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Improving Vitamin D testing and supplementation in children with newly-diagnosed cancer: A Quality Improvement Initiative at Rady Children's Hospital San Diego

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Abstract

Background: Vitamin D deficiency and insufficiency have been associated with poorer health outcomes. Children with cancer are at high risk for Vitamin D deficiency and insufficiency. At our institution, we identified high variability in Vitamin D testing and supplementation in this population. Of those tested, 65% were Vitamin D deficient/insufficient. We conducted a quality improvement (QI) initiative with aim to improve Vitamin D testing and supplementation among children aged 2-18 years old with newly-diagnosed cancer to ≥ 80% over 6 months.

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1. Improving the approach for Vitamin D diagnostic testing and supplementation in newly diagnosed pediatric cancer patients at Rady Children's Hospital San Diego. Pediatrics Research Symposium, San Diego, January 2017.
2. You Can't Find What You Don't Seek: Vitamin D Testing and Treatment in Pediatric Cancer Patients. PAS, San Francisco, May 2017.

Methods: An inter-professional team reviewed baseline data, then developed and implemented interventions using Plan-Do-Study-Act (PDSA) cycles. Barriers were identified using QI tools, including lack of automated triggers for testing and inconsistent supplementation criteria and follow-up testing post-supplementation. Interventions included an institutional Vitamin D guideline, clinical decision-making tree for Vitamin D deficiency, insufficiency and sufficiency, electronic medical record triggers, and automated testing options.

Results: Baseline: N=26 patients, four (15%) had baseline Vitamin D testing; two (8%) received appropriate supplementation. Post-intervention: N=33 patients; 32 (97%) had baseline Vitamin D testing; 33 (100%) received appropriate supplementation and completed follow-up testing timely (6-8 weeks post-supplementation). Change was sustained over 24 months.

Conclusions: We achieved and sustained our aim for Vitamin D testing and supplementation in children with newly-diagnosed cancer through inter-professional collaboration of hematology/oncology, endocrinology, hospital medicine, pharmacy, nursing, and information technology. Future PDSA cycles will address patient compliance with Vitamin D supplementation and impact on patients' Vitamin D levels.

Keywords

pediatric cancer; Vitamin D deficiency; Vitamin D supplementation; quality improvement; clinical guidelines

Introduction

Vitamin D plays an important role in calcium homeostasis and bone health.[1, 2] Large ecological studies have suggested a link between Vitamin D deficiency and low UVB irradiation with increased cancer incidence and mortality.[3, 4] These studies highlight a broader role for Vitamin D in the human body than previously believed, with effects on immune function, metabolism [5, 6] and cancer pathophysiology.[7, 8]

Adequate calcium and Vitamin D levels are important for growing children and essential for adult bone health. Adequate calcium and Vitamin D intake, in conjunction with adequate physical activity, are recommended for cancer survivors, as well as for the general population. Children diagnosed with acute lymphoblastic leukemia are treated with systemic corticosteroids and have increased rates of skeletal complications such as osteoporosis and vertebral fractures during and after their treatment.[9, 10] Additionally, suboptimal Vitamin D levels have been associated with lower survival rates after stem-cell transplantation[11] and in patients with Hodgkin Lymphoma.[8]

Data on Vitamin D deficiency and insufficiency among children with newly-diagnosed cancer are very limited. Children with cancer are at high risk for Vitamin D deficiency and insufficiency due to inadequate sun exposure and treatment-related complications, such as poor diet, hepatotoxicity and/or nephrotoxicity of chemotherapeutic agents, impaired absorption due to mucositis and/or colitis, and interference of Vitamin D metabolism by glucocorticoids. Current Endocrine Society Clinical Practice Guidelines on the evaluation, treatment, and prevention of Vitamin D deficiency recommend testing patients at risk for deficiency with the measurement of serum 25(OH)D concentrations, followed by treatment

with either oral Vitamin D2 or Vitamin D3 supplementation in patients found to be deficient or insufficient.[12] Research from our group showed that Vitamin D supplementation significantly increases serum 25(OH)D concentrations.[13]

Low bone mineral density has been reported in pediatric cancer survivors even several years after completion of cancer therapy.[14, 15] Current national survivorship guidelines[16] recommend a baseline bone mineral density evaluation followed by laboratory assessments, in order to evaluate bone health beginning two years after therapy completion, particularly for patients with history of acute lymphoblastic leukemia.[15, 16]

Clinical research and Quality Improvement (QI) initiatives aimed at improving Vitamin D status in this population are lacking. We have previously reported that Vitamin D deficiency and insufficiency are common in children with newly-diagnosed cancer. Hispanic patients, females and older children were at higher risk for Vitamin D deficiency and insufficiency at our institution.[13]

At Rady Children's Hospital San Diego, we noted high variability in Vitamin D testing, supplementation and follow-up testing post-supplementation for children with newly-diagnosed cancer. We conducted a QI initiative with the global aim to improve overall bone health among children with newly-diagnosed cancer by standardizing Vitamin D testing and supplementation (from November 1, 2015 to January 31, 2016 - baseline phase; from February 1, 2016 to June 30, 2016 – intervention phase) and monitored sustainability of the intervention phase until June 2018.

Methods

Clinical Setting and Electronic Medical Record

This study was conducted at Rady Children's Hospital San Diego, a large tertiary academic institution. Pediatric cancer care is provided at the Peckham Center for Cancer and Blood Disorders, the largest pediatric cancer care facility in a region that includes around one million children. Approximately 260 new cases of pediatric cancer are diagnosed annually at our institution. Most patients require treatment with chemotherapy, radiation, immunotherapy, stem-cell transplant, or a combination of these modalities.

