Knowledge of Coumadin Use in Atrial Fibrillation Patients

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KNOWLEDGE OF COUMADIN USE IN ATRIAL FIBRILLATION PATIENTS

by

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Abstract

Background: Atrial fibrillation (AF) is the most common observed arrhythmia in clinical practice. Over the next decades, the number of people affected by AF is estimated to be anywhere from 5.6 to over 12 million. In patients with AF, thromboembolism is a central concern, as it can lead to stroke with significant morbidity and mortality. Coumadin anticoagulation has been shown to significantly reduce stroke risk, particularly in patients with other risks, such as hypertension, diabetes, prior stroke, or heart failure. Although Coumadin is effective in reducing stroke, its chronic use requires frequent international normalized ratio (INR)/protime monitoring. This is necessary because nutritional status, compliance, and drug interactions can lead to under- or over-coagulation. There can be numerous interactions with food and medications in patients using Coumadin. In addition, Coumadin carries with it the major concern of intracranial bleeding. Consequently, identifying knowledge deficits related to Coumadin use is critical to improving patient outcomes.

Methods: This study took place at Intermountain Medical Center, Murray, Utah, in collaboration with Utah State University, Logan, Utah. Patients with known AF, who were receiving treatment from the Utah Heart Clinic (n=75), were asked to complete a one-time questionnaire. The data thus obtained was analyzed to identify any knowledge deficits related to Coumadin use.

Results: It was found that 90.7 percent of the sample had at least one stroke risk factor. Descriptive data indicated 21.3 percent of all participants reported consuming grapefruit and/or grapefruit juice and were unaware of the interaction with Coumadin.

Conclusions: This is of great clinical significance as lack of knowledge increased the risk for thromboembolism and intracranial bleeding. The results may be skewed due to the common knowledge of grapefruit-drug interactions. We conclude that better strategies need to be devised to effectively educate AF patients on Coumadin to improve treatment outcomes in the future.
Research Objective

Patient outcomes can be improved through intervention and education pertaining to nutrition, compliance, and understanding of drug interactions. Variability in dietary consumption of vitamin K destabilizes anticoagulation control of Coumadin. Consumption of grapefruit alters the metabolism of the drug and can lead to intracranial bleeding. Many prescription drugs, over-the-counter medications, and herbal products/supplements interact with the metabolism of Coumadin and can lead to over- or under-anticoagulation. Noncompliance with Coumadin has been estimated at 21 percent in the elderly, who often perceived that they were more compliant than they actually were. Patient education communicating these ideas is widely available and frequently used for patients with cardiovascular disease but is neither widely available nor frequently used for patients taking Coumadin. The objective of this study is to assess the understanding of the AF population related to their role in reducing the risks associated with Coumadin and the effects of proper understanding on stroke risk.
Introduction

Atrial fibrillation (AF) is the most commonly observed arrhythmia in clinical practice. Over the next decades, the number of people affected by AF is estimated to be anywhere from 5.6 to over 12 million (1,2). While age is a key risk factor for AF, other population demographics will also likely contribute to the increased AF prevalence. Both the Framingham study and a cohort from Olmsted County, Minnesota have shown age-adjusted increases in the prevalence and incidence of atrial fibrillation from the 1960's to 1989 (3-4). The epidemiologic changes of AF are a global phenomena with incidence and prevalence data from the Netherlands similar to the US. AF admissions are also on the rise in China (5-6).

In patients with AF, thromboembolism is a central concern as it can lead to stroke with high rates of morbidity and mortality. Coumadin anticoagulation has been shown to significantly reduce stroke risk, particularly in those with other risk factors of stroke such as hypertension, diabetes, prior stroke, or heart failure (7-11). Although Coumadin is effective in reducing stroke, its chronic use requires frequent INR/protime monitoring. Nutritional status, hepatic function, intestinal absorption, compliance, and genetic polymorphisms are factors that can lead to under- or overanticoagulation with long-term use of Coumadin. There are also numerous dietary and medication interactions and the major concern of intracranial bleeding, all of which could lead to stroke (12).
Review of Literature

It is generally accepted that certain foods may interact with the pharmacokinetics of certain medications (13). In 1991, researchers inadvertently discovered the drug-grapefruit juice interaction that enhances the area under the concentration time curve (AUC) and the maximum plasma concentration (Cmax) of orally administered drugs (13). Drugs with lower oral bioavailability are affected to a greater degree. This interaction has been reported with 40 pharmaceutical products, including the vitamin K antagonist, Coumadin (13).

