PRACTICAL POINTERS

FOR

PRIMARY CARE MEDICINE

ABSTRACTED MONTHLY FROM THE JOURNALS

A Free Public-service Publication

MAY 2012

JAMA, NEJM, BMJ, LANCET
ARCHIVES INTERNAL MEDICINE
ANNALS INTERNAL MEDICINE

PUBLISHED BY PRACTICAL POINTERS, INC.
EDITED BY RICHARD T. JAMES JR. MD
400 AVINGER LANE, SUITE 203
DAVIDSON NC 28036 USA

www.practicalpointers.org A free public-service publication. To request monthly issues go to Rjames6556@aol.com

26th YEAR OF PUBLICATION

This document is divided into two parts

1) The **HIGHLIGHTS AND *EDITORIAL COMMENTS* SECTION**

   HIGHLIGHTS condenses the contents of studies, and allows a quick review of pertinent points of each article.

   EDITORIAL COMMENTS are the editor's assessments of the clinical practicality of articles based on his long-term reviews of the current literature and his 26-year publication of Practical Pointers.

2) The **FULL ABSTRACTS** section is designed as a reference. It presents structured summaries of the contents of articles in much more detail.

I hope you will find *Practical Pointers* interesting and helpful. The complete content of all issues for the past 10 years can be accessed at www.practicalpointers.org

Richard T. James Jr. M.D.
Editor/Publisher.

Practical Pointers is published every month on the internet as a public service. It is available on a more timely basis by e-mail attachment. It contains no advertising. It is completely without bias. There is never any charge.

Requests for "subscription" to rjames6556@aol.com

HIGHLIGHTS AND *EDITORIAL COMMENTS* MAY 2012

Patient Autonomy Is Not Synonymous With Endless Choice. Shifting All The Burden To The Patient Or Family Is Not Patient-Centered Care At All.

5-1 FREEDOM FROM THE TYRANNY OF CHOICE—TEACHING THE END-OF-LIFE CONVERSATION

Thirty years ago, an intern had a conversation with a patient he still regrets to this day. The patient, a young man with widely metastatic lymphoma, unresponsive to chemotherapy, now had progressive dyspnea. The internist knew that, even with intubation, his patient would soon die. The norm at that time was for physicians to make end-of-life (**e-o-l**) decisions without involving the patient. The medical team, struck by the patient's youth, asked the intern to elicit the patient's wishes. Uncertain, and frightened, the patient said "I want everything". Intubation followed, and then multi-organ failure. The patient died on the ventilator weeks later, never getting an opportunity to say goodbye to those he loved.

More recently another resident made a decision he feared he would regret. A women in her 30s with widely metastatic breast cancer presented with shortness of breath due to bilateral malignant effusions. His job was to triage the patient to the proper level of care. Although her cancer had been diagnosed a decade earlier, no physician had discussed her e-o-l wishes. In the middle of the night, the patient was in respiratory extremis. Intubation was necessary if her life was to be prolonged. The resident decided to make it clear that she was dying. Comfort measures were initiated. The resident feared he had overstepped his bounds and that the patient's oncologist would be angry. Instead, when the patient died peacefully 3 days later, the oncologist and the family expressed their gratitude.

In the 3 decades between these 2 experiences, the typical approach to discussing resuscitation has evolved from paternalism to discussions in which the patient and family are often asked to choose from a bewildering array of medical possibilities. To rectify perceived violation of patients' autonomy, healthcare institutions now require physicians to involve patients and families in e-o-l decisions. But physicians may lack the required trainees to lead such conversations confidently and effectively. A recent survey of internal medicine residents reported that they were frequently asked to lead such conversations, but only a third felt comfortable doing so.

Miscommunications may occur. When patients request "Do not resuscitate", such orders may not be placed in the medical record. They may be disregarded. In other cases, patients may not recall ever having such a conversation

Conversations with patients and families may focus on specific interventions rather than on the overarching goals of care. “Do you want us to pound on your chest if you need it?” “Do you still want antibiotics?” “Do you want intravenous fluids administered?” This ignores the fact that most patients and families have no basis on which to make such decisions. Patient autonomy is not synonymous with endless choice.

