Reducing vitamin test ordering in primary care; the effectiveness of professional and patient oriented strategies in a Cluster randomized Intervention Study

Vugt, Saskia van; de Schepper, Evelien; van Delft, Sanne; Zuithoff, Nicolaas; de Wit, Niek; Bindels, Patrick

DOI: https://doi.org/10.3399/BJGPO.2021.0113

To access the most recent version of this article, please click the DOI URL in the line above.

Received 17 June 2021
Revised 17 June 2021
Accepted 05 July 2021

© 2020 The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 License (http://creativecommons.org/licenses/by/4.0/). Published by BJGP Open. For editorial process and policies, see: https://bjgpopen.org/authors/bjgp-open-editorial-process-and-policies

When citing this article please include the DOI provided above.

Author Accepted Manuscript
This is an ‘author accepted manuscript’: a manuscript that has been accepted for publication in BJGP Open, but which has not yet undergone subediting, typesetting, or correction. Errors discovered and corrected during this process may materially alter the content of this manuscript, and the latest published version (the Version of Record) should be used in preference to any preceding versions
Reducing vitamin test ordering in primary care; the effectiveness of professional and patient oriented strategies in a Cluster Randomized Intervention Study

Saskia F van Vugt MD,PhD (Researcher, General Practitioner)¹; Evelien IT de Schepper MD,PhD (Researcher, Assistant Professor)²; Sanne van Delft PhD (Researcher)³; Nicolaas PA Zuithoff PhD (Statistician)¹; prof Niek J de Wit MD,PhD (Head Department of General Practice)¹; prof Patrick JE Bindels² MD,PhD (Head Department of General Practice)².

1. Department of General Practice, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, The Netherlands
2. Department of General Practice, Erasmus Medical Center Rotterdam, The Netherlands
3. Saltro, Diagnostic Center for Primary Care, Utrecht, The Netherlands

Corresponding author
Saskia F. van Vugt, MD, PhD.
Department of General Practice, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Str.6.131
PO Box 85500, NL-3508 GA Utrecht, the Netherlands
Phone: +31-6-33802678
E-mail: saskiavvugt@gmail.com
Reducing vitamin test ordering in primary care; the effectiveness of professional and patient oriented strategies in a Cluster Randomized Intervention Study

ABSTRACT

Background: Vitamin tests are increasingly ordered by GPs, but a clinical and evidence based indication is often lacking. Harnessing technology, i.e. decision support tools and redesigning request forms, have been shown to reduce vitamin D requests.

Aim: Could the number of vitamin tests also be reduced by providing a multi-level intervention program based on training, monitoring and feedback?

Design & Setting: In a Cluster Randomized Intervention Study performed in 26 primary care health-centres (200.000 patients) the relative reduction in ordered vitamin D and B12 tests was determined after introduction of two de-implementation strategies (may 2017-may 2018).

Method: Health-centers randomized to de-implementation strategy 1 received education and 3-monthly benchmarking of their own vitamin test ordering behavior. Health-centers in de-implementation strategy 2 received the same education and benchmarking but supplemented with educational material for patients.

Results: The number of vitamin D tests decreased 23% compared to the one-year pre-intervention period. For vitamin B12 tests an overall reduction of 20% was found. Provision of patient educational information showed additional value over training and benchmarking of GPs alone, but only for vitamin D test ordering (10% extra reduction, OR 0.88, 95%CI 0.83-0.92, compared to 4% extra reduction for vitamin B12, OR 0.96, 95%CI 0.91-1.02). Nationwide, this would result in over € 3.200.000 saving on healthcare expenditure per year.

Conclusion: A structured intervention program, including training and benchmarking of GPs regarding their diagnostic test ordering resulted in a significant reduction in ordered vitamin tests. Additional information provision to patients resulted in a small but still relevant additional reduction. If implemented on a national level, a substantial cost saving can be achieved.