Subsequent investigations of this interaction indicated that grapefruit juice acts by inhibiting cytochrome P450 3A4 (CYP3A4) expression (14). Cytochrome 450 (CYP450) enzymes are in a class of over 50 enzymes. Six of those are responsible for metabolizing 90 percent of drugs, with the two most significant enzymes being CYP3A4 and CYP2D6 (15).

Drug metabolism may be the result of one or several CYP450 enzymes. For example, Coumadin is metabolized by CYP1A2, CYP2D6, and CYP3A4 (15). Drugs that interact with CYP450 enzymes are known as either inhibitors or inducers. Inhibitors block the activity of one or more CYP450 enzymes, amplifying the effect of the drug (15). A drug can both inhibit an enzyme and be metabolized by the same enzyme. Conversely, inducers enhance the synthesis of CYP450 enzymes, thus reducing the drug's effect. Adverse effects are more common if the drug has a narrow safety range and if it is metabolized by only one enzyme (15).

Grapefruit juice inhibits CYP3A4 synthesis and accelerates CYP3A4 degradation, which indicates the process is mechanism-based opposed to competitive (13). Mechanism-based inhibition involves an inhibitor being metabolically activated by an enzyme and then irreversibly inactivating that same enzyme. This means that the return of enzyme activity will require de novo enzyme synthesis and prolong the effect of the inhibitor (13). For this reason, the effects of
grapefruit juice typically last 24 hours (14). Drug-grapefruit juice interactions, therefore, cannot be fully avoided by taking them at a different time (16).

Drug-grapefruit juice interactions are unique in that while apical enterocytes and hepatocytes both contain CYP3A4, ingestion of normal amounts of grapefruit juice only appears to alter intestinal CYP3A4 expression (14). Studies demonstrated a 62 percent reduction in intestinal CYP3A4 protein content after consuming grapefruit juice over 5 days (14). However, repeated dosing of large amounts of grapefruit juice over several days can also inhibit hepatic CYP3A4 synthesis (16). The content of intestinal and hepatic CYP3A4 can vary tenfold among individuals and appears to be regulated independently of the other. Therefore, the magnitude of the interaction is highly variable (14).

Identification of the active ingredients in grapefruit juice is important, as it would enable researchers to evaluate its effect on CYP3A4 with other foods. In addition, the active ingredients may be used in commercial products to produce higher drug bioavailability (14). Several components of grapefruit juice have been proposed as the cause of this interaction, including flavonoids and furanocoumarins.

The most prevalent flavonoid in grapefruit juice is naringin (14). Naringin is in high concentration in grapefruit juice and absent from orange juice, which does not interact with Coumadin. While naringin has potential to inhibit CYP3A4 synthesis, it is less potent than its aglycone, naringenin (14). Naringenin is typically not present in grapefruit juice, but studies demonstrated renal excretion of naringenin conjugates after administration of grapefruit juice, suggesting in vivo naringenin formation. However, ingestion of commercial pure naringin in the same amounts as grapefruit juice produced little to no effect (14).
More recent studies concluded that furanocoumarins are the major CYP3A4 inhibitors in grapefruit juice. Bergamottin and 6',7'-dihydroxybergamottin (DHB) are the two most abundant furanocoumarins in grapefruit juice (17). In order to accurately evaluate their impact on CYP3A4 inhibition, a furanocoumarins-free (FC-free) formula was created. The recorded results reported the AUC of grapefruit juice to be 30 to 370 percent higher than that of the FC-free grapefruit juice (17). The FC-free formula behaved in a similar manner to orange juice. It produced some effects, but to a much lesser degree (17). While furanocoumarins appear to be the active ingredient in grapefruit juice, no individual furanocoumarin is able to completely reproduce the inhibitory effect of whole juice. It is not possible to determine which furanocoumarin contributes the most to the grapefruit juice-drug interaction (17).