During clinic visits and hospital admissions, patients with cancer are seen either by advanced practice providers (8) and fellow physicians (6), with a supervising pediatric hematology/oncology attending physician (18) acting as the preceptor, or solely by an attending physician. All clinical documentation is completed electronically in a commercial electronic medical record (EMR) [Epic® Systems Corporation, Verona, Wisconsin], which was implemented six years prior to the beginning of our QI initiative.

Target oncology population

We previously conducted a retrospective research study to assess Vitamin D status and its socio-demographic and clinical correlates in 163 children with cancer, using 25-hydroxy vitamin D (25(OH)D) concentrations.[13] Based on the Endocrine Society guidelines,[12] we found that 65% of the patients with newly-diagnosed cancer had low Vitamin D levels.

Fifty-two patients (32%) were Vitamin D deficient, and 53 (33%) were insufficient. Age over 10 years, Hispanic ethnicity, and female sex were significantly associated with lower 25(OH)D concentration at diagnosis.[13] Based on these research findings, we initiated our QI initiative in November 2015. Prior to the start of the project, our institution did not have a written guideline for Vitamin D testing, supplementation, and follow-up testing post-supplementation in children with newly-diagnosed cancer. Testing for Vitamin D and supplementation was done at the discretion of the treating oncology provider, with only 15% of patients having baseline Vitamin D testing and 8% receiving appropriate supplementation. Our QI initiative included children with newly-diagnosed cancer 2-18 years of age who needed treatment with chemotherapy and/or radiation.

QI Team and Specific Measurable Achievable Relevant and Timely (SMART) Aim

After reviewing the data from our retrospective study revealing high prevalence of Vitamin D deficiency and insufficiency, we assembled an inter-professional QI team.

Our QI team followed the Institute for Healthcare Improvement's Model for Improvement[17] and the QI leader completed formal QI training. The QI leader was a pediatric Hematology/Oncology physician who worked closely with the team that included physician champions, nursing staff, QI advisors, and content experts from pediatric hematology/oncology, pediatric endocrinology, hospital medicine, pharmacy, and information technology (IT).

In person QI team meetings were held every two weeks, beginning with the planning phase and throughout the project to address interventions, discuss unexpected observations and problems encountered, review study data and decide on interventions to be implemented.

The entire team participated in development of the Key Driver and Ishikawa diagrams (Figures 1 & 2), the SMART Aim, the decision-making tree (Figure 3) and reviewed the Plan-Do-Study-Act (PDSA) cycles. Input from other key stakeholders (physicians, advanced practice providers, oncology case managers, pharmacists, inpatient and outpatient nurses) was obtained about potential barriers and facilitators to Vitamin D testing at the time of initial cancer diagnosis and proposed supplementation strategies. The QI team leader contributed approximately six hours of time each week during the first four months of the project and then approximately four hours per week during subsequent months.

Our SMART Aim was: Increase compliance with institutional guidelines for Vitamin D testing and supplementation in children with newly diagnosed cancer (age 2-18 years) from 15% to ≥80% by June 30, 2016 and sustain over 6 months.

Interventions

Our institution has successfully used and sustained evidence-based order sets that include clinical decision-making elements for other conditions.[18] The team used this existing framework, QI tools, and the PDSA methodology[17] to understand barriers to improvement and implement interventions. To enable rational design of interventions, the QI team identified factors that drive the Vitamin D testing, supplementation and follow-up testing post-supplementation. Potential barriers and facilitators and primary drivers are described in Ishikawa (Figure 1) and Key Driver (Figure 2) diagrams.

After considering the feasibility, published evidence, and local culture, the team decided on the following interventions: 1) development of an institutional guideline for Vitamin D testing, supplementation and follow-up testing post-supplementation; 2) education on Vitamin D deficiency and insufficiency testing and supplementation for oncology providers (N=32); 3) creation and distribution of a clinical decision-making tree for Vitamin D deficiency, insufficiency, and sufficiency [Figure 3]; 4) incorporation of EMR triggers and Vitamin D automated testing options; 5) inclusion of the Vitamin D laboratory order into the pre-existing oncology order sets; and 6) creation of a Best Practice Advisory (BPA) alert to be triggered if the patient did not have recent Vitamin D testing, or if testing was done but the patient was not prescribed Vitamin D (Figure 4). *Baseline-Pre-intervention assessment, Ishikawa and Key Driver diagrams, process map, and development of institutional guideline (November 1, 2015 to January 31, 2016).*

We collected baseline data, compiled and analyzed Ishikawa results, and completed a process map. Barriers such as lack of automated triggers/reminders for testing, inconsistent criteria used for testing and supplementation, and inability to obtain follow-up testing post-supplementation were identified. Key drivers included (Figure 2): physicians' knowledge about when to test and how to supplement Vitamin D; guideline and decision-making tree widely available; integration into clinical workflows and facilitated by automated triggers in EMR; and leadership awareness and support. In collaboration with a pediatric endocrinologist we reviewed national best practices and created an institutional guideline and clinical decision-making tree for Vitamin D testing, supplementation and follow-up testing post-supplementation (Figure 3). We utilized 25(OH)D as the most accurate way to measure Vitamin D status in our patients. The pediatric endocrinologist provided input regarding supplementation and follow-up testing post-supplementation based on the Endocrine Society Guidelines.[12] We defined Vitamin D deficiency as 25(OH)D concentration of <20 ng/ml, insufficiency ≥20 and <30 ng/ml, and sufficiency ≥30 ng/ml. Based on the patient's 25(OH)D concentration, supplementation was prescribed and follow-up testing post-supplementation was completed per the clinical decision-making tree (Figure 3).

