Original Research

Assessment of Healthcare Professionals' Knowledge About Warfarin-Vitamin K Drug-Nutrient Interactions

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Objective: Dietary vitamin K can interact with oral anticoagulant drugs and interfere with their therapeutic safety and efficacy. Therefore, knowledge about drug-nutrient interactions involving vitamin K possessed by physicians, pharmacists, dietitians and nurses practicing anticoagulant therapy was assessed.

Methods: Healthcare practitioners were surveyed using a 30-question, 98-item questionnaire on the most common and/or important food interactions with warfarin, drug interactions with warfarin and general drug-nutrient interactions involving vitamin K. The study sample included 160 randomly selected healthcare providers (40 physicians, pharmacists, dietitians and nurses) from 10 hospitals with 200 to 1000 beds from six Massachusetts regions. Random selection was conducted from a pool of selected healthcare providers practicing anticoagulant therapy who counsel patients receiving warfarin.

Results: All surveys were completed within three months of the start of the study, and all participants provided usable data for statistical analysis. The mean scores ($\pm$SD) on the overall test were 72.5$\pm$9.0 for pharmacists, 62.5$\pm$10.6 for physicians, 56.9$\pm$8.8 for dietitians and 50.2$\pm$9.3 for nurses, with 100 being a perfect score. Pharmacists scored significantly higher in the area of drug interactions (75.9$\pm$11.3, $p<0.05$). Dietitians scored higher in the area of food interactions (73.0$\pm$10.3). No significant differences between physicians and pharmacists were evident on general drug-nutrient interactions. While over 87% of the healthcare professionals correctly identified some common foods containing large amounts of vitamin K, such as broccoli and spinach, fewer than 25% were able to identify others such as pea soup, coleslaw and dill pickles.

Conclusions: Although the healthcare professionals surveyed in this study appear to have demonstrated some proficiency in their respective areas of expertise, they exhibited less knowledge in others. Therefore, additional training and integration of knowledge and expertise about drug-nutrient interactions among healthcare professionals are essential to provide appropriate patient counseling and optimal therapeutic outcomes.

INTRODUCTION

Drug-nutrient interactions are responsible for a variety of adverse medical consequences [1]. For example, generous or poor intake of vitamin K can interact with the oral anticoagulant warfarin to yield non-therapeutic anticoagulation or life-threatening hemorrhagic complications [2–5]. Standards regarding drug-nutrient interactions have been developed by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). They mandate the need for healthcare professionals to counsel their patients on these relationships [6]. Thus, clinicians who prescribe and/or monitor patients receiving warfarin should routinely counsel these patients about warfarin-vitamin K interactions and on the vitamin K content of foods [7]. This recommendation presumes an expertise of relevant drug-nutrient interactions among healthcare providers. However, Lasswell *et al.* [8] indicate family practice residents could correctly identify only 61% of 14 common drug-nutrient interactions. Whereas most (94%) of the residents did note that vitamin K could interfere with anticoagulant therapy, only 43% identified broccoli as a food rich in vitamin K. Lack of knowledge about warfarin-vitamin K drug-nutrient interactions is noteworthy because changes in vitamin K intake have been known since 1965 to affect warfarin therapy [9,10].

Oral anticoagulants are administered to create a partial deficiency of the active form of vitamin K, thereby reducing

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risks of abnormal blood coagulation [11]. Since its introduction almost 60 years ago, warfarin, a coumarin-based anticoagulant, has become the principal oral anticoagulant for the treatment of thromboembolic disease [12]. Warfarin is typically prescribed for three to six months to treat conditions such as deep venous thrombosis, pulmonary embolism and myocardial infarction. It is also prescribed for longer periods of time to treat individuals who have prosthetic heart valves, atrial fibrillation, atrial fibrillation with embolization and hereditary disorders characterized by a chronic hypercoagulable state [13–15]. Dosing with oral anticoagulants must be carefully monitored to achieve optimal therapeutic efficacy and safety. The challenge in warfarin therapy is to obtain stable therapeutic anticoagulation indices which prevent thrombosis and minimize the risk of hemorrhage [16]. Formulas for predicting warfarin-maintenance dose requirements from a patient's initial response to treatment are sometimes employed early in the therapy [17–19]. Nonetheless, the predictability of appropriate warfarin dosing remains inadequate and the interaction of diet with the drug is frequently noted as a contributing factor in unstable anticoagulation.