This impulse to offer patients a menu of options reflects fundamental insecurity about ability to prognosticate. Who are we to know when a patient will die?

Trainees are often the first initiators of e-o-l conversations. A survey of 2500 patients with metastatic cancer reported that only 20% of the patients’ oncologists had documented their patients’ code status.

We do not have suitable guidelines about e-o-l conversations. Experts suggest that these conversations should clarify prognosis and end with the physician’s recommendations. This approach is not widely disseminated to trainees. And may even be rare in attending physicians.

Despite the current push toward patient-centered care, when it comes to the e-o-l, some patients and families prefer more physician-driven decision- making. In one study of seriously ill hospitalized patients, only 16% wanted to make treatment decisions alone. Shifting all the burden to the patient or family is not patient-centered care at all.

End of life conversations should be treated like any other competency. Every individual admission of a seriously ill patient should include an assessment of prognosis.

Leading conversations about e-o-l requires skills that are difficult to teach. There is a tendency to shy away from death. Conversations should include the words “death” and dying”.

These conversations will not get easier. The population is aging. Hospitalists have assumed care that would once have been followed by primary care physician. Long work hours erode relationships with patients. With medical advances, there is almost always something else that could be offered.

“A physician who merely spreads an array of vendibles in front of the patient and then says ‘Go ahead and choose it’s your life’ . . . does not warrant the somewhat tarnished, but still distinguished title of doctor.” [1]

NEJM May 3 2012; 266: 1655-57 “Perspective” first author Daniela Lamas, editorial fellow at NEJM

1 Statement from Franz Ingefinger, former editor of NEJM , who died of esophageal cancer, published posthumously in the journal.

There would have been ample time and opportunity for discussions of e-o-l concerns of the two patients described in the anecdotes. In both instances, the attending physicians left the responsibility to residents when the patients were dying. This responsibility should not be transferred.

The article is slanted to academic medical centers in which residents are being trained. Primary care clinicians do not usually have this advantage They have to plan ahead and act alone. They must practice the art of communicating about death.

I believe decisions about interventions when patients are approaching death depend on this judgment: What will this patient's life be like if death is postponed and the patient regains her previous status? What will this patient look forward to if life is prolonged? Prognosis should not be limited only to the short term. Would the patient choose a longer life of complete dependence and dementia?

"Hope springs eternal". But we can often be sure than there is no hope for survival or improvement. This does not mean that there is nothing left to do for patient and family. They should not be abandoned.

Death is one of the two most important episodes in life. And is the one for which we may make plans. Primary care clinicians may shy away from these discussions for lack of a perceived opportunity. There may be a helpful introduction—simply ask the patient "Are you at peace?", and proceed from there. This can permit discussions at a time when stress is not so great.

Confused communications are common. Communications must be repeated. The wishes of a patient in a nursing home may be overlooked in the confusion of sudden collapse. The patient meanwhile may have lost the ability to communicate his wishes. There are times when patients may wish to change a decision temporarily –e.g. when a family wedding or graduation is approaching.

Most patients die in institutions. Most would rather die at home. Do not delay calling for help from Palliative Care and Hospice. Often their aid is requested at the last moments. They may help the patient to stay at home and support the family to care for the dying patient. Chaplains and clergy can be very helpful.

There are cultural differences which primary care clinicians should consider. Not too many decades ago, in some ethnicities, it was the norm to avoid mentioning the word "cancer". This was considered to indicate loss of hope. Fortunately, times have changed, and I believe most Americans are becoming more comfortable with contemplating death.

Some interventions at the time of death may be considered to be cruel. Although patients and families may refuse interventions, they may not demand them if they are not considered appropriate or indicated. Physicians can refuse to intervene. They may do so indirectly as when responding very slowly to an emergency call for resuscitation.