Intervention phase (February 1, 2016 to June 30, 2016).—We conducted an educational intervention focused on Vitamin D deficiency and insufficiency testing and supplementation for oncology providers (physicians and advanced practice providers), nurses, case managers, and pharmacists via direct one-on-one in-person communication, structured in-person lectures and secure e-mails.

The decision-making tree was not built into the BPA, but it was distributed as hardcopy to team members. It was also posted in the inpatient unit, outpatient clinic working area, and was made electronically available via our secure shared oncology folder online.

EMR triggers and Vitamin D automated testing options were incorporated. A Vitamin D laboratory order was added into the pre-existing oncology admission order set as well as in Beacon chemotherapy treatment plans, an Epic® oncology module for physicians and pharmacists to create treatment and supportive care plans based on standardized protocols that also allows for easy modification. A BPA alert was created (Figure 4) that triggered

if the patient had a chemotherapy treatment plan in place but did not have recent Vitamin D testing, or if Vitamin D testing was done but the patient was not prescribed Vitamin D. BPA alert was sensitive to the Vitamin D level and suggested appropriate supplementation depending on the Vitamin D level result.

In order to assess our process and balancing measures and end-user value, we created a 6-question secure online de-identified survey utilizing the SurveyMonkey® platform. The survey was administered to oncology providers after interventions were executed. The survey included the following questions: 1) What are the barriers preventing Vitamin D initial testing at the time of cancer diagnosis? (Free text response); 2) Do you use the Vitamin D supplementation decision-making tree? (Likert scale); 3) Do you find the Vitamin D supplementation decision-making tree helpful? (Likert scale); 4) What are the barriers preventing repeat Vitamin D testing at 6-8 weeks after Vitamin D supplementation initiation? (Free text response); 5) Do you use the Vitamin D BPA? (Likert scale); 6) Do you find Vitamin D BPA reminders helpful? (Likert scale). For questions 2, 3, 5 and 6, a traditional Likert scale with 1-5 ratings was used to assess value/usefulness, with 1 = none, 2 = little, 3 = some, 4 = moderately high, and 5 = high. The percentage of results for “moderately high“ or “high” for each question were reported.

Data collection and analysis

The QI leader identified newly-diagnosed patients through an automated new diagnosis banner in the EMR. We performed frequent monitoring of newly-diagnosed patients to ensure that all cases were captured.

Standardized definitions for Vitamin D deficiency, insufficiency and sufficiency were used.[12] EMRs of patients aged 2–18 years old with newly-diagnosed cancer were reviewed, including provider notes, lab testing orders and results, and prescriptions. Rates of Vitamin D testing, supplementation and follow-up testing post-supplementation were obtained at different time points, from November 1, 2015 to January 31, 2016 (baseline) and from February 1, 2016 to June 30, 2016 (post-intervention), and averaged over seven-day periods. To assess sustainability, we obtained data every two months until June 2018.

Outcome measures of testing and supplementation were chosen to assess the system improvement; supplementation was also identified as a feasible proxy for clinical outcome improvement by the team. We chose decision-making tree use as process measure and perceived utility of the decision-making tree and automated triggers were chosen as balancing measures to assess end-user buy-in.

Weekly documentation rates were plotted on a control chart during the study phase of each PDSA cycle to identify non-random signals of change in Vitamin D testing (Figure 5) and supplementation and follow-up testing post-supplementation (Figure 6). We used statistical process control with our primary outcomes measure of proportion of patients who had a Vitamin D test and appropriate supplementation, displayed on a p-chart. We followed established rules for differentiating special versus common cause variation. We used proportions to track process and balancing measures. Both the run chart and p-control chart were generated with QI Macros® for Microsoft Excel™[19].

Ethics and Project Communication

This QI study was reviewed and deemed to not be human subjects research and a QI exemption waiver was granted by the University of California San Diego/Rady Children's Hospital San Diego Institutional Review Board.

The results, successes and barriers we encountered during the project were shared with the oncology providers on a regular basis. Communications included weekly updates on the progress of the initiative, monthly updates to division leadership, and annual reports to hospital leadership.

Results

Twenty-six patients were evaluated during the initial baseline three-month period:11 patients (42%) with hematological malignancies, 15 patients (58%) with malignant solid tumors, mean age at the time of diagnosis was 8.9 years ±5.4, 10 patients (38%) were males and 16 (62%) females. Only four (15%) patients had baseline Vitamin D testing. Three patients had concentrations that should have required supplementation, but only two (66%) were prescribed the appropriate supplement.