Deficiencies in the knowledge of vitamin K-warfarin interactions could result in inappropriate patient counseling, disruptions in warfarin anticoagulant outcomes that may result in bleeds or clots and adverse medical consequences [5,6,20]. Thus, we assessed the knowledge of a representative sample of healthcare providers practicing anticoagulant therapy on the most common and/or important interactions between diet and warfarin. We examined their general knowledge of drug-nutrient interactions as well as used the questionnaire previously employed by Lasswell *et al.* [8].

METHODS

Survey Questionnaire

The survey questionnaire was designed to examine the knowledge of clinicians practicing anticoagulant therapy in the areas of warfarin-drug and warfarin-food interactions. We incorporated into the questionnaire the items on general drug-nutrient interactions previously used to test family practice medicine residents by Lasswell *et al.* [8] with permission. Additional questions focused on common interactions mentioned in the medical literature [3,5,21]. The validity and importance of the knowledge items in a draft questionnaire were assessed by an expert panel consisting of a pharmacologist, a clinical pharmacist, a registered dietitian, a physician and a registered nurse, all of whom were educators in their respective fields. The panel eliminated items deemed uncommon in usual clinical practice and revised some questions to improve their clarity.

The final survey consisted of 30 questions. Part I had five questions containing 19 items. These questions were relevant to drug interactions with oral warfarin anticoagulant therapy (anti-inflammatory agents, antibiotics, cardiac agents, gastrointestinal agents and vitamin supplements) (Table 1). Part II had seven questions containing 54 items and employed sample menus of common foods to test knowledge of food interactions with warfarin (Table 2). As noted above, Part III had fourteen questions about general drug-nutrient interactions that were incorporated from Lasswell *et al.* [8]. Demographics such as profession, age and gender, as well as information sources used to obtain knowledge about drug-nutrient interactions were collected from the first four questions. It took subjects approximately 15 minutes to complete the survey form.

Study Population

A random sample of clinicians practicing anticoagulant therapy who counsel patients receiving warfarin was obtained from 10 hospitals in six previously stratified geographical regions in Massachusetts. A table of random numbers was utilized to select 10 hospitals with 200 to 1000 beds from within these regions. Four hospitals were identified from metropolitan Boston, two from Springfield and one each from Worcester, Fall River, South Shore and North Shore. The director of pharmacy at each hospital served as a site coordinator to distribute and collect the surveys. Using a table of random numbers, the directors selected four physicians, four registered pharmacists, four registered dietitians and four registered nurses practicing anticoagulant therapy at their respective hospital. If a selected individual refused or was unable to participate, another respondent was randomly selected from the remaining pool of clinicians at that institution. One hundred sixty clinicians composed of 40 physicians, 40 registered pharmacists, 40 registered dietitians and 40 registered nurses practicing anticoagulant therapy were surveyed.

Statistical Analysis

Multifactor analysis of variance (ANOVA) was used to compare responses of the four groups of clinicians on their level of knowledge in the areas of drug interactions with warfarin, food interactions with warfarin and general drug-nutrient interactions. Occupation was treated as a fixed factor and hospitals as a random factor. The scores of the occupational groups were compared using Tukey's Honestly Significant Differences (HSD). Results were considered to be statistically significant when the observed significance level (p value) was less than 0.05.

RESULTS

Survey Respondents

Within six weeks of receiving the survey, 120 clinicians submitted completed questionnaires. A second wave of recruitment was conducted after seven weeks in a similar manner to obtain an additional 40 clinicians from the same pool. All surveys were completed within three months of the start of the

Table 1. Part I. Drug Interactions with Oral Warfarin Anticoagulant Therapy
Please check √ whether each drug enhances, inhibits, or has no effect on warfarin action