There have been recent attempts to remove FCs from grapefruit juice, which include chemical, physical, and microbiological methods. One of these methods involves the use of autoclaved fungus to absorb and remove FCs, specifically *M. esculenta* (18). *M. esculenta* efficiently absorbed all non-polar FCs in grapefruit juice. However, polar FCs were not absorbed, which caused 40% of the CYP3A4 inhibition to remain (18). The binding of FCs to the fungi is believed to be due to passive interaction. This interaction was successful in reducing the potency of the inhibitory effect of grapefruit juice on CYP3A4 (18).

The vitamin K antagonist Coumadin has multiple food-drug and drug-drug interactions, including grapefruit juice. Coumadin is the most extensively used oral anticoagulant worldwide. It is indicated to prevent thromboembolism, myocardial infarction, and stroke in patients with atrial fibrillation (AF) and prosthetic heart valves (19). AF increases the risk of stroke five-fold. Coumadin reduces the risk of AF-related stroke by 64 to 70 percent (20).
Coumadin acts by inhibiting the vitamin K-dependent coagulation factors II, VII, IX, and X. The drug is promptly absorbed and its concentration peaks around 4 hours (19). Coumadin is eliminated through metabolism by hepatic CYP2C9. There are several variations in the gene that encodes CYP2C9 among different ethnic groups. These variants are associated with an increase in negative clinical outcomes, including over- and under-anticoagulation, both of which can lead to stroke (19). Inadequate amounts of Coumadin can increase the risk for a thromboembolism leading to an ischemic stroke. An abundance of Coumadin can increase the risk of intracranial bleeding, which could cause a hemorrhagic stroke (19).

The dose-response to Coumadin has a large range due to intrinsic genetic factors, comorbid diseases, other medications, and dietary factors, all of which can alter drug metabolism. While grapefruit juice can significantly amplify the effects of Coumadin, it does not appear to alter the anticoagulant response (19). Due to the wide dose-response of Coumadin and the wide dose-response of grapefruit juice, medical professionals cannot safely recommend a specific amount of grapefruit juice that one could ingest while taking Coumadin.

The current patient education methods utilized in health care facilities may not be adequate to convey the importance of adherence to the prescription and the seriousness and understanding of food-drug interactions, especially concerning grapefruit juice. Adverse effects of Coumadin are common with non-adherence. Poor adherence is estimated to cause 5 percent of all hospital admissions, which accrue 8 billion dollars in cost every year (20). Anticoagulants are believed to be the leading cause of preventable adverse drug-related events among the elderly.

The INR Adherence and Genetics (IN-RANGE) study demonstrated that over 40 percent of participants were less than 80 percent adherent with their Coumadin prescription (20).
Overall non-adherence was significantly associated with underanticoagulation and altered INR levels. No differences were found when examining compliance with initiation versus maintenance of Coumadin. These findings are significant as even moderate fluctuations in INR are associated with increased risk of thromboembolism, additional visits, increased need for dose changes, and a higher potential for dosing errors (20).

The latest results from the IN-RANGE study lend support to the hypothesis of poor compliance among those taking Coumadin. Non-adherence was reported in 21 percent of the days observed, with individual numbers ranging from 0.9 to 79 percent (21). Increased non-adherence was significantly associated with those with education beyond a high school diploma, those with active employment, and those with lower cognitive functioning.

Poor adherence in educated populations may be due to more independent decision-making or decreased trust in physicians (21). The negative association with employment and medication adherence is consistent with other studies and other disease settings. While the underlying relationship is not definite, it is hypothesized that employment may represent several factors, which take priority over consistent pill taking (21). Lower cognitive function was associated with non-adherence, but there was no association with depressive symptoms. Patient adherence to Coumadin appears to be related to factors involving time, memory, and mental health functioning (21).