The message is—plan ahead. Be prepared for the second most important event of your life,

Probiotics Are Associated With Lower Risk For AAD.

5-2 PROBIOTICS AND THE PREVENTION AND TREATMENT OF ANTIBIOTIC-ASSOCIATED DIARRHEA

Antibiotics that disturb the gastrointestinal flora are associated with diarrhea, which can occur in up to 30% of patients. Symptoms may be mild and self-limiting, or severe (as with *Clostridium difficile* infection).

Probiotics may maintain or restore gut micro-ecology during or after antibiotic treatment.

This systematic review and meta-analysis evaluated and updated the available evidence on live probiotics on incidence of antibiotic-associated diarrhea (**AAD**).

Selected randomized controlled trials (**RCT**) that compared probiotics use as an adjunct to antibiotics vs. a concurrent control group. (As a supplement given with antibiotic at onset of treatment.)

The majority used *Lactobacillus* alone or in combination with other genera.

The primary outcome was the number of participants with diarrhea in each treatment group.

The quality of the trials was low. Questions about conflict of interest and bias remained.

Efficacy: 63 RCTs reported the number of participants with diarrhea, and the number randomized to both groups. Most trials did not show a statistically significant advantage for probiotic use. However, across the 63 RCTs (N = 11 811) probiotic use was associated with a lower relative risk (**RR**) of developing AAD compared with the control groups. (RR = 0.58; Number needed to treat = 13.)

Trials that reported incidence of AAD after cessation of antibiotic therapy reported that the number of patients experiencing AAD was lower in those who had received probiotics. (RR = 0.44)

No adverse effects were reported, and the probiotics were considered safe.

The main limitations of the study are unexplained heterogeneity, poor documentation of probiotic strains, and lack of assessment of probiotic-specific adverse effects.

The study was not able to determine:

Any difference in response depending on age.

Which probiotic or combination resulted in greatest benefits.

The effect of probiotics treatment of AAD (ie, after start of symptoms).

Whether probiotic treatment is more effective in preventing *C difficile* AAD than other types of AAD.

If probiotics are entirely harmless.

Conclusion: Adjunct probiotic administration is associated with lower risk for AAD. This generalized conclusion likely obscures heterogeneity of effectiveness among the patients, the antibiotics, and the probiotic strains and blends.

(See the full abstract for details and the citation. Ed.)

Obviously a weak study. How should the primary clinician respond?

What is the benefit / harm-cost ratio of probiotics? I believe it is high.

The harm is very low. Yoghurt has been used as a food for centuries. We should know any adverse events by now.

Costs are very low

Benefits may be great, especially if a case of C difficile colitis is prevented.

Should probiotics be used routinely when antibiotics are prescribed? I believe this should be a decision by the individual patient. If the patient enjoys yogurt and consumes it regularly, I see no reason not to suggest it. Certainly, it should be prescribed for patients who have experienced AAD before.

We still do not know much about probiotics to treat AAD once AAD has begun. It is worth a try.

Associated With An Increased Risk Of Total Mortality, CHD Mortality, And AF

5-3 SUBCLINICAL HYPERTHYROIDISM AND THE RISK OF CORONARY HEART DISEASE AND MORTALITY

Subclinical hyper-thyroidism (**sc-hyper-t**) is defined by a low thyrotropin (**TSH**) level and normal concentrations of free thyroxine (**FT4**) and triiodothyronine (**T3**).

This study included individual data on 52 674 participants pooled from 10 cohorts. Median age= 59; 58% women; median duration of follow-up = 8.8 years. Defined sc-hyper-t as a second

generation, more accurate, TSH level lower than 0.45 mIU/L with normal FT4 levels; euthyroidism as TSH between 0.45 and 4.49.

Sc-hyper-t was further categorized as levels of TSH below 0.10, and levels of 0.10 to 0.44. This included 1884 (3.6%) with TSH (0.10 to 0.44) and 304 (0.15%) with TSH <0.10.