1. How do these anti-inflammatory agents affect oral warfarin anticoagulant therapy?			
	Enhance	Inhibit	No Effect
aspirin	■	□	□
ibuprofen	□	□	■
topical salicylates	■	□	□
2. How do these cardiac agents affect oral warfarin anticoagulant therapy?			
	Enhance	Inhibit	No Effect
propranolol (Inderal®)	■	□	□
cholestyramine (Questran®)	□	■	□
atenolol (Tenormin®)	□	□	■
3. How do these gastrointestinal agents affect oral warfarin anticoagulant therapy?			
	Enhance	Inhibit	No Effect
antacids	□	□	■
cimetidine (Tagamet®)	■	□	□
Metamucil®	□	□	■
sucralfate (Carafate®)	□	■	□
4. Most antibiotics affect warfarin anticoagulant therapy by the process of			
	Yes	No	Don't Know
potentiation	■	□	□
inhibition	□	■	□
both	□	■	□
neither (other process)	□	■	□
5. How do these vitamin supplement(s) affect oral warfarin anticoagulant therapy?			
	Enhance	Inhibit	No Effect
multivitamin	□	□	■
multivitamin & minerals	□	□	■
antioxidant formula	□	□	■
1200 IU vitamin E	■	□	□
1000 mg vitamin C	■	□	□

■ indicates correct answer

study. Seventy-three percent of the physicians and 63% of the pharmacists were male; all the nurses and dietitians were female. The mean age (±SD) for the groups was physicians: 39.0±10.7 years, pharmacists: 38.3±9.7 years, dietitians: 36.6±9.8 years and nurses: 41.2±8.8 years.

Drug-Nutrient Interaction Knowledge

The score for each section was the fraction of items answered correctly, expressed as a percent. A perfect score was 100 points. The overall test score was calculated by averaging the three section scores. The mean scores (±SD) on the individual sections and overall test are presented in Table 3. The distributions of section and overall scores are shown in Fig. 1. The ANOVA ($p<0.01$) and Tukey's HSD ($p<0.05$) revealed that pharmacists scored significantly higher overall than did members of the other three groups. Physicians scored higher than nurses, dietitians fell between the physicians and nurses, but were not significantly different from either.

Test results on warfarin-drug interactions (Part I) revealed that pharmacists scored significantly higher (ANOVA $p<0.01$; Tukey's HSD $p<0.05$) than the other groups. Physicians scored higher on warfarin-drug interactions than nurses and dietitians; however, differences between nurses and dietitians were not significant. Dietitians scored significantly higher than nurses (ANOVA $p<0.01$; Tukey's HSD $p<0.05$) on the section on warfarin-food interactions (Part II). Physicians' and pharmacists' scores were neither significantly different from one another nor from those of dietitians and nurses. On the section on general drug-nutrient interactions (Part III), pharmacists' and physicians' scores were not significantly different from each others'. They both performed better than nurses and dietitians, whose scores also were not significantly different from each others' (Table 3).

The overall scores (±SD) of healthcare professionals practicing in hospitals with anticoagulation clinics tended to be higher than those from institutions without this resource, 62.1±12.8 *versus* 58.1±11.6, respectively. No significant differences were found in the subsections or in total scores between clinicians practicing in the six teaching *versus* the four non-teaching facilities.

Vitamin K Food Content Knowledge

The questionnaire examined the knowledge of the subjects with respect to five foods containing medium to high amounts

Table 2. Part II. Food Interactions with Oral Warfarin Anticoagulant Therapy (Case Menus)

1. Please check √ which of the following items in Patti's Menu contain Vitamin K.

Patti's Menu

Food Item	Vitamin K		
Breakfast:	Yes	No	Don't Know
Brewed black tea	☐	■	☐
Orange juice	☐	■	☐
Blueberry muffin	■	☐	☐
Lunch:	Yes	No	Don't Know
Split pea soup	■	☐	☐
Fish sandwich (fast food)	■	☐	☐
Coleslaw w/dressing	■	☐	☐
Dill pickle	■	☐	☐
Cola carbonated beverage	☐	■	☐
Dinner:	Yes	No	Don't Know
Chinese beef chow mein	■	☐	☐
White rice (steamed)	☐	■	☐
Broccoli (steamed)	■	☐	☐
Red wine	☐	■	☐
Brewed black tea	☐	■	☐
Apple pie	■	☐	☐

Standard serving size assumed

2. Please check √ which of the following items in Kymberly's Menu contain Vitamin K

Kymberly's Menu

Food Item	Vitamin K		
Breakfast:	Yes	No	Don't Know
Coffee	☐	■	☐
Grapefruit juice	☐	■	☐
Cream	☐	■	☐
Danish	■	☐	☐
Lunch:	Yes	No	Don't Know
Tacos (fast food)	■	☐	☐
Cola carbonated beverage	☐	■	☐
Dinner:	Yes	No	Don't Know
Tuna casserole	■	☐	☐
Spinach (steamed)	■	☐	☐
Carrots (steamed)	■	☐	☐
White wine	☐	■	☐
Coffee	☐	■	☐
Cream	☐	■	☐
Pumpkin Pie	■	☐	☐