Health literacy may also play a role in patient compliance and understanding. Previous studies demonstrated decreased patient knowledge and lack of Coumadin education are associated with reduced anticoagulant control and increased risk of hemorrhagic events (22). Health education brochures are typically written at a ninth-grade level or higher. A recent study demonstrated that out of 179 interviewed patients, 33.5 percent reported having no more than an
eighth-grade level education (22). Limited health literacy was prevalent in 60.9 percent of the multi-cultural population and was more likely to occur in those that were older, female, non-white, and have less than a high school education.

Limited health literacy increased the amount of incorrect answers concerning Coumadin related knowledge (22). The patients taking Coumadin for atrial fibrillation were more likely to report that their physician had not explained that they had atrial fibrillation (60 percent vs. 9.7 percent) and were less likely to understand that it increased their risk of stroke (42 percent vs. 70 percent). Despite these differences, limited health literacy was not significantly associated with poor INR control (22).

Coumadin is a beneficial but potentially hazardous medication. Appropriate education has a profound impact on patient knowledge of Coumadin use, INR control, and prevalence of drug-related complications.
Methods

This study was conducted at Intermountain Medical Center (Murray, Utah) in collaboration with Utah State University (Logan, Utah). Patients with known AF who were receiving treatment from the Utah Heart Clinic (n=75) and were currently taking Coumadin were asked to complete a one-time questionnaire of 52 questions. The questionnaire was completed under the supervision of a registered dietitian or student dietitian. Data collected was analyzed to assess the descriptive characteristics of the data and to identify any knowledge deficits related to Coumadin use and was stratified based on stroke risk versus non-stroke risk. This study was approved by the Institutional Review Board at Utah State University (protocol #2187).
Results

The mean age of the patient population was 69.2 (n=75). The data was stratified by gender to assess differences between male and female. The patients were categorized according to stroke risk, based on the CHADS$_2$ Score. The CHADS$_2$ score is used to estimate risk of stroke in AF patients.

Sixty-eight of the patients had at least one risk factor for stroke (see Table 1). The seven remaining patients with no stroke risk factors were taking Coumadin because they had recently undergone a cardiac ablation.

Hypertension was the most common stroke risk factor (58.7 percent of the population). Age > 75 years was the second most common, followed by heart failure.

<table>
<thead>
<tr>
<th>Item</th>
<th>M+P</th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>75</td>
<td>47</td>
<td>28</td>
</tr>
<tr>
<td>Age</td>
<td>69.2</td>
<td>66.7</td>
<td>72.3</td>
</tr>
</tbody>
</table>

**Stroke Risk**

1. Hypertension 44(58.7) 28(59.6) 16(57.1)
2. Heart failure 25(33.3) 14(29.8) 11(39.3)
3. Age > 75 26(34.7) 12(25.5) 14(50.0)
4. Diabetes 12(16.0) 7(14.9) 5(17.9)
5. TIA 19(25.3) 11(23.4) 8(28.6)
6. TIA on Coumadin 6(8.0) 3(6.6) 3(10.7)

Table 2 represents the patient population (n=16) who reported having consumed grapefruit or grapefruit juice and were not aware that grapefruit interacts with Coumadin.
Possible responses to the grapefruit or grapefruit juice consumption question ranged from “every day” to “less than once a month.” Table 2 reveals that 21.3 percent of those that consumed grapefruit or grapefruit juice were unaware of this interaction.

Table 2. Those Who Were Not Aware Of Grapefruit Interaction With Coumadin

<table>
<thead>
<tr>
<th>Item</th>
<th>M+F n(%)</th>
<th>M n(%)</th>
<th>F n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grapefruit</td>
<td>16(21.3)</td>
<td>10(21.3)</td>
<td>6(21.4)</td>
</tr>
</tbody>
</table>

Table 3 presents the data from the grapefruit or grapefruit consumption question only with respect to members of the population having stroke risk (n=68). Surprisingly, there was no difference in the proportion (21.3 percent) that were not aware of the grapefruit interaction with Coumadin.