Thirty-three patients were included in the intervention group: 27 patients (88%) with hematological malignancies and six patients (12%) with malignant solid tumors, mean age at the time of diagnosis was 8.6 years ±5.2, 19 patients (57%) were males and 14 (43%) females. We calculated a centerline rate of 80% of patients having a baseline Vitamin D test performed and receiving appropriate supplementation and follow-up testing. After our interventions, we noted special cause variation with 97% of patients having a baseline Vitamin D testing performed, starting in May 2016. A hundred percent of patients received appropriate supplementation and completed follow-up testing at the appropriate time (6-8 weeks post-supplementation). Compared to baseline, we tested 27 more patients and identified 10 more patients. From July 2016 to June 2018, over 80% of patients had both baseline Vitamin D testing performed, received appropriate supplementation and completed follow-up testing post-supplementation, demonstrating post-intervention sustainability over time (Figures 4 and 5). The perceived utility and use survey was completed by 16 out of 24 clinicians. Process and balancing measures were assessed and showed 1) end-user perceived utility of the decision-making tree was 67%, and 3) end-user perceived utility of automated triggers was 86%.

Discussion

Summary

Through inter-professional collaboration with hematology/oncology, endocrinology, hospital medicine, pharmacy, and IT, we successfully improved the testing, diagnosis, supplementation and monitoring of Vitamin D deficiency and insufficiency for children with newly-diagnosed cancer and demonstrated sustainability over 24 months. We achieved and sustained our aim to improve Vitamin D testing, adequate Vitamin D supplementation and accurate and timely follow-up testing post-supplementation. We exceeded our SMART

Aim of ≥80% compliance with the newly developed institutional guideline and clinical decision-tree after implementation and sustained our aim of ≥80% over time.

Our QI methodology led to successful establishment of the QI team, with specific roles for team members; continued communication of the QI initiative aim and progress to staff; two-way feedback on processes implementation; and accurate and efficient patient identification for data analysis. Particular strengths of our project include the implementation of higher reliability level EMR-based interventions by the IT team, such as automated BPA alerts and triggers for Vitamin D laboratory testing and monitoring. These interventions may have contributed to the observed increase in compliance with the newly developed institutional guideline for Vitamin D testing and supplementation.

Interpretation

After conducting educational interventions regarding the standardized criteria for Vitamin D deficiency and insufficiency diagnoses, and the clinical decision-making tree for adequate supplementation, we observed a significant increase in testing and supplementation rates. This finding is consistent with previous studies showing that passive EMR features such as BPA alerts need to be accompanied by complementary strategies such as educational interventions to improve compliance with guidelines and achieve sustainability over time.[20]

Regular feedback (every two weeks) about group performance, compared to prior performance was provided via email and during routine division meetings. Feedback was positively received, and helped motivate oncology providers to further adhere to the newly implemented practices. Although additional research is needed to establish the benefit of performance feedback (individual or group) in improving guideline compliance and sustained culture change, our findings support previous studies showing the positive impact of providing timely feedback on improving clinical practice and EMR documentation.[21] Additionally, hospital leadership support and awareness of the clinical need, and frequent communication with key stakeholders contributed to achieving and sustaining our aim. There were no added costs associated with this project: EMR changes were completed by existing IT staff. We did not specifically assess loss of the ability to perform other tasks or meet other responsibilities resulting from instituting this initiative. However, the survey did query on barriers, and the lack of comments about competing priorities suggests this project did not adversely affect clinical workflows.

Limitations

There are several limitations in our project to be discussed. First, we reviewed data for three months prior to our interventions on a small group of patients. Studying pre-intervention data in a larger group and over a longer period may help to determine temporal variation. Second, our EMR interventions were geared toward BPA alerts and automated testing options in our admission and chemotherapy order sets, which are specific components of our EMR and may not be reproducible in other practices that do not use a similar EMR. While motivations for performing testing or prescribing supplementation were not explored, providers' perceived utility of the decision-making tree and automated triggers, and positive feedback of frequent reports and reminders, contributed to steady improvement over the

first 4 months of the QI initiative and sustainability for 24 months. Our QI initiative could have been further strengthened by assessing additional balancing measures to determine whether there were unintended consequences in other parts of the clinical workflow as a result of our QI initiative, such as documentation of time spent by the provider reviewing the clinical decision-making tree, ordering tests and prescribing supplementation. We did encounter barriers while implementing our QI initiative that may be helpful to highlight for other institutions. Providers had different testing habits, personal beliefs, and varied degrees of resistance to change. Prescription processes and coverage varied by insurance type, which required some added steps for some patients. Lastly, our intervention included BPA alerts, which are carefully managed and in limited number at our institution. In order to engage end-users, the BPA was constructed with team input. Sites with multiple active BPAs may find that this intervention adds to alert fatigue.[22]

Conclusion

Our inter-professional QI initiative, which incorporated automated tools within the EMR, demonstrated success in improving Vitamin D testing and supplementation in children with newly-diagnosed cancer in a large tertiary academic institution with a high prevalence of Vitamin D deficiency and insufficiency. This QI approach may be replicated in similar settings. Future PDSA cycles will address patient compliance with Vitamin D supplementation. QI methodology will continue to be used in the future to improve adherence to other testing and medication prescribing procedures for children with cancer at our institution.

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Conflict of Interest statement

This project was partially supported by the National Cancer Institute K08 CA230306 (Aristizabal) and Dedman Family (Shliakhtsitsava). The content is solely the responsibility of the authors and does not represent the official views of the National Cancer Institute or the National Institutes of Health.