Keywords: vitamins, overdiagnosis, primary care
**Abbreviations:**

General Practitioner (GP)  
Julius General Practitioners’ Network Utrecht (JGPN)  
Social Economic Status (SES)  
Social and Cultural Planning Office (SCP)

**How this fits in:**

Vitamin tests are increasingly ordered by GPs, but a clinical and evidence based indication is often lacking.  
This cluster randomized intervention study showed that with a structured time limited intervention program, including training and benchmarking of GPs, a significant reduction of the number of vitamin tests in primary care can be achieved with a substantial cost saving.
INTRODUCTION

Medical overuse, including both overdiagnosis and overtreatment is a growing problem in healthcare.\(^1\) Overuse is increasingly recognized around the world, but quantifying it is often challenging. Estimates of cost related to overuse vary widely, but overuse of individual services may be as high as 80% of cases.\(^2\)

Despite the growing awareness and recommendations from the Choosing Wisely campaign, several studies illustrate how difficult it is to achieve substantial reduction in unnecessary testing.\(^3\)-\(^6\) A recent UK study showed that diagnostic testing in primary care substantially increased.\(^6\) Over 10 years, testing for vitamin D increased exponentially with an average annual increase of 54%. Also, a linear increase pattern emerged for vitamin B12, with an annual increase of 17%.\(^6\) Although recommended for specific patient populations\(^7,8\), laboratory tests for vitamin D and B12 are mainly used for patients with non-specific symptoms.\(^9,10\)

Although many consider vitamin testing as ‘harmless’, it may lead to medicalisation, due to untargeted testing in response to (irrational) health perceptions of patients, to overdiagnosis (‘iatrogenic illness’\(^11\)) and to an unnecessary increase of healthcare expenditure.\(^6,12\) This stresses the need to rationalize vitamin test ordering, especially vitamin D and B12, the most frequently ordered vitamin tests in clinical practice, through influencing both medical professionals and patients.\(^13\)

A systematic review showed how involving patients through patient-targeted educational materials is effective in decreasing the use of low-value care.\(^13,14\) Further, previous studies showed how redesign of the electronic request form\(^15\) and 3 clinical decision support tools (e.g. guideline development, a ‘stop alert’ shown to the ordering clinician and removal from the laboratory ordering preference list)\(^16\) reduced vitamin D testing respectively 36 and 30%. However, the individual impact of these tools could not be assessed, the follow-up period was limited to 6 months and implementation is only possible in a setting where decision support tools can be integrated in Electronic Health Records.\(^14,15,16\) Therefore, we aimed at other simple intervention strategies that can be implemented in every primary care system and can be evaluated separately. In this study we therefore assess the effect of a GP targeted intervention program based on training, monitoring and feedback to rationalize the vitamin D and B12 test ordering in primary care, and the added value of practice based patient information about vitamins and health.
METHOD

Design
A Cluster Randomized Intervention Study comparing two de-implementation strategies.

Setting
Health-centres from two regional academic primary care networks in the Netherlands were invited to participate in a one year intervention study. All vitamin D and B12 tests requested by GPs working in the 26 health-centres during the intervention year (01/05/2017-01/05/2018) and the pre-intervention year (01/05/2016-01/05/2017) were extracted.

Participants
All health-centers from the Julius General Practitioners' Network Utrecht (JGPN, 59 centres), 2 health-centers of the Academic Primeur network and 8 other health-centers in the Rotterdam area were invited to participate. Criteria for inclusion were willingness to attend 2 obligatory educational sessions by at least one GP of the participating center, and permission to extract data from the regional diagnostic laboratory on their vitamin D and B12 test ordering. There were no exclusion criteria.

Interventions
The participating health-centers were randomized to either de-implementation strategy 1 ('GP only') or strategy 2 ('GP+patient'), Figure 1. Strategy 1 included two training sessions of 1.5 hour addressing the evidence and indications for vitamin D and B12 testing, and communication strategies regarding (withstanding) patients' requests for testing. At least one GP per center had to attend the plenary meeting. All other GPs were allowed to follow the e-learning of this educational session. GPs received 3-monthly emails with the number of ordered vitamin tests, benchmarked to the numbers of the other participating health-centers.