Table 3. Those At Stroke Risk Who Were Not Aware Of Grapefruit Interaction With Coumadin

<table>
<thead>
<tr>
<th>Item</th>
<th>M+F n(%)</th>
<th>M n(%)</th>
<th>F n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grapefruit</td>
<td>16(21.3)</td>
<td>10(21.3)</td>
<td>6(21.4)</td>
</tr>
</tbody>
</table>
Discussion

Seventy-five patients participated in this study. Of these, 68 had at least one stroke risk factor, which included hypertension, heart failure, age over 75 years, diabetes, and prior stroke. The study demonstrated that 21.3 percent of those who consumed grapefruit or grapefruit juice were not aware of its interaction with Coumadin. While this study was the first to assess patient knowledge of specific drug-nutrient and drug-drug interactions, our results are similar with other research assessing overall patient understanding of Coumadin (23).

A recent study demonstrated that 83 percent of patients were aware that too little Coumadin could lead to an ischemic stroke, but only 21 percent were aware that too much could lead to a hemorrhagic stroke (23). Thirteen percent of patients did not know that Coumadin could cause bruising or internal bleeding. Patient beliefs also included 12 percent claiming they were able to determine if the Coumadin was at the right level by how they felt and 13 percent stating that missing a lab appointment was not that important (23).

Appropriate education tools are essential to overcome these barriers. There has been debate about the effectiveness of presenting statistics in educational materials compared with narratives (23). A growing amount of literature suggests that even well educated patients struggle comprehending quantitative information. Narratives may be more engaging, memorable, and realistic than statistics, but may induce inaccurate beliefs or lead to non-optimal decision-making (23).

Patients viewing a video education tool with evidence presented in a narrative format showed greater knowledge gains than those that received statistical evidence (p=0.006). There were no significant differences in the narrative version compared to the video with narrative plus statistical evidence (23). Narrative evidence may be more effective in Coumadin education. The
videos used in this study did have a positive impact; however, they did not correct knowledge
gaps, reduce incorrect beliefs, or improve non-adherence. Patients may benefit from periodic
Coumadin education. Clinicians should not assume that those who have been taking Coumadin
for months or years have adequate knowledge of its drug-nutrient and drug-drug
interactions (23).

The results of this study may have been skewed by common knowledge that grapefruit
interacts with most medications, especially many cardiovascular and hypertensive agents. With
that in mind while completing the questionnaire, the participants may have merely guessed,
rather than answering based on their specific knowledge, that Coumadin interacts with
grapefruit.
Conclusion

This is the first study to assess and compare the association of various risk factors with Coumadin knowledge. Stroke risk patients (n=68) had limited knowledge related to Coumadin use. As most patients had at least one stroke risk factor, comparison of stroke risk patients and their non-stroke counterparts was not possible. AF patients did not ask professionals about Coumadin interactions. Specifically, 21.3 percent of those consuming grapefruit or grapefruit juice did not ask a professional if the product interacts with Coumadin. Only 63.9 percent of participants were knowledgeable about at least one dietary influence on Coumadin metabolism.

Lack of patient knowledge may increase the risk for thromboembolism and intracranial bleeding in patients taking Coumadin. Dietary factors, drug compliance, and interactions with Coumadin can be positively influenced through intervention and education. Better strategies need to be devised to effectively educate AF patients on Coumadin to improve treatment outcomes in the future. Further data analysis will take place to identify specific correlations in order to improve patient education in the future.
References


Appendix 1

Survey Instrument
Age ______

Please circle:

Gender
Male
Female

Education Level
Less than the 8th Grade
8-12th Grade
High School Graduate
College Graduate
Advanced Degree

Stroke Risk Factors
1. High blood pressure: Yes/No
2. Heart failure: Yes/No
3. Age greater than 75 years: Yes/No
4. Diabetes: Yes/No
5. Prior stroke or mini-stroke (TIA): Yes/No
7. Prior stroke or mini-stroke when on Coumadin: Yes/No

If you had a stroke on Coumadin, was your blood level:

a. Too low
b. Normal
c. Too high
d. Not sure
**Other Cardiac Problems**

1. Have you had a prior heart attack: Yes/No
2. Have you had a stent or bypass surgery: Yes/No
3. Do you have any problems with your heart valves: Yes/No
   