Risks (hazard ratios [**HR**]) were consistently greater in the sc-hyper-t groups. However, absolute risks were small. Stroke and cancer mortality did not differ.

	HR for sc-hyper-t vs euthyroid	Risks per 1000-person-years
Total mortality	1.24	+3.6
CHD mortality	1.29	+0.6
CHD events	1.21	+3.2
Incident AF[a]	1.68	+4.6

(a atrial fibrillation)

CHD events and incident AF (but not other outcomes) were significantly greater in those with lower TSH levels

A. TSH 0.10 to 0.44	HR	
	CHD mortality	Incident AF
	1.24	1.63
B. TSH lower than 0.10		
	1,84	2.54

The population-attributable risk was 0.7% for total mortality, and 6.2% for incident AF.

Recent guidelines suggest that treatment of sc-hyper-t should be strongly considered in all individuals age 65 and older with TSH levels below 0.10. And treatment should be considered in individuals age 65 and over with TSH levels 0.10 to 0.44.

Conclusion: Endogenous sc-hyper-t is associated with an increased risk of total mortality, CHD mortality, and AF, with higher risks in those with TSH levels below 0.10 mIU/L. The study is observational and cannot assess whether the risks associated with sc-hyper-t are lowered by treatment.

(See the full abstract for details and the citation. ED)

This is not a strong study. I believe their estimate of prevalence of sc-hyper-t is too high. There is doubt about application of the data to younger patients.

There is a distinction between screening and testing, which I believe should be preserved. Screening applies to performance of a test for a disease or condition for which the patient has no

symptoms or signs. Screening the general population for sc-hyper-t is discouraged. Testing applies to patients who have signs or symptoms of a disease of interest.

TSH screening has an advantage in that it will diagnose hypo-thyroidism as well.

The prevalence of sc-hyper-t is low, and, if diagnosed, treatment, in absolute terms, yields relatively few benefits. We should focus on those who are at higher risk: eg, with nervousness, fatigue, weakness, heat intolerance, palpitations, new onset AF, supraventricular tachycardia, unexplained weight loss, fatigue, and signs such as thyroid enlargement, and thyroid nodules, use of causative medications, and older women with osteoporosis. Indeed screening may be more effective in women older than 50 because 1 of every 71 has unsuspected sc-hyper-t or overt hyperthyroidism.

The term apathetic hyperthyroidism applies to those with fatigue, depression, weight loss, and AF.

Thyroid disease is common. Prevalence in the US is estimated to be about 1%; 40% overt ant 60% subclinical . Primary care clinicians, usually the first to encounter these patients, should be constantly aware.

The reference range of TSH has been disputed and changed over the years, depending on the technique and the laboratory In 2004 the SI units defined the range as 0.5 to 4.7 mIU/L, My local laboratory defines it as 0.3 to 3.0. Certainly, the lower the TSH, the more likely is sc-hyper-t.

The distinction between exogenous hyperthyroidism and endogenous hyperthyroidism is important. Exogenous hyper-t may occur when the dose of therapeutic levothyroxin is too high or when patients take it surreptitiously.

I would not hasten to treat sc-hyper-t. Many patients are asymptomatic, or have mild symptoms. There is substantial disagreement about how and when to treat. TSH levels may return to normal without treatment. Those with TSH < 0.10 and those with convincing symptoms should be treated. Clinical judgment is required.

(Some of these editorial comments were based on an excellent review in the July 3 2012 issue of the Annals of Internal Medicine. Written by Michael T McDermott.)

5-4 WHAT IS THE IMPORTANCE OF SUBCLINICAL HYPER-THYROIDISM?

(This commentary expands on the previous article. Ed.)

Subclinical hyper-thyroidism (**sc-hyper-t**) is defined as having a normal free thyroxine (FT4) and a normal total triiodothyroninee (T3) in conjunction with a thyrotropin (TSH) level persistently below the reference range, in the absence of factors known to suppress TSH.

