Immunoassay
25OH D2 and 25OH D3 separately	6	HPLC LC-MS/MS
25OH D2, 25OH D3 Total 25OH D (by addition)	6	HPLC LC-MS/MS
Not given	2	

Question 14

What is your Turnaround Time for 25OH D?

	Number of Trust Laboratories
<1 week	11 *
1 – 2 weeks	5
>2 weeks	3**
Not given	2
* Measured in laboratory, ** Referred	

Question 15

What serum 2OH D Reference Ranges do you quote for **Deficiency**?

Deficient 25 OH D (nmol/L)	Number of Trust Laboratories
<10	1
<12.5	1
<20	1
<25	7
<30*	5
<40	2
Not given	4

*1 Lab does not quote ranges - local guidelines recommend treatment if <30 nmol/L

Question 15

What serum 25OH D Reference Ranges do you quote for **Insufficiency**?

Insufficient 25OH D (nmol/L)	Number of Trust Laboratories
<35	1
<50	6
<70	2
<75	4
<80	3
Not reported	5

Question 15

What serum 2OH D Reference Ranges do you quote for **Replete**?

Replete 25OH D (nmol/L)	Number of Trust Laboratories
>36	1
>50	6
>70	2
>75	5
>80	3
Not Reported/not available	4

Question 15

What serum 2OH D Reference Ranges do you quote for **Toxic**?

Toxic 25OH D (nmol/L)	Comments	Number of Trust Laboratories
>150	Bone added	1
>200	Reduce dose	5
>225		1
>250	If sustained	3
>500		1
Not recorded		10

Source of Reference Ranges

Source of Reference Range	Number of Trust Laboratories
Referral Lab (current or previous)	10
Determined within Laboratory	5
Kit manufacturer insert	2
Institute of Medicine 2010 report	1
Local Guidelines	1
Not recorded	2

Question 16

What percentage of patients have serum 25OH D concentrations in the deficient range (please give approximate figure)?

Percentage of Patients with deficient 25OH D	Number of Trust Laboratories
5 – 10	4
11 – 20	5
21 - 30	4
40 - 50	5
68 - 80	2

Where Labs have specified time of year, “summer” percentages were used
1 Lab: depends on time of year but percentage not given

Acknowledgements

- Thank you for returning completed questionnaires
- Thank you to Clinical Audit Department, West Hertfordshire Hospitals NHS Trust

Draft Laboratory Guidelines for Serum 25 Hydroxyvitamin D (25OH D) Requests

Laboratories should

Manage the increasing request numbers for serum 25OH D by:

1. Producing Local Guidelines (together with Endocrine, Renal, Rheumatology and Pharmacy Departments) as to which patient groups require 25OH D measurements
2. Rejecting 25OH D requests made within 3 months of vitamin D replacement therapy
3. Discouraging routine monitoring in patients on long term maintenance doses

Draft Laboratory Standards for Serum 25 Hydroxyvitamin D (25OH D) Methods

Laboratories should:

1. Use methods with good performance in terms of precision and accuracy particularly at deficient/insufficient 25OH D concentrations
2. Use methods calibrated with standards that are traceable to NIST (National Institute of Standards and Technology)
3. Belong to an EQA Scheme
4. Use chromatographic methods that measure 25OH D2 and 25OH D3 separately
5. Use immunoassays that measure Total 25OH D using antibodies with an equimolar response to 25OH D2 and 25OH D3
6. Use methods that can distinguish and/or show no cross reactivity with C-3 epimers of 25OH D2 and 25OH D3 (especially when the laboratory processes paediatric samples)

Draft Laboratory Standards for Serum 25 Hydroxyvitamin D (25OH D) Results

Laboratories should:

1. Report Total 25OH D concentrations (by addition of 25OH D2 and 25OH D3 for chromatographic methods)
2. Report 25OH D results within 2 weeks of receipt of sample
3. Whenever possible use Serum 25OH D “consensus” reference ranges
 - less than 25 nmol/L: profound vitamin D **deficiency**
(symptomatic osteomalacia or rickets)
 - between 25 and 50 nmol/L: vitamin D **insufficiency**
(associated with several common diseases including cardiovascular disease, diabetes, cancer, multiple sclerosis)
 - greater than 500 nmol/L: associated with Vitamin D **toxicity**

Pearce SHS, Cheetham TD. Diagnosis and management of vitamin D deficiency. BMJ 2010; 340: 142 - 147