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**Letter to the Editor**

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# Long-term effects of interventions applied to optimize the use of 25-OH vitamin D tests in primary health care

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To the Editor,

In our previous publication [1], we evaluated the effects of six combinations of four different interventions on optimizing the use of biochemical tests in primary healthcare: A) sending out official guidelines from the Danish Board of Health [2], B) sending feedback reports periodically, C) non-interruptive alert and D) interruptive alert), using 25-OH vitamin D as a model test. We found that pop-up alerts caused a significant reduction in the number of tests requested (up to 46 %), whereas the guidelines and feedback reports, in the way that they were presented in our study, did not cause significant changes. A major concern of our findings was that test utilization did not become more appropriate in any of the intervention groups [1]. On the contrary, in the groups where the total number of tests decreased, the number of low results decreased proportionally.

As detailed in ref. [1], the interventions were randomly applied to six groups of primary healthcare clinics in the Region of Southern Denmark (RSD) from March 1, 2020 to February 28, 2021 A total of 313 clinics completed the original study and they were randomly divided into the seven groups (including the control group, also referred to as group 1). The randomization of the clinics was maintained in the present study. We chose 25-OH vitamin D as the model test because it was frequently requested by general practitioners (GPs) and because of the availability of official guidelines from the Danish Health Authority on the recommended use of the 25-OH vitamin D test. Here, we refer to this period as the "intervention period", while the pre-period, which includes data from March 1, 2019 to February 28, 2020, is referred to as the "background period."

In the present study, we report data on the annual number of ordered 25-OH vitamin D tests and the number of tests with 25-OH vitamin D measured at ≤50 nmol/L during two follow-up years after removal of the interventions from the same groups of GP clinics. The first year of follow-up (follow-up 1) started March 1, 2021 and lasted until February 28, 2022, and the second year of follow-up (follow-up 2) started March 1, 2022 and lasted until February 28, 2023.

The levels of 25-OH vitamin D measured with the tests were dichotomized, where results ≤50 nmol/L were considered insufficient and those >50 nmol/L were considered normal in accordance with the guideline concerning 25-OH vitamin D launched by the Danish Board of Health [3] and used in our study [1]. The number of tests where 25-OH vitamin D was measured in the blood at ≤50 nmol/L was used as an indicator of the appropriateness of the test.

A total of 279 primary healthcare clinics were eligible for inclusion in the follow-up years because they were active during all four study periods (background, intervention, follow-up 1, and follow-up 2; see Supplementary Material 1). Full calendar years were used in order to avoid any bias caused by seasonal variations in 25-OH vitamin D. During follow-up 1 and follow-up 2, a total of 34 clinics (12 %) dropped out of the study because their identification numbers were no longer active (see Supplementary Material 1). To investigate any possible bias caused by these dropouts, the patient

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characteristics across the groups were compared in terms of gender and age, and no differences were observed between follow-ups 1 or 2 and the intervention period (see Supplementary Material 2).

Statistical tests were performed on the patients' first measurements in each of the four periods using Stata/BE (Basic Edition) v. 17.0 [4]. A Poisson Generalized Estimating Equation (GEE) model using robust standard errors was utilized to obtain population-averaged incidence rate ratios (IRR) of the effect of the interventions on the number of 25-OH vitamin D tests requested by GPs during the first and the second years of follow-up. The statistical analysis was applied both to individual groups and to combined groups (guidelines ± feedback reports, non-interruptive pop-up ± feedback reports, and interruptive alerts ± feedback reports) (see Supplementary Material 3). Mixed effects logistic regression was applied to the dichotomized variable (i.e., 25-OH vitamin D tests measuring ≤50 nmol/L or >50 nmol/L). The model included follow-up 1 and follow-up 2, as well as interaction terms between follow-up 1 and follow-up 2 and the intervention group. The results are reported as odds ratios (ORs) (see Supplementary Material 4).

In follow-ups 1 and 2, the number of 25-OH vitamin D test requests increased significantly in all groups, including the control group compared to the intervention period ($p<0.05$). Figure 1 shows the mean number of 25-OH vitamin D tests per 1,000 patients in each group in the different periods. As shown in the figure, the number of 25-OH vitamin D tests rose in all groups during the follow-up periods compared to the intervention period. However, the statistical GEE model used to compute IRRs considered all time points and GPs in each group and revealed that the impact of the interventions persisted in groups 4, 5, 6, and 7 during follow-up 1, as these groups requested 12–29 % fewer 25-OH vitamin D tests compared to the control group ($p<0.05$). Groups 5, 6, and 7 still requested significantly fewer tests compared to the control group in follow-up 2, while group 4 was no longer significantly different compared to the control group at this time ($p=0.346$). Similar outcomes were observed in the combined groups (see Supplementary Material 3).

Consistent with that previously reported for the intervention period [1], no significant differences were observed between the groups that received feedback reports and those that did not in both the follow-up 1 and follow-up 2 periods ($p>0.05$) (Supplementary Material 3).

Across all groups, the number of 25-OH vitamin D test requests steadily increased from the intervention period to follow-up 1 and follow-up 2, indicating that discontinuing the interventions prompted GPs to return to their previous behavior. The groups in which the interventions had no significant effects during the intervention period surpassed their background levels of requests, whereas the groups with a significant decrease in the number of test requests during the intervention period still requested fewer 25-OH vitamin D tests during follow-up 1, and, for Groups 5, 6, and 7, this effect persisted in follow-up 2. However, all groups showed a steady increase in test requests, indicating that they already have or may soon surpass their previous levels if no further action is taken.