Factors that may alter thyroid function tests include medications (eg, corticosteroids, dopamine), pituitary and hypothalamic dysfunction and non-thyroid illness—a wide variety of illnesses that can alter thyroid function tests.

In general, the diagnosis of sc-hyper-t is made in ambulatory outpatients who are not taking medications known to affect thyroid function, The most common causes include Graves disease (usually younger patients), multi-nodular goiter (usually older patients) and solitary autonomous thyroid nodules.

The incidence of sc-hyper-t in the population is about 1%.

The distinction between endogenous and exogenous disease is important since exogenous sc-hyper-t can be treated by modulating the levo-thyroxine dose.

In addition to adverse cardiovascular (CVD) effects, sc-hyper-t is associated with risk of osteoporosis.

The main conclusion of the preceding study was that sc-hyper-t is associated with increased mortality and AF regardless of age, sex, and previous CVD. There was a trend for increased risk if TSH was lower than 0.10 mIU/ L.

Given the potential adverse effects of sc-hyper-t, how should primary care clinicians respond? The editorialists suggest considering tests to assess possible causes:

Complete history and physical exam
Thyroid ultrasound
Radioactive iodine uptake and scan
Bone mineral density
Electrocardiography
Comprehensive metabolic package
Repeat TSH, FT4, T3
Thyroid antibodies
Thyroid stimulating immune globulin

Prior to treatment, guidelines suggest repeating the thyroid function tests at 3 and 6 months to confirm stability. Sc-hyper-t may not be persistent. TSH levels may return to normal, or rarely progress to overt hyperthyroidism (~1%).

Once sc-hyper-t has been established, and external causes are considered (eg, medications, systemic illness), the most salient issue is whether to treat, and by what modality.

Recent guidelines indicate:

When TSH is persistently less than 0.1 mIU/L treatment should be strongly considered in an individual age 65 and older and in postmenopausal women who are not on estrogen or bisphosphonates; in patients with CVD risk factors; heart disease; osteoporosis; and individuals with hyperthyroid symptoms.

When TSH is persistently below the lower limits of normal, but over 0.10 mIU/L, treatment should be considered in individuals age 65 and older and in patients with heart disease or osteoporosis.

Treatment modalities and underlying principles of treatment are compatible with overt hyperthyroidism, including anti-thyroid drugs, radioactive iodine, and surgery. Methimazole is the first-line drug (compared with prophythiuracil) except during the first trimester of pregnancy. However, it is often difficult to formulate the optimum approach. Sc-hyper-t is usually milder than overt hyperthyroidism and may be controlled with lower doses of methimazole. Patients may be reluctant to accept surgery or radio-iodine therapy when the disease is mild and the patient asymptomatic. Older patients are usually treated with low doses of methimazole with periodic monitoring.

The preceding study provided information regarding the importance of recognizing sc-hyper-t. Until more information is available, the relationship between sc-hyper-t and total- mortality, CVD-mortality, and AF presently provides sufficient evidence to consider treatment, especially in patients with CVD risks, hyperthyroidism or osteoporosis**.**

While writing abstracts on sc-hyper-t and sc-hypo-t (Practical Pointers March 2012) I began to think how much primary care practice these days depends on laboratory and imaging reports. We order screening packages routinely, sometimes without much thought about the risk of underlying disease. And without any knowledge and consent by the patient.

As a result, patients are entered into the medical "system". The system goes on to more and more tests and consultations, with increasing costs, inconvenience and anxiety. We rely less on patient symptoms and concerns. We examine the patient less frequently.

Sc-hyper-t is a good example. A "routine" blood test suggests something amiss. More and more tests are ordered even though the patient feels well and has no suggestive symptoms or signs of the disorder. We follow the lab reports, not the patients. Would it not be better to simply follow the patient in the old-fashioned clinical way—continuing history and physical examinations. Little harm will be done in delaying the diagnosis.

Screening tests do indeed have a place in medical practice. They should be applied judiciously. Thee is a downside.