In strategy 2, the health-centers received the same training, monitoring and feedback as in strategy 1, but in addition these centers were equipped with educational material for patients through video screens in the waiting room and leaflets in Dutch, Turkish and Arabic languages about health effects of vitamins.

Outcomes and measurements
Primary outcome was the difference in the number of vitamin D and B12 blood tests ordered by GPs during the intervention year controlled for the number in the pre-intervention year.
Secondary outcomes were the number of abnormal test results and the direct cost savings.

Data on pre-intervention and intervention vitamin testing were collected through the primary care laboratory organisations in Utrecht (Saltro) and Rotterdam (Star-shl). Both organisations have a very long standing relation with their regional GPs, handling >90% of the laboratory tests ordered by GPs in their region. GP and health-center identity (code), age and gender of patient, date, test (e.g. vitamin D or B12) and test result were extracted anonymously from existing registries.

**Randomisation**
Randomisation was performed by the Data Management Department of the Julius Center Utrecht and controlled for region (Utrecht/Rotterdam) and health-center size to ensure proper distribution over both intervention arms. The intervention allocation within this cluster randomised intervention study could not be blinded.

**Sample size calculation**
Based on a two-sample Wilcoxon sample size calculation with data on the achieved absolute reduction in vitamin D tests in an earlier performed ‘practice improving project’ in the Rotterdam region (i.e. Poisson means of 850 tests before and 638 after intervention), an alpha of 0.05 and a power of 0.90, a minimum number of 36 individual GPs (with a mean of 2095 patients each) was needed to achieve significance. When taking an expected cluster correlation of 0.15 into account, the number of individual GPs increased to 66. Allowing for drop-outs we aimed to include 75 individual GPs, with a resulting patient population of 157,125.

**Data analysis**
The primary outcome, the difference in the number of requested tests (divided by the number of patients) in pre and post intervention year per health-center was analysed with a generalized linear mixed model for binomial outcomes. We included a random intercept to correct for clustering (due to the repeated measurement in each center). The comparison between strategy 1 and 2 during the intervention year was included separately. In an additional step, we included predefined confounders, i.e. the number and gender of GPs per health-center, and (to correct for composition of the patient population\(^1\)) the average social economic status (SES) of patients per center. SES data were retrieved from the Social and Cultural Planning Office (SCP) and calculates social economic status scores based on information regarding education, income and position in the labor market.\(^2\)
Effect of the intervention strategies was reported in ORs with 95% CIs and p-values.
To externally validate our results, comparison to the number of ordered vitamin tests in the same period by non-participating health-centers was performed. These (anonymous) data were retrieved from Saltro’s laboratory registry, containing routine data of all tests requested by primary care health-centers in the Utrecht region.

Presuming that the average test result is an adequate proxy for the quality of the indication of a performed test, the number of tests indicating a vitamin deficiency was determined (based on reference values from the Dutch GP Guidelines on vitamin D\textsuperscript{20} and B12\textsuperscript{21}).

Finally, direct cost-savings were determined by calculating savings from the reduction in the number of vitamin D and B12 tests. Standard national tariffs for vitamin D and B12 laboratory tests were used\textsuperscript{22}(i.e. €7,62-€8,38 (average € 8,00) for vitamin D and €5,81-€6,39 (average €6,10) for vitamin B12). Other (indirect) cost-savings, e.g. number of GP consultations, cannot be calculated from this study.

All analysis was performed using SPSS Statistics version 25 and SAS v9.4.
RESULTS

Baseline characteristics
22 health-centers with 117 GPs in the Utrecht region and 4 health-centers with 41 GPs in the Rotterdam region participated in the study, with a corresponding total population of 195,000 patients (134,000 in the Utrecht region and over 61,000 in the Rotterdam region). Table 1. No significant differences in baseline characteristics were seen between health-centers in de-implementation strategy 1 and 2. None of the participating centers discontinued the intervention or was lost to follow-up.