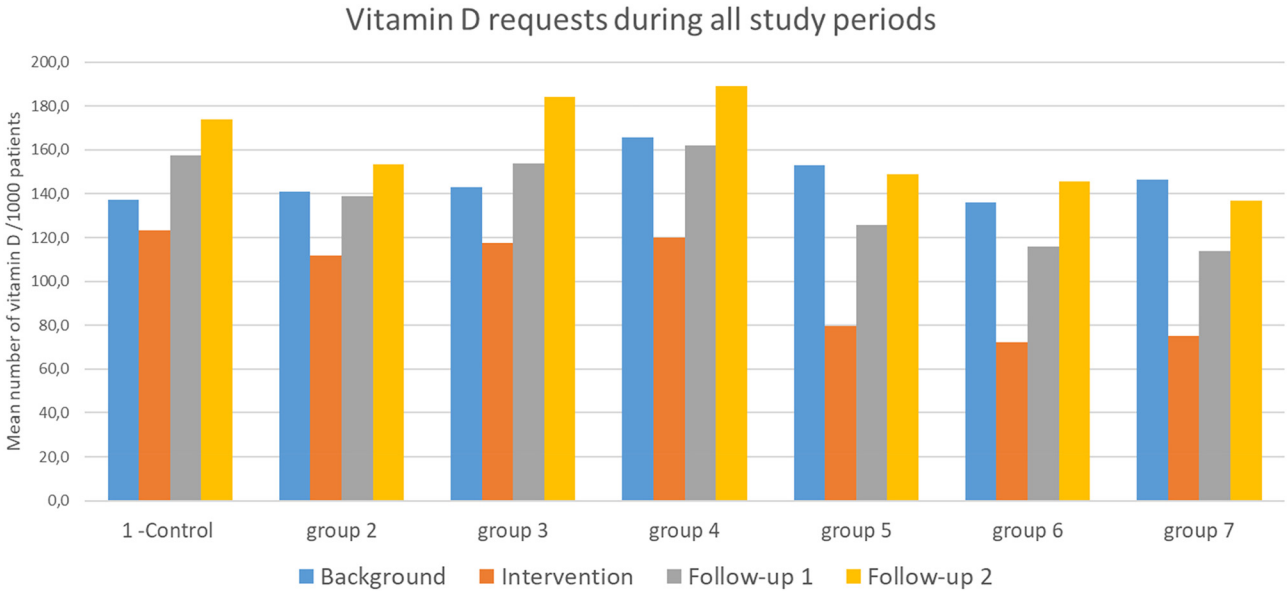


**Figure 1:** Vitamin D test requests by all groups throughout the entire study of four years. All periods had a duration of one year.

The relative number of tests where 25-OH vitamin D levels were measured at ≤50 nmol/L increased in all groups during both the follow-up 1 and follow-up 2 periods. In addition, the odds of doctors identifying patients with 25-OH vitamin D levels ≤50 nmol/L significantly increased compared with the background period in all groups (including the control group) in both follow-up 1 (ranging from 15 to 31 %) and follow-up 2 (ranging from 20 to 42 %; see Supplementary Material 4), indicating a generally more appropriate use of the test. This is in contrast to the intervention period, where a more appropriate use of 25-OH vitamin D tests was not observed [1]. The increase in appropriateness during the follow-up period could not be related to the interventions as this observation was made in all groups, including the control group. Thus, the change towards increased appropriateness may be attributable to the unspecific effects of a strong focus on the use of 25-OH vitamin D tests in the region caused by the large, long-lasting, and unblinded study [1].

Very few studies have examined the long-term effects of interventions on test ordering [5–8]. Existing studies have tended to focus on educational interventions combined with administrative changes, such as revising requesting profiles or changing requesting forms. The effects of these types of interventions seem to help ensure that changes persist, even in case of doctor turnover in the clinics, which may be one of many reasons why interventions lose their effectiveness over time. However, similar to that observed in the current study, others have reported that when administrative interventions are disrupted, GPs quickly return to their previous ordering patterns [5].

To our knowledge, this investigation is the first to evaluate the long-term effects of several different interventions on test ordering in the primary healthcare setting. The most important limitation of this study lies in the fact that several clinics dropped out before the study was completed. While it cannot be excluded that this may have affected our results, dropout is a natural consequence of a long study period of four years and is consistent with the turnover rate of GP clinics in this region. However, we did not observe differences in the patients' ages or genders between the intervention period and the follow-up periods in any of the groups. Thus, we believe that our results are not biased due to clinic dropout.

The current results highlight the challenges of maintaining the impact of interventions on laboratory test ordering behavior over time. Our findings indicate that, even in groups receiving interventions that resulted in considerably fewer requested tests, test requests increased when the interventions were removed. Thus, there is a need to develop more effective and long-lasting interventions to optimize laboratory test ordering in the primary healthcare setting.

Our results must be also evaluated in the context of a healthcare system where neither the patient nor the requestor is charged for laboratory tests. In other healthcare systems, it may be possible to make the requestors financially responsible for all requested tests or for inappropriate tests. However, these systems may suffer from other drawbacks, such as the underuse of relevant tests due to economic reasons.

One potentially effective intervention that would be applicable worldwide involves implementing educational strategies that aid doctors in comprehending and identifying the factors that contribute to the inappropriate use of laboratory tests. This approach can assist doctors in revising their test-requesting profiles. Additionally, displaying alerts periodically and reevaluating traditional feedback reports by providing information on clinically relevant results along with (or instead of) the traditionally reported total number of tests requested may prove beneficial, as it has been demonstrated that feedback reports are tools with a high visibility among GPs [9]. Combining and integrating these various approaches may optimize laboratory test utilization and ensure a sustained impact of interventions over time.

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**Informed consent:** Informed consent was obtained from all individuals included in this study.
**Author contributions:** All authors have accepted responsibility for the entire content of this manuscript and approved its submission. The author TRL changed job position during the study period.
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