Data availability statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Abbreviations key:

BPA	Best Practice Advisory
ng/ml	Nanogram/milliliter
PDSA	Plan-Do-Study-Act

QI	Quality Improvement
UVB	Type B ultraviolet

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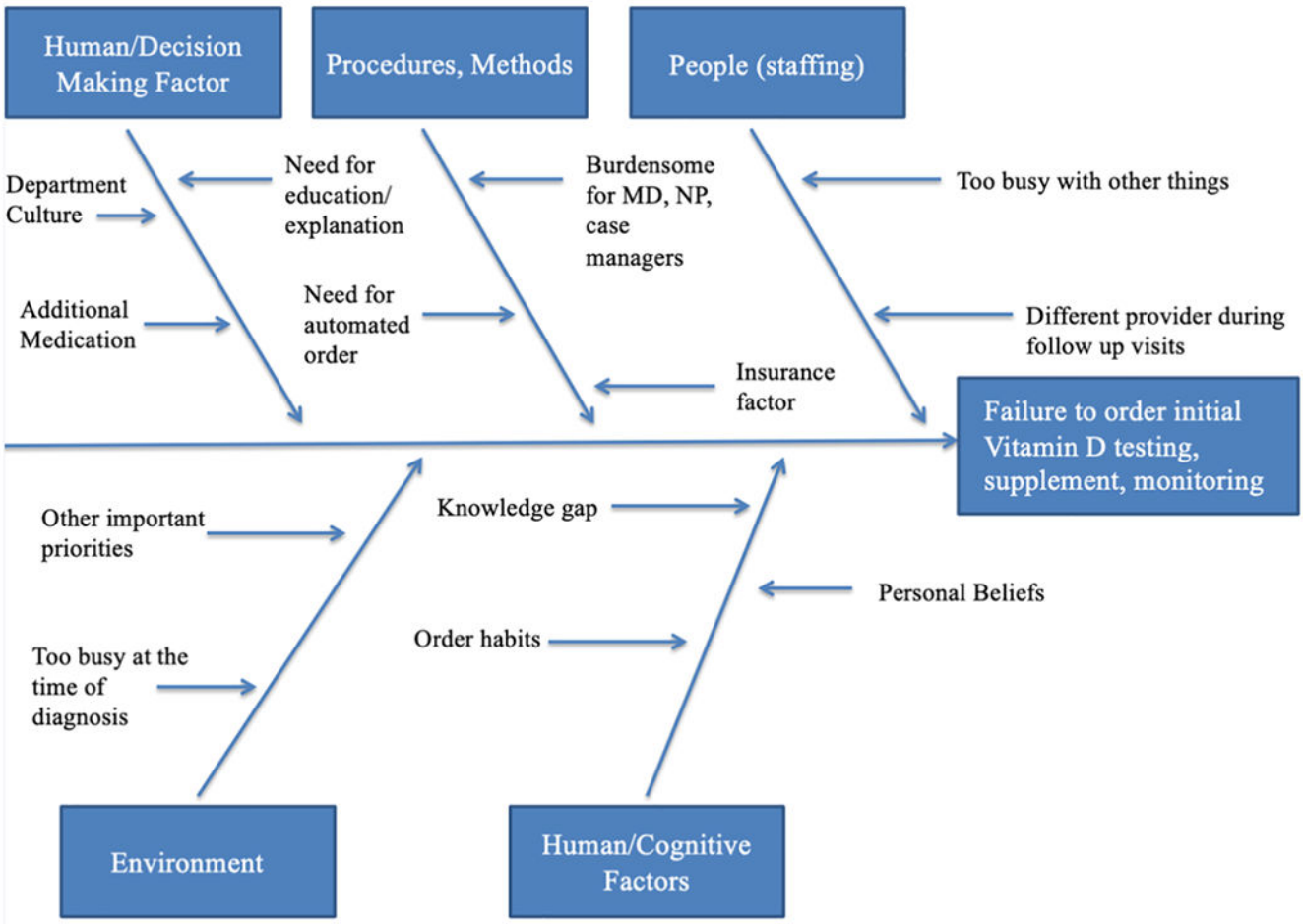

FIGURE 1.
Ishikawa diagram.