Number of vitamin D and B12 tests
The total number of vitamin D tests ordered by GPs in strategy 1 and 2 decreased from 17,527 to 13,447 (-23%, OR 0.73 [95%CI 0.71-0.75]) with a range of -9 to 70%.

The mean number of vitamin D tests ordered in the pre-intervention year was 88/1000 patients (SD 57), ranging per center from 12 to 262/1000 patients. During the intervention year this was 66 vitamin D tests/1000 patients (SD 51), resulting in a decrease of 22/1000 [95%CI -32- -13, p<0.001]).

The total number of ordered vitamin D tests in non-participating health-centers remained stable during the intervention year (-0.4%).

For vitamin B12 the total number of tests reduced from 12,304 (pre-intervention) to 9,891 (-20%, OR 0.79 [95%CI 0.76-0.81]) with a range of -19 to 63%. Overall, a mean of 59 vitamin B12 tests/1000 patients (SD 43), was ordered during the pre-intervention year, compared to 47/1000 patients (SD 32) during the intervention year, resulting in a mean difference of 12/1000 [95%CI -20 - -5, p=0.003]). The number of ordered vitamin B12 tests/1000 patients per center varied from 7 to 198/1000 patients during the pre-intervention year. A marked difference between the pre-intervention numbers for Utrecht (46/1000 patients, SD 26) and Rotterdam (106/1000 patients, SD 62) was found, which reduced to 38/1000 (SD 22) and 79/1000 (SD 43) respectively.

In non-participating health-centers the number of tests decreased with 4.3%.

The variation between centers was substantial, both in number of ordered vitamin tests in the pre-intervention period (range of 12 to 262 and 7 to 198/1000 patients for vitamin D and B12 respectively), as in the observed reduction in tests during the intervention period (-9 to 70% for vitamin D and -19 to 63 for vitamin B12). Therefore, all health-centers were divided in quartiles according to the pre-intervention test ordering. Per category the mean reduction in ordered vitamin tests was calculated (Figure 2), which increased with higher pre-intervention test-rates.
Comparison between de-implementation strategy 1 and 2
In centers randomized to the de-implementation strategy 1 (GP only) there was a 19% reduction in total number of vitamin D tests, compared to a reduction of 29% in centers randomized to de-implementation strategy 2 (GP+patient intervention), odds ratio 0.88, 95%CI 0.83-0.92 (Table 2).
For vitamin B12 a reduction of 18% was found in centers of strategy 1 compared to a reduction of 22% in strategy 2 (odds ratio 0.96, 95%CI 0.91-1.02, non-significant).

Vitamin test results
The mean test result of vitamin D tests did not differ before and during the intervention (56 nmol/l versus 55 nmol/l), neither for vitamin B12 (304 pmol/l). Also the proportion of tests results below the reference values for vitamin D and B12 did not differ (around 17%, Table 3).

Cost benefit analysis
With an observed reduction of 4080 vitamin D and 2413 vitamin B12 tests, a saving of €32.640 plus €14.719 can be calculated. Total savings were €47.359, compared to €20.340 related to development and implementation of the intervention (i.e. development of patient education material (i.e. videos €12.566, booklets €1.266, posters €787), organization of GP training sessions (€1.096), development of e-learning (€4.625)). In case of an endurable implementation, only expenses for printing patient education material (€972), organization of GP training sessions (€1.096) and laboratory costs (€3.000) for regular collection and (secured) communication of the number of test requests will continue, which is 11% of the total savings.
With an observed average reduction of 22 vitamin D and 12 vitamin B12 tests/1000 patients, a cost reduction of €361 plus €375 per standard primary care practice (2095 patients) per year can be calculated. In Dutch context (with a total of around 5000 primary care practices) this would mean a total cost reduction of €3.681.701 per year, lowered by 11% intervention costs resulting in total savings of €3.276.714 per year. This estimate is likely lower than the true savings because exact data on indirect cost reduction (e.g. GP consultations) were not available for this analysis.
DISCUSSION