   If yes, was the problem:
   
   a. Narrow
   b. Leaky
   c. Not sure
4. Have you had surgery for your heart valves: Yes/No

**Please answer the following questions:**

1. Have you ever experienced bleeding in your urine or stools? Yes/No

2. Have you ever received a blood transfusion because of bleeding? Yes/No

3. Have you fallen in the past year? Yes/No

4. If you have fallen in the past year, how many times? _____

5. How long have you been on Coumadin?
   
   a. Less than 1 year
   b. 1 year – 5 years
   c. 5 years – 10 years
   d. Greater than 10 years
   e. Not sure
6. Do you take your Coumadin as prescribed by your doctor? Yes/No

7. Do you ever skip your Coumadin dose? Yes/No

8. Do you ever double up your Coumadin dose? Yes/No

9. Do you ever not refill your Coumadin because of cost? Yes/No

10. What is the most common reason why you may not take your Coumadin dose?
    a. Cost
    b. Forgetting
    c. Mixing up medications
    d. Lack of desire
    e. Illness
    f. None of the above

11. Have you gained weight after starting Coumadin? Yes/No

12. If yes, approximately how much weight have you gained? _____

13. If yes, why do you think you gained the weight? (Circle all that apply)
    a. Changed diet and avoided vegetables
    b. Exercised less
    c. Ate more at each meal
    d. Craved new foods that were less healthy
14. Have you lost weight after starting Coumadin? Yes/No

15. If yes, approximately how much weight have you lost? _____

16. If yes, why do you think you lost the weight? (Circle all that apply)
   a. Changed diet and avoided many foods
   b. Illness
   c. Ate less at each meal
   d. Stopped drinking alcohol

17. What is considered a normal INR (blood Coumadin level)?
   a. Less than 1
   b. 2-3
   c. 4-5
   d. Greater than 5
   e. Not sure

18. Do you know what your current INR (blood Coumadin level) is? Yes/No

19. Approximately how often do you get your INR (blood Coumadin level) checked?
   a. Once a week
   b. Twice a month
   c. Once a month
   d. Twice a year
   e. Once a year
   d. Never
   f. Not sure
20. Do you ever not get your INR (blood Coumadin level) checked because of cost? Yes/No

21. Are you aware that your other medications can interact with Coumadin? Yes/No

22. Do you ask your pharmacist before starting a new medication if it interacts with Coumadin? Yes/No

23. Do you ever take over-the-counter pain medications? Yes/No

24. If yes, which ones? (Circle all that apply)
   Excedrin® Tylenol® (Acetaminophen) Aleve® (Naproxen)
   Advil® (Ibuprofen) Motrin® (Ibuprofen) Aspirin

25. Do you ask your doctor before using over-the-counter pain medications? Yes/No

26. Do you ever take over-the-counter stomach remedies? Yes/No

27. If yes, which ones? (Circle all that apply)
   Tagamet HB® (Cimetidine) Pepto Bismol® (Bismuth Subsalicylate)
   Laxatives Stool Softeners
   Alka-Seltzer®

28. Do you ask your doctor before using over-the-counter stomach remedies? Yes/No

29. Do you take vitamin supplements? Yes/No
30. If yes, which ones (Circle all that apply)
   - Multivitamin (Dose:  )
   - Vitamin A (Dose:  )
   - Vitamin E (Dose:  )
   - Vitamin D (Dose:  )
   - Vitamin C (Dose:  )

31. Are you aware that vitamin supplements can interact with Coumadin? Yes/No

32. Do you ask your doctor before using a vitamin supplement if it interacts with Coumadin? Yes/No

33. Do you think getting enough Vitamin K is important?
   a. Yes
   b. No
   c. Not sure

34. What do you think Vitamin K does for us? (Circle all that apply)
   a. Improves eye sight
   b. Strengthens bones
   c. Improves the texture and softness of skin
   d. Helps to form clots
   e. It is an anti-oxidant to help the body