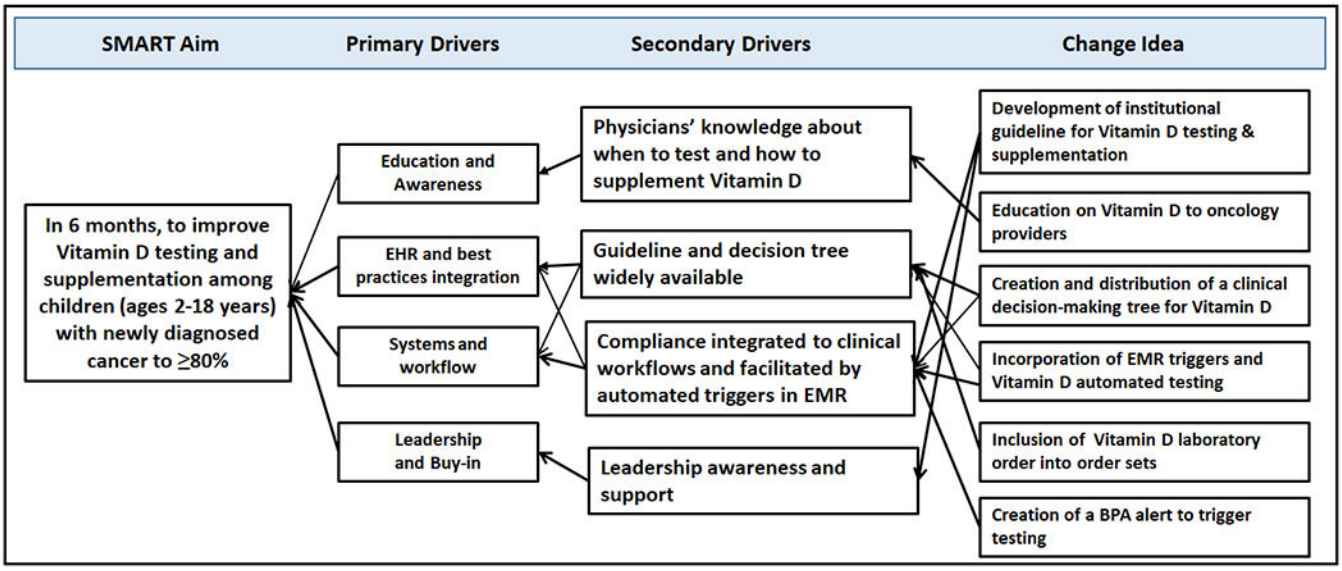

FIGURE 2.
Key driver diagram.

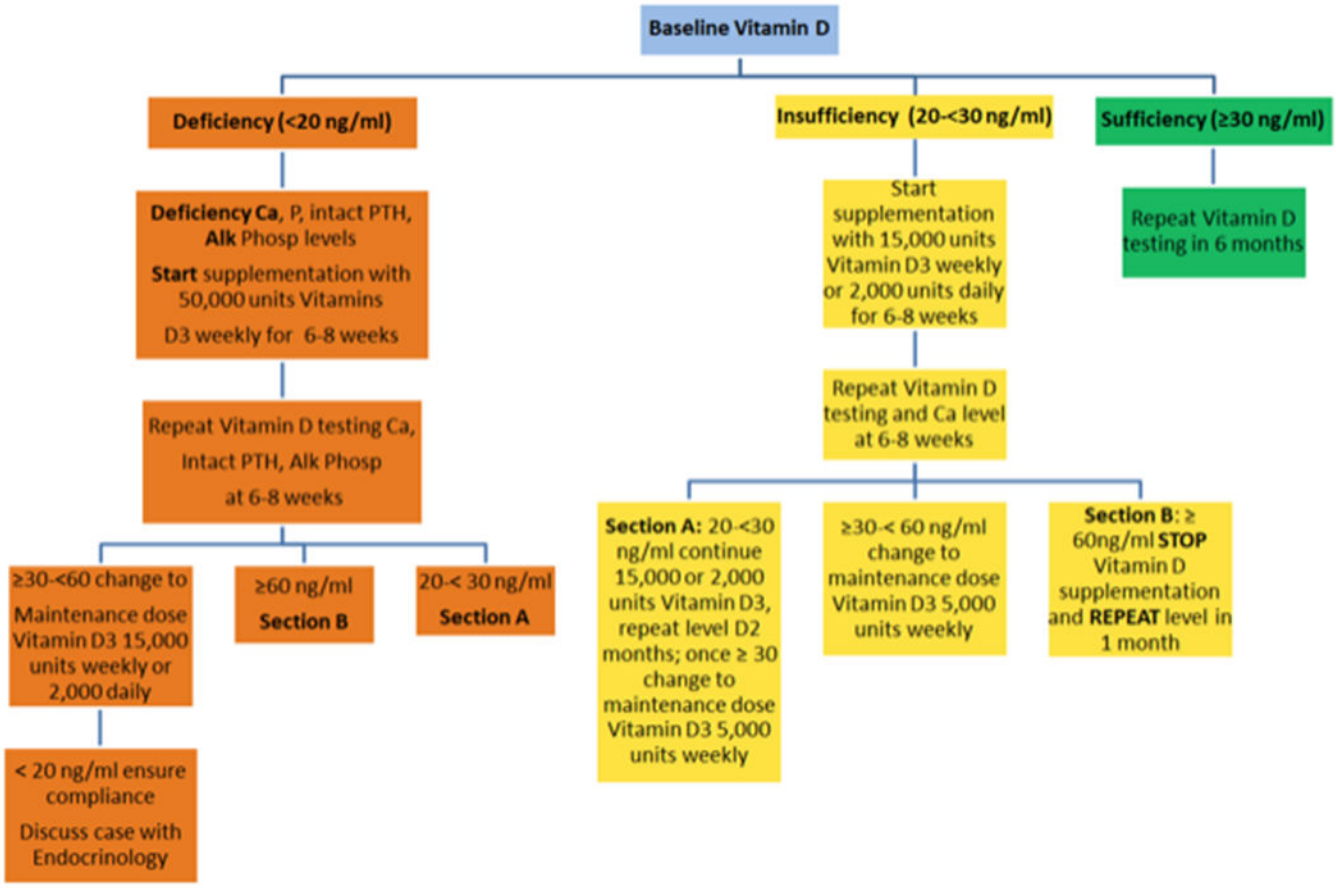

FIGURE 3.
Decision-Making Tree.