Summary. This study demonstrates that with relatively simple and limited time-consuming interventions the number of vitamin tests ordered in primary care can be reduced substantially. We found a 23% reduction of vitamin D tests and 20% of vitamin B12 tests ordered after one year, resulting in substantial cost savings. Additional provision of patient information resulted in a 10% extra reduction of vitamin D tests on top of training and benchmarking of GPs, and a non-significant 4% additional reduction for vitamin B12 tests. The decrease was most prominent in centers that already had a high test ordering rate before the intervention.

Strengths and limitations. A major strength of this study is the inclusion of a relatively high number of GPs. Furthermore, a simple and limited time-consuming intervention was used which is easy to implement in daily practice. However, some limitations need to be considered. First, primary care assistants were not included in the intervention, whereas they sometimes issue laboratory forms on a patient request. Including primary care assistants might improve test reduction even more. Second, benchmarking was provided at center level, whereas provision of individual feedback could possibly result in further reduction of test ordering. Furthermore, presence of at least one GP per center was obligatory for participation in this study. We were not able to check whether the lessons learned during the training sessions were actually shared with fellow GPs. However, an e-learning of the training sessions was available and 80% of all 158 GPs from the participating centers was reached via either the training session (32%) or e-learning (48%). Besides, participating GPs could have been influenced by other training programs on the same topic during the intervention period, although we did not receive any notifications of such programs. Selection bias may have occurred, because the GPs joining our study may have been more motivated compared to non-participating GPs. Also, regional differences were observed: Rotterdam region showed a much higher pre-intervention test-rate and reduction in test ordering for vitamin B12. When interviewing participating GPs at the end of the intervention year, several Utrecht GPs mentioned that they experienced how the provided patient information raised awareness for vitamin testing, encouraging patients to ask for a vitamin B12 blood test. Reviewing the patient education material would therefore be required before using it further. Finally, reason of testing was not studied during this project. It would have been interesting to know whether the GP training sessions helped to improve evidence based testing behavior. Presuming that the average test result is an adequate proxy for the quality of the indication of
a performed test, the number of tests indicating a vitamin deficiency was determined, which did not differ during the intervention period.

**Comparison with existing literature.** Several medical specialty societies have identified unnecessary laboratory testing as a target for overuse reduction in campaigns aimed at avoiding low-value care.\textsuperscript{23,24} Several studies focusing on vitamin D request reduction have been performed. Harnessing technology, such as redesigning electronic request forms\textsuperscript{15}, decision support tools\textsuperscript{16} and obligatory addition of test indication on request forms\textsuperscript{5}, showed reductions in vitamin D test requests of 36%, 67% and 92% respectively. Systematic reviews have also showed how performance feedback and clinician education\textsuperscript{25,26} as well as patient education\textsuperscript{13,14} are useful strategies with a solid evidence base for reducing use of low-value health services.

In the present study the proportion of tests with a result below the reference values remained stable, suggesting that, even in the intervention period, many vitamin tests are still done without a valid indication. Several recent studies confirmed that a large proportion of vitamin D tests in primary care lacks a valid clinical indication.\textsuperscript{15,27,28}

**Sustainability.** In order to gain understanding of the sustainability of our intervention, we looked at the number of vitamin D tests ordered in the two years following the pilot ‘practice improvement project’ performed in 11 primary care health-centers (patient population 120,000) in Rotterdam. One year after the intervention the numbers remained stable; in the second year the number of vitamin D tests was only slightly higher (+0.3%, unpublished data). Because these results are based on a small project, further studies with a longer follow-up are necessary.

**Implications for practice.** We demonstrated that a limited time requiring intervention, consisting of training of GPs and benchmarking their diagnostic test ordering, a significant reduction in ordered vitamin laboratory tests can be achieved. This strategy is most successful among GPs who are frequently ordering vitamin levels and who are willing to improve their testing behavior.