Standard serving size assumed

3. Please check √ which of the following items in Tiffany's Menu contain Vitamin K.

Tiffany's Menu

Food Item	Vitamin K		
Breakfast:	Yes	No	Don't Know
Brewed black tea	☐	■	☐
Grapefruit juice	☐	■	☐
Bagel (plain)	☐	■	☐
Cream Cheese	☐	■	☐
Lunch:	Yes	No	Don't Know
Ham luncheon meat	☐	■	☐
Mustard (yellow)	☐	■	☐
Roll (white)	☐	■	☐
Tomato	☐	■	☐
Cola carbonated beverage	☐	■	☐
Dinner:	Yes	No	Don't Know
Chicken breast (roasted)	☐	■	☐
Potato (baked)	☐	■	☐
Corn (steamed)	☐	■	☐
White wine	☐	■	☐
Brewed black tea	☐	■	☐
Vanilla ice cream	☐	■	☐

Standard serving size assumed

4. Please check √ which Menu contains the least amount of vitamin K.

☐ Patti's Menu ☐ all Menus have equal amounts
☐ Kymberly's Menu ☐ don't know
■ Tiffany's Menu

5. Please check √ the Menus by the total amounts of vitamin K they provide.

	Low	Medium	High
Patti's Menu	☐	☐	■
Kymberly's Menu	☐	☐	■
Tiffany's Menu	■	☐	☐

6. Menus high in vitamin K affect warfarin anticoagulant therapy. Please check √ which Menu(s) have the potential for such effects.

■ Patti's Menu
■ Kymberly's Menu
☐ Tiffany's Menu

7. Please check √ the food categories that affect oral warfarin anticoagulant therapy.

	Yes	No	Don't Know
fruits	☐	■	☐
vegetables	■	☐	☐
dairy products	☐	■	☐
meat, fish, poultry	☐	■	☐
grain products	☐	■	☐
fats	■	☐	☐
alcohol	■	☐	☐

■ indicates correct answer

of vitamin K listed in a commonly used patient education brochure, the Dupont Patient Counseling Guide [7]. Chi-square tests revealed no significant difference between the healthcare professionals in their ability to identify the vitamin K content of specific foods. However, there were significant differences between the foods clinicians were able to identify (Fig. 2). All of the registered dietitians and over 87% of the other healthcare professionals surveyed correctly identified broccoli and spinach as foods rich in vitamin K. Coleslaw was correctly identified as a good source of vitamin K by 75% of the dietitians and 60% of the pharmacists, but fewer than 50% of the physicians

Table 3. Scores on Drug-Nutrient Interactions

Test Section	Profession			
	Physicians	Pharmacists	Dietitians	Nurses
Overall Score	62.5±10.6[a]	72.5±9.0	56.9±8.8[ab]	50.2±9.3[b]
Part I Drug Interactions with Warfarin	50.9±13.7	75.9±11.3	34.5±15.7[a]	40.9±11.7[a]
Part II Food Interactions with Warfarin	59.8±18.4[ab]	62.5±16.0[ab]	73.0±10.3[a]	53.5±21.4[b]
Part III General Drug-Nutrient Interactions	76.8±10.5[a]	79.1±10.8[a]	63.2±12.7[b]	56.1±12.2[b]

test scores (mean±SD)

[a, b] within test section, professions sharing the same superscript are not significantly different from each other (Tukey's HSD, $p<0.05$)