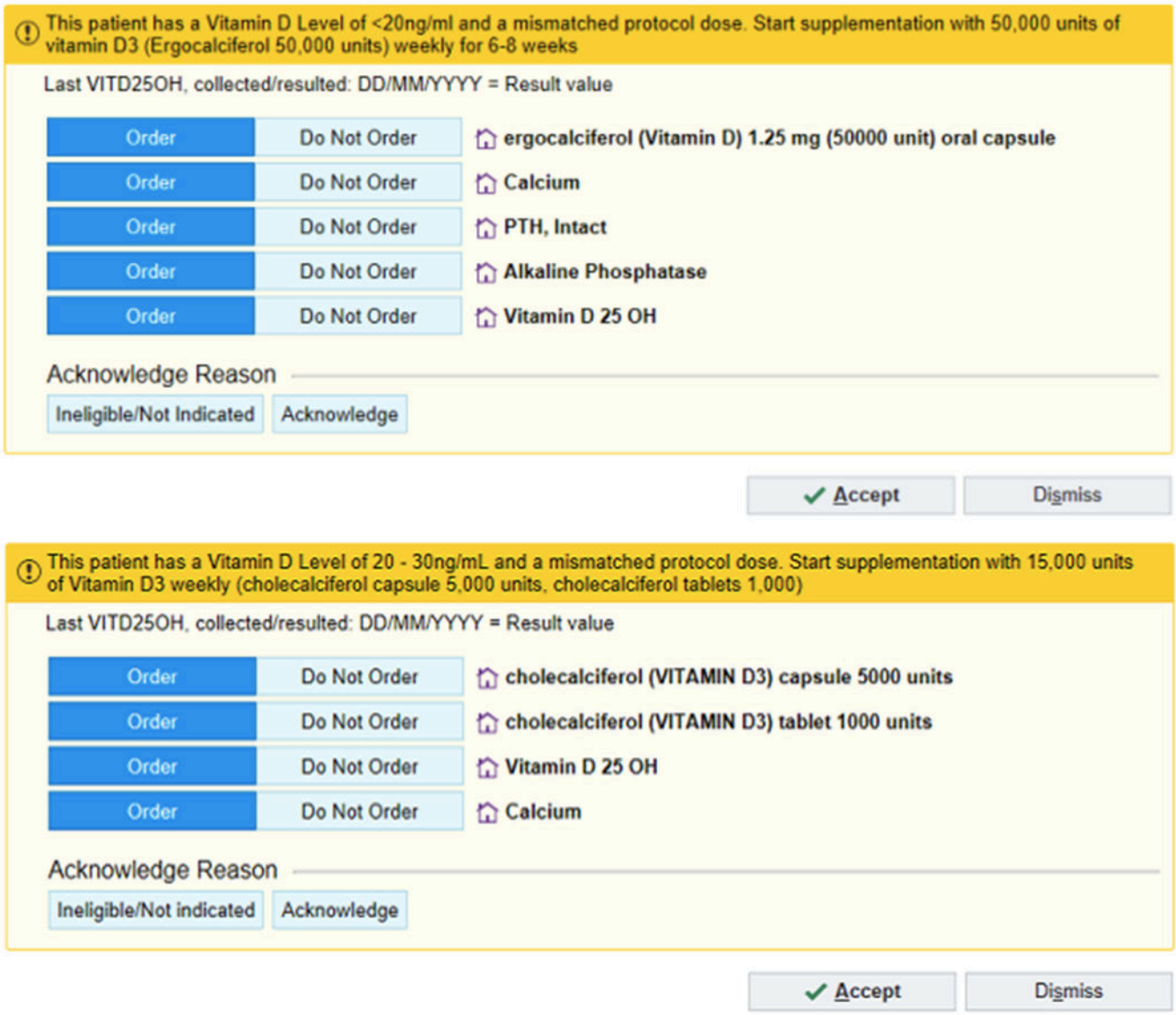

FIGURE 4.
Best Practice Alert (BPA).