The low number of abnormal test results illustrates the need for training on evidence-based indications for vitamin test ordering. Training programs and individual monitoring and feedback should be implemented on a national level to achieve a further reduction of the number of vitamin tests in primary care with substantial cost savings.
**Funding**
The study was funded by the Citrien Fund, a national program of the Dutch government initiated in 2015 (i.e. “Do or don’t” program) to reduce lower-value services. The funding source was not involved in the design, conduct, analysis and interpretation of the data, nor in the writing and decision to submit the paper.

**Ethical approval**
The Medical Ethics Committee of the University Medical Centre Utrecht assessed this study’s design and procedures, and in accordance with the local regulatory guidelines and standards for human subjects protection in the Netherlands (Medical Research Involving Human Subjects Act (WMO), 2005), this study proved to be exempt from further medical ethical review.

**Competing interests**
All authors have no conflict of interest to report.

**Acknowledgements**
We thank Sacha de Lathouder from STAR-shl Diagnostic Center for Primary Care and Lara Harmans and Sanne van Delft from Salto Diagnostic Center for Primary Care for their participation in the data collection. We also thank all included GPs for their enthusiastic participation during the intervention year.

**References**
1. Morgan DJ, Dhruva SS, Coon ER, Wright SM, Korenstein D. 2019 Update on Medical Overuse: A Review. JAMA Intern Med. 2019 Sep 9.
2. Brownlee S, Chalkidou K, Doust J, et al. Evidence for overuse of medical services around the world. Lancet. 2017 Jul 8;390(10090):156-168.
3. American Board of Internal Medicine. Choosing Wisely. [Internet]. Available from: http://www.choosingwisely.org. [Accessed 10th August 2019].
4. Rosenberg A, Agiro A, Gottlieb M, et al. Early Trends Among Seven Recommendations From the Choosing Wisely Campaign. JAMA Intern Med. 2015 Dec; 175(12):1913-20.
5. Ferrari R, Prosser C. Testing Vitamin D Levels and Choosing Wisely. JAMA Intern Med. 2016 July 1; 176(7):1019–1020.
6. O’Sullivan JW, Stevens S, Hobbs FDR, et al. Temporal trends in use of tests in UK primary care, 2000-15: retrospective analysis of 250 million tests. BMJ. 2018 Nov 28; 363:k4666.
7. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2011 Jul; 96(7):1911-30.

8. Harrington D, Robinson S. Vitamin B12 deficiency. BMJ. 2014 Sep 4; 349:g5226.

9. Hofstede H, van der Burg HAM, Mulder BC, et al. Reducing unnecessary vitamin testing in general practice: barriers and facilitators according to general practitioners and patients. BMJ Open. 2019 Oct 7;9(10):e029760.

10. Koch H, van Bokhoven MA, ter Riet G, et al. What makes general practitioners order blood tests for patients with unexplained complaints? A cross-sectional study. Eur J Gen Pract. 2009; 15(1):22-8.

11. Kahwati LC, Weber RP, Pan H, et al. Vitamin D, Calcium, or Combined Supplementation for the Primary Prevention of Fractures in Community-Dwelling Adults. Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2018 Apr 17; 319(15):1600–1612.

12. Sattar N, Welsh P, Panarelli M, et al. Increasing requests for vitamin D measurement: costly, confusing, and without credibility. Lancet. 2012 Jan 14; 379(9811):95-6.

13. Légaré F, Stacey D, Turcotte S, et al. Interventions for improving the adoption of shared decision making by healthcare professionals. Cochrane Database Syst Rev. 2014 Sep 18;(9):CD006732.

14. Sypes EE, de Grood C, Whalen-Browne L, et al. Engaging patients in de-implementation interventions to reduce low-value clinical care: a systematic review and meta-analysis. BMC Med. 2020 May 8; 18(1):116.

15. Patel V, Gillies C, Patel P, et al. Reducing vitamin D requests in a primary care cohort: a quality improvement study. BJGP Open. 2020 Dec 15;4(5):bjgopen20X101090.