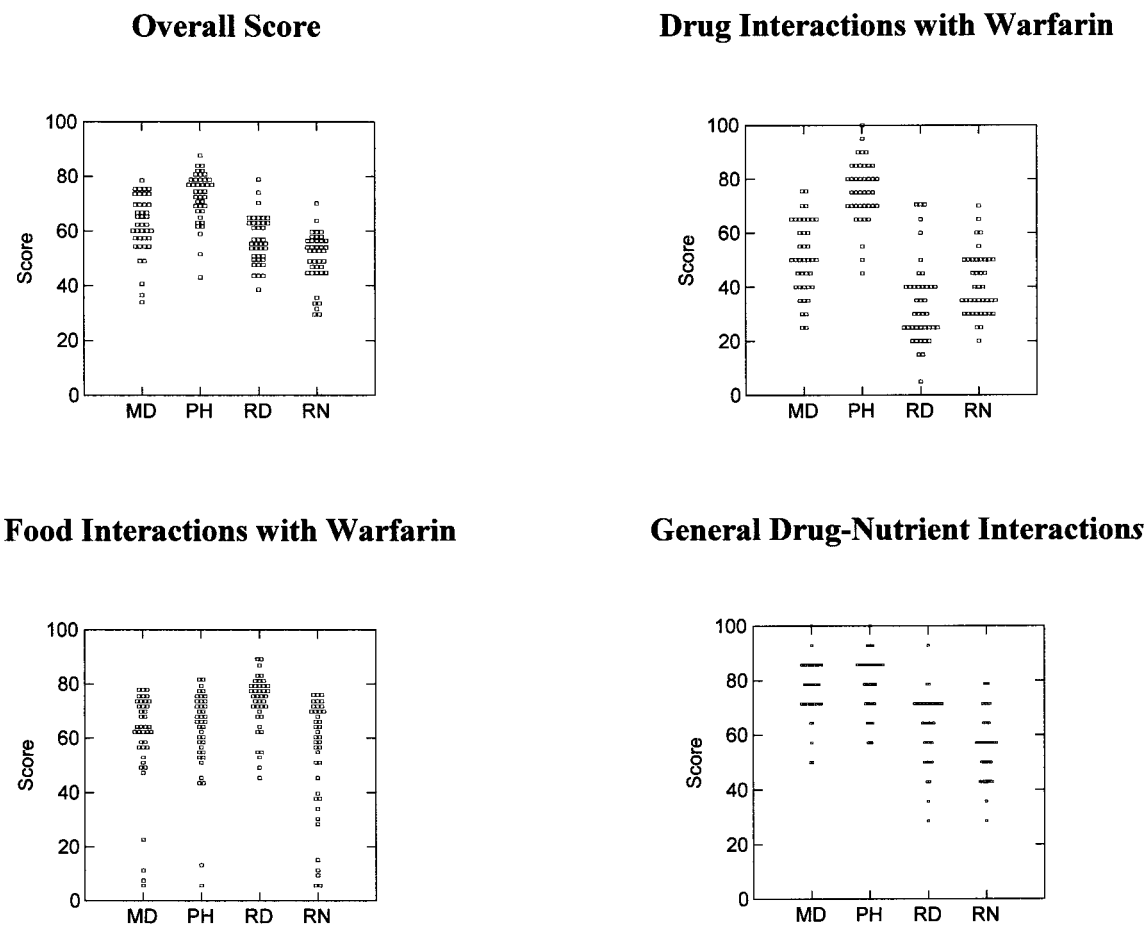

Fig. 1. Distribution of Overall and Section Scores on Drug-Nutrient Interactions. MD = Physicians, PH = Pharmacists, RD = Dietitians, RN = Nurses.

and nurses. Conversely, 60% of the physicians identified pea soup as a source of vitamin K, while fewer than 50% of the other respondents were able to do so. Dill pickles were recognized as a source of vitamin K by fewer than 25% of the participants. The vitamin K content of the foods which appear in Part II of the survey can be found in Booth *et al.* [22–24].

The survey included questions concerning the vitamin K content of processed and mixed foods such as beef chow mein, tacos, muffins and pie, items not listed in the Dupont Patient Counseling Guide [7]. These foods are not rich sources of vitamin K, but may contribute significantly to total intake when consumed frequently or in large quantities. Knowledge about this information was poor among all respondents with fewer than 25% correctly identifying tacos, muffins and pie as food sources of vitamin K.