35. Do you take any herbal or natural medications or supplements? Yes/No
36. If yes, which ones? (Circle all that apply)

- Garlic
- Ginger
- Glucosamine
- Ginko Biloba
- CoEnzyme Q10
- Green Tea
- St. John’s Wort
- Flaxseed
- Melatonin
- Papaya Extract
- Ginseng
- Soy Protein Products
- Fish oil supplements that contain EPA or DHA

37. Are you aware that natural medications or supplements can interact with Coumadin? Yes/No

38. Do you ask your doctor before using a natural medication or supplement if it interacts with Coumadin? Yes/No

39. Do you know how to interpret a supplement facts label on natural medications or supplements? Yes/No

40. How often do you drink alcoholic beverages?
   a. Every day
   b. 4-6 days a week
   c. 2-3 days a week
   d. Once a week
   e. 2-3 times a month
   d. Once a month
   e. Less than once a month
   f. Never
41. How often do you use tobacco products?
   a. Every day
   b. 4-6 days a week
   c. 2-3 days a week
   d. Once a week
   e. 2-3 times a month
   d. Once a month
   e. Less than once a month
   f. Never

42. Can changing your diet change your Coumadin dose?
   a. Yes
   b. No
   c. Not sure

43. How often do you drink grapefruit juice or eat grapefruit?
   a. Every day
   b. 4-6 days a week
   c. 2-3 days a week
   d. Once a week
   e. 2-3 times a month
   d. Once a month
   e. Less than once a month
   f. Never
44. Are you aware that grapefruit and grapefruit juice interact with Coumadin?
   a. Yes
   b. No
   c. Not sure

45. Are you aware that you get Vitamin K from the foods you eat?
   a. Yes
   b. No
   c. Not sure

46. How much Vitamin K do the following foods contain? Please circle the amount:

<table>
<thead>
<tr>
<th>Food</th>
<th>0-9 mcg</th>
<th>10-29 mcg</th>
<th>30-89 mcg</th>
<th>99-1200 mcg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooked broccoli (1 cup)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetable Oil (1 Tbsp)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Canned tuna in oil (3 oz)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Iceberg lettuce (1 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Cooked spinach (1 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Coleslaw (3/4 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Red grapes (1 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Green leaf lettuce (1 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Walnuts (14 halves)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Grapefruit juice (1 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Item</td>
<td>Calories</td>
<td>Calories</td>
<td>Calories</td>
<td>Calories</td>
</tr>
<tr>
<td>-------------------------------------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Red wine (3.5 fl oz)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Olive Oil (1 tbsp)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Cooked asparagus (4 spears)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Raw celery (1 stalk)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Vanilla ice cream (1/2 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Avocado (3 oz)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>75% lean ground beef (3 oz)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Roasted chicken (1 drumstick)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Raw pineapple (1 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Cooked salmon (1/2 fillet)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Swiss cheese (1 oz)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>2% milk (1 cup)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Hard-boiled egg (1 large)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
<tr>
<td>Chunky peanut butter (1 Tbsp)</td>
<td>0-9 mcg</td>
<td>10-24 mcg</td>
<td>25-99 mcg</td>
<td>100-499 mcg</td>
</tr>
</tbody>
</table>

47. Do you know how to interpret a nutrition facts label on food products? Yes/No
48. How many meals do you eat each day?
   a. One
   b. Two
   c. Three
   d. Four
   e. Five
   f. Less than one
   g. More than 5

49. How many meals do you eat each day with Vitamin K?
   a. One
   b. Two
   c. Three
   d. Four
   e. Five
   f. Less than one
   g. More than 5
   h. Not sure

50. Is it important to watch how much Vitamin K you get each day when you are on Coumadin?
   a. Yes
   b. No
   c. Not sure

51. Do you believe that taking Coumadin negatively influences your quality of life?
Yes/No
52. If yes, why do you think Coumadin negatively influences your quality of life? (Circle all that apply)

   a. Frequent blood draws
   b. Don't get to eat your favorite foods
   c. Diet is too restrictive
   d. No longer drink alcohol or only occasionally
   e. Worry about bleeding
   f. Feel unwell or experience side effects on the medication