16. Felcher AH, Gold R, Mosen DM, et al. Decrease in unnecessary vitamin D testing using clinical decision support tools: making it harder to do the wrong thing. J Am Med Inform Assoc. 2017 Jul 1; 24(4):776-780.

17. Grobbee DE, Hoes AW, Verheij TJ, et al. The Utrecht Health Project: optimization of routine healthcare data for research. Eur J Epidemiol. 2005; 20(3):285-7.

18. Sociaal Cultureel Planbureau. SCP Statusscores 2016. [Internet]. Available from: https://www.scp.nl/Onderzoek/Lopend_onderzoek/A_Z_alle_lopende_onderzoeken/Statusscores/statusscores_2016. [Accessed 19th September 2017].

19. Knol FA. Van hoog naar laag; van laag naar hoog. Den Haag: Sociaal en Cultureel Planbureau; 1998.

20. Nederlands Huisartsen Genootschap. Laboratoriumdiagnostiek Vitamine D-deficiëntie (LESA). [Internet]. Available from: https://www.nhg.org/themas/publicaties/laboratoriumdiagnostiek-vitamine-d--deficiëntie-volledige-tekst. [Accessed 6th June 2018].

21. Nederlands Huisartsen Genootschap. Laboratoriumdiagnostiek Vitamine B12-deficiëntie (LESA). [Internet]. Available from: https://www.nhg.org/themas/publicaties/laboratoriumdiagnostiek-vitamine-b12-volledige-tekst. [Accessed 6th June 2018].

22. Nederlandse Zorg Autoriteit. Kengetallen en statistiek (Bijlage 1 bij Beoordelingsrapport pakket 2017). [Internet]. Available from: https://puc.overheid.nl/nza/doc/PUC_13003_22. [Accessed 2nd November 2019].

23. Levinson W, Kallewaard M, Bhatia RS, et al. 'Choosing Wisely': a growing international campaign. BMJ Qual Saf. 2015 Feb; 24(2):167-74.
24. Venkatesh AK, Hajdasz D, Rothenberg C, et al. Reducing Unnecessary Blood Chemistry Testing in the Emergency Department: Implementation of Choosing Wisely. Am J Med Qual. 2018 Jan/Feb;33(1):81-85.

25. Colla CH, Mainor AJ, Hargreaves C, Sequist T, Morden N. Interventions Aimed at Reducing Use of Low-Value Health Services: A Systematic Review. Med Care Res Rev. 2017 Oct;74(5):507-550.

26. Cadogan SL, Browne JP, Bradley CP, Cahill MR. The effectiveness of interventions to improve laboratory requesting patterns among primary care physicians: a systematic review. Implement Sci. 2015 Dec 5;10:167.

27. Crowe FL, Jolly K, MacArthur C, et al. Trends in the incidence of testing for vitamin D deficiency in primary care in the UK: a retrospective analysis of The Health Improvement Network (THIN), 2005-2015. BMJ Open. 2019 Jun 4;9(6):e028355.

28. Woodford HJ, Barrett S, Pattman S. Vitamin D: too much testing and treating? Clin Med (Lond). 2018 Jun;18(3):196-200.
Figures

Figure 1. Flow Diagram of the study and its participating health-centers.

Figure 2. Number of ordered vitamin tests in pre-intervention period (in quartiles) related to reduction in number of ordered tests during intervention period.