DISCUSSION

Since the influence of vitamin K on oral warfarin was demonstrated in humans [9,10], many reports have implicated

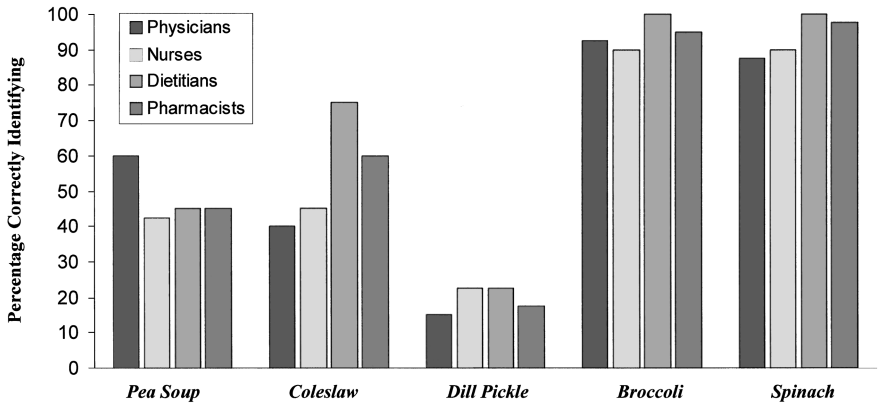

Fig. 2. Percent of Respondents Correctly Identifying Selected Vitamin K Rich Foods. No significant difference exists between clinicians in their ability to identify the vitamin K content of specific foods ($p>0.05$). Significant differences exist between the foods clinicians were able to identify ($p<0.05$).

dietary vitamin K as a factor contributing to unwanted disturbances in anticoagulation, sometimes with life-threatening consequences [25–30]. Increases in vitamin K intake can precipitate abnormal clotting or warfarin-resistance [25–28]. For example, Kempin [25] reported a diet-induced warfarin resistance in two patients consuming large amounts of broccoli. Similarly, Walker [26] noted myocardial infarctions due to warfarin resistance in patients following weight loss diets, including large amounts of green leafy vegetables rich in vitamin K. In contrast, decreases in vitamin K intake are associated with warfarin potentiation and a tendency for abnormal bleeding. Colvin and Lloyd [29] documented severe coagulation defects attributed to dietary deficiencies of vitamin K1, and Chow [30] reported instability of anticoagulation with hemorrhagic complications in two warfarin-anticoagulated patients due to dietary modifications that lowered intake of vitamin K. Therefore, when the amount of vitamin K in the diet remains constant, regardless of the level of consumption, it poses little problem to anticoagulant dosing. Experts recommend that patients who are receiving warfarin therapy limit their daily variations in vitamin K consumption to no more than 250 to 500 μg from baseline intakes [31].

Lasswell [8] has previously reported gaps in the knowledge of physicians about drug-nutrient interactions. However, such deficiencies among any member of the healthcare team with regard to warfarin-vitamin K interactions could lead to inappropriate patient counseling, disruption in anticoagulant outcomes and adverse medical consequences [5,6,20]. In this assessment of knowledge among healthcare professionals, pharmacists and dietitians scored well in their respective areas of expertise, i.e., drug and food interactions, respectively, but did not perform as well in other areas. Scores of physicians were similar to those of pharmacists in general drug-nutrient interactions but were lower in other areas assessed by the questionnaire. Our results are similar to those of Lasswell *et al.* [8], who found a lack of knowledge about drug-nutrient interactions and general nutrition among family practice residents. Nurses tended to score the lowest among the groups.

A limitation of this study was the inability to ascertain the respondents' knowledge of quantitative amounts of vitamin K contained in foods. This limitation was due to the fact that our survey questionnaire only asked respondents to identify foods containing vitamin K and not to rank these foods according to low, medium or high K content. Our study was conducted to establish if in fact a problem existed in the ability of clinicians to identify foods containing vitamin K regardless of the quantity. Therefore, if a clinician demonstrated minimum competency by identifying foods high in vitamin K content as foods having vitamin K, he or she then would be aware of variations in the dietary intakes of his or her patients receiving warfarin that would have a clinical significance on anticoagulant therapy.

CONCLUSIONS

Although the healthcare professionals surveyed in this study demonstrated proficiency in their respective areas of expertise, they exhibited lack of knowledge in others. Inadequate knowledge of drug-nutrient interactions may lead to inappropriate patient counseling and result in adverse medical consequences. Deficiencies in knowledge of warfarin-vitamin K interactions may result in insufficient anticoagulation or hemorrhagic complications. Therefore, additional training and integration of knowledge and expertise about drug-nutrient interactions among healthcare professionals is essential to provide appropriate patient counseling and optimal therapeutic outcomes. Further study is required to document the extent and nature of gaps in knowledge, attitudes and practices of healthcare professionals in this area and the best ways to provide basic

academic and continuing education about clinically significant drug-nutrient interactions such as those between warfarin and vitamin K.

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