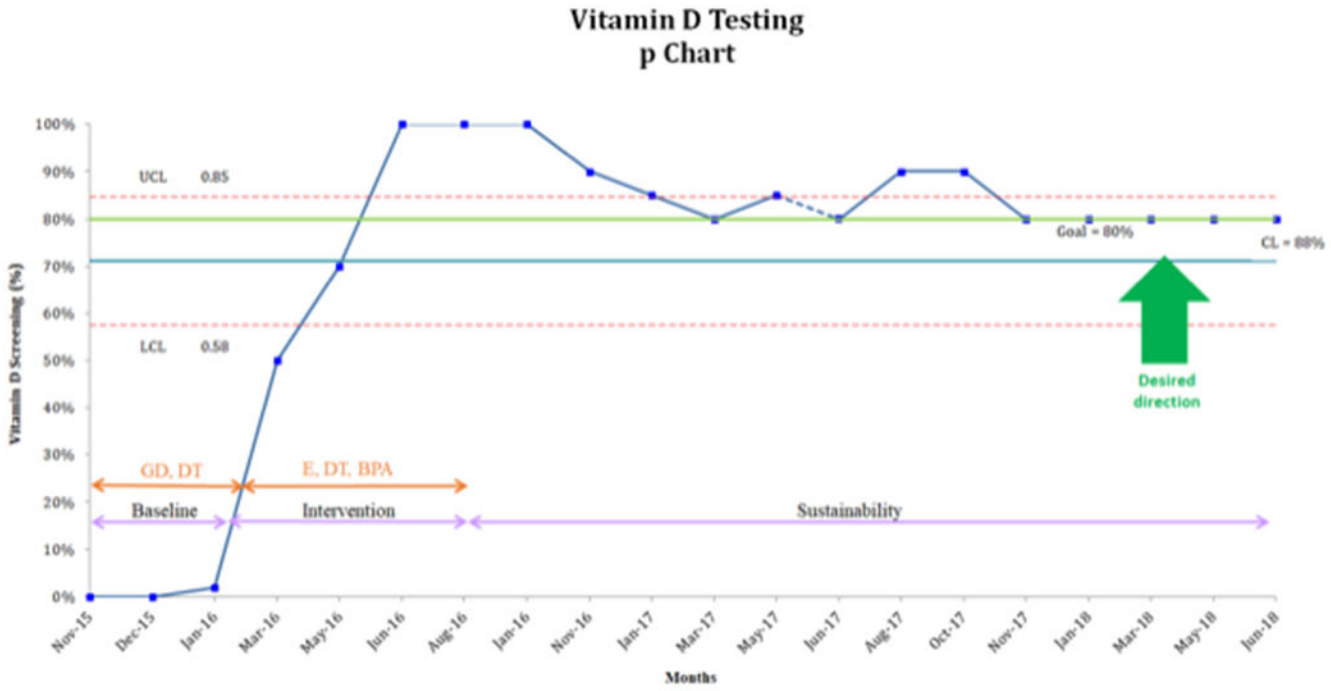

FIGURE 5.

Vitamin D testing rates. P-chart with vitamin D testing and annotated improvement interventions in orange. Desired direction of change is noted in bold green arrow. GD Guideline development; E, Education; DT, Decision making tree; BPA, Best Practice Alert; CL, centerline; LCL, lower control limit; UCL, upper control limit. Baseline phase= GD and DT development; Intervention phase = E, DT implementation, Electronic Medical Record (EMR) triggers (BPA). Baseline phase start date: November 1, 2015; intervention phase start date: February 1, 2016, interventions were launched at the same time in February, 2016; sustainability phase start date: July 1, 2016.

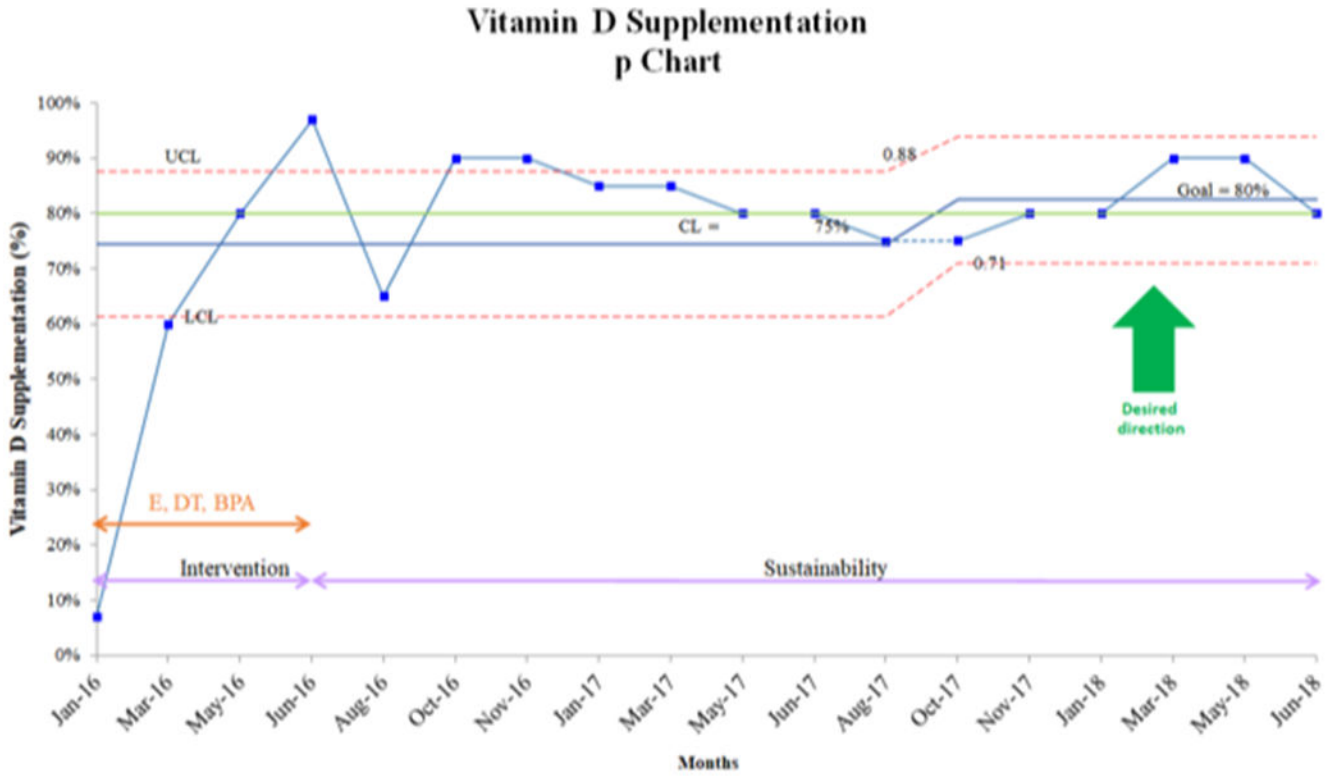

FIGURE 6.

Vitamin D supplementation and follow-up post-supplementation rates. P-chart with vitamin D supplementation. Desired direction of change is noted in bold green arrow. E, Education; DT, Decision making tree; BPA, Best Practice Alert; CL, centerline; LCL, lower control limit; UCL, upper control limit. Intervention phase = E, DT implementation, Electronic Medical Record (EMR) triggers (BPA). Intervention phase start date: February 1, 2016, interventions were launched at the same time in February, 2016; sustainability phase start date: July 1, 2016.