Tables

Table 1. Baseline characteristics of participating GPs, including pre-intervention numbers of vitamin testing.

| Characteristic                                      | Total | Intervention group                      | p-value |
|-----------------------------------------------------|-------|----------------------------------------|---------|
|                                                     |       | Strategy 1 (GP only)                   |         |
| Number of health-centers; N                         | 26    | 13                                     |         |
|                                                     |       | Strategy 2 (GP and patient intervention)|         |
| Number of GPs; N                                   | 156   | 78                                     | 0.85    |
| Male GPs; N (%)                                    | 47 (30)| 26 (32)                                | 0.72    |
| Population; N                                      | 195.394 | 97.658                                | 0.99    |
| SES; mean (range)                                  | 0.26 (-2.58-2.06) | 0.53 (-2.40-2.06) | 0.48    |
| Vitamin D tests pre-intervention; N                | 17.527 | 10.277                                | 0.30    |
| Vitamin D/1000 patients pre-intervention; N (range)| 88 (12-262) | 102 (32-262)                           | 0.22    |
| Vitamin B12 tests pre-intervention; N              | 12.304 | 7.242                                 | 0.36    |
| Vitamin B12/1000 patients pre-intervention; N (range)| 59 (7-198) | 69 (7-198)                           | 0.21    |
| GPs who followed e-learning                        | 76    | 28                                     | 0.11    |
| GPs present at 1st training session                | 50    | 26                                     | 0.86    |
| GPs present at 2nd training session                | 50    | 24                                     | 0.85    |

a SES data, linked by four digital postal codes to location of health-center
b Mean difference Utrecht-Rotterdam is -60 (95% CI -94- -26), p=0.06.
Table 2. Reduction in number of vitamin D and B12 tests.

| Characteristic                  | Total | De-implementation strategy |
|---------------------------------|-------|-----------------------------|
|                                 |       | Strategy 1 (GP only)        | Strategy 2 (GP and patient intervention) |
| Number of centers; N           | 26    | 13                          | 13                                      |
| **Vitamin D**                  |       |                             |                                         |
| Reduction; % (range)           | 23% (-9-70) | 19% (-4-70) | 29% (-9-28) |
| Absolute reduction in vit D/1000 patients; mean (range) | 22 (-6-98) | 24 (-6-98) | 21 (-6-51) |
| **Vitamin B12**                |       |                             |                                         |
| Reduction; % (range)           | 20% (-19-63) | 18% (-3-63) | 22% (-19-42) |
| Absolute reduction in vit B12/1000 patients; mean (range) | 12 (-6-69) | 15 (-3-69) | 9 (-6-63) |

Table 3. Results of ordered vitamin D and B12 tests.

|                      | Vitamin D | Vitamin B12 |
|----------------------|-----------|-------------|
|                      | Pre-intervention year | Intervention year | Pre-intervention year | Intervention year |
| **Average value**    | 56 nmol/l (5-327) | 55 nmol/l (10-309) | 304 pmol/l (34-1476) | 304 pmol/l (36-1476) |
| **Female pts, %**    | 72%       | 72%         | 72%                   | 72%                   |
| **Age pts; mean**    | 48 yr (SD 20) | 47 yr (SD 20) | 51 yr (SD 21)       | 50 yr (SD 20)         |
| **<Ref value; %**    | <50 nmol/l if >70yr: 30% | <50 nmol/l if >70yr: 32% | <148 pmol/l: 17% | <148 pmol/l: 16% |
|                      | <30 nmol/l if <70yr: 17% | <30 nmol/l if <70yr: 18% |                 |                      |
Figure 1. Flow Diagram of the study and its participating health centers

Primary Care Health Centers invited to participate (n=69)

Excluded (n=43)
- Not responded to invitation (n=40)
- Declined to participate (n=2)
- Other reasons (n=1)

Randomized (n=26)

Allocation

Allocated to de-implementation strategy 1 (n=14)
- Received allocated intervention (n=14)
- Did not receive allocated intervention (n=0)

Allocated to de-implementation strategy 2 (n=14)
- Received allocated intervention (n=14)
- Did not receive allocated intervention (n=0)

Follow-Up

Lost to follow-up (n=0)
Discontinued intervention (n=0)

Analysis

Analysed (n=14)
- Excluded from analysis (n=0)

Analysed (n=14)
- Excluded from analysis (n=0)
Figure 2. Number of ordered vitamin tests in pre-intervention period (in quartiles) related to reduction in number of ordered tests during intervention period.

357x166mm (96 x 96 DPI)