Clearly, There Are Areas In Which Health Care Spending Does Not Add To The Health Of Individuals Or Communities.

5-5 CHOOSING WISELY: ***Helping Physicians And Patients Make Smart Decisions About Their Care***

The US is grappling with the costs of health care and quality care. Clearly there are areas in which health care spending does not add to the health of individuals or communities.

An initial focus should be on the overuse of medical resources, which is not only a leading factor on the high level of spending on health care, but also places patients at risk of harm. Some estimates suggest that as much as 30% of all healthcare spending is wasted.

Physician's decisions about tests and procedures account for about 80% of health care expenditures. Yet physicians do not always have the most current effectiveness data. They can recommend diagnostic and therapeutic interventions that are no longer considered essential. Physicians may need help in communicating these matters to their patients. This may be especially difficult when clinicians and consumers are deluged with advertising and promotions. Physicians often report feeling compelled to accommodate patient's requests for interventions they know are unnecessary.

Patients need trustworthy information to help them better understand that more care is not always better care, and in some cases actually cause more harm than good. Patients need transparent and creditable information about the relative value and risks of various diagnostic and therapeutic interventions

To help reduce waste in the US health care system, and promote physician-patient conversations about making wise choices, 9 medical specialties have joined the *American Board of Internal Medicine Foundation* and *Consumer Reports* in the first phase of the "choosing wisely" campaign. Each society developed a list of 5 treatments or tests that are commonly used, which should be re-evaluated. The lists were released in April 2012 at a national event in Washington. It articulated the professional responsibility of physicians to improve quality and access to care, and to advocate for just and cost-effective distributing of finite resources. It specifically calls on physicians to be responsible for the appropriate allocation of resources and to avoid superfluous tests and procedures.

In 2010, a *Consumer Report* survey of nearly12 000 healthy 40- to 60-years old men and women with no heart disease risk factors or symptoms, showed that 44% had received screening tests for heart disease that were unlikely to have benefits that outweigh harms. Those who received testing did so without first getting crucial information from their physician. Only a few patients discussed with their physician how accurate the tests were, whether they reduced mortality, the potential complications that might occur due to the tests, or what the patient would need to do if the tests indicated a problem.

There is need to dispel the myth that " if some medical care is good, more is better".

The hope is that the lists will spark discussions between physician and patients about the need—or lack thereof—for many frequently ordered tests and treatments.

Consumer Reports, an independent non-profit consumer organization, in consultation with professional societies, will create and disseminate consumer-friendly versions of the lists to help patients understand the recommendations and be prepared to talk with their physicians about them.

The medical organizations demonstrate leadership, vision, and courage in highlighting overuse in their specialty. This is the highest form of medical professionalism.

The complete lists can be found at http://www.choosingwisely.org

Also see Consumer Reports – acting wisely

(See the Full Abstract for a selected list. Ed.)

JAMA May 2, 2012; 307: 1801-02 First author Christine K Cassel, ABIM Foundation, Philadelphia, PA

This is a good start—a work in progress. The goal is to achieve just and cost-effective distribution of finite clinical resources. We must be good stewards of medical interventions and costs. This is an ethical imperative.

It may take decades of experience with tests to determine the benefit / harm-cost ratio. Note the long debate about the value of prostate-specific antigen testing. And screening mammography in women age 40-49.

FULL ABSTRACTS MAY 2012

Probiotics Are Associated With Lower Risk For AAD.

5-2 PROBIOTICS AND THE PREVENTION AND TREATMENT OF ANTIBIOTIC-ASSOCIATED DIARRHEA

Antibiotics that disturb the gastrointestinal flora are associated with diarrhea, which can occur in up to 30% of patients. Symptoms may be mild and self-limiting, or severe (as with *Clostritium difficile* infection).

Antibiotic-associated diarrhea (**AAD**) is an important reason for non-adherence with antibiotic treatment.

Probiotics are living microorganisms intended to have health benefits. Symbiotics refer to preparations containing both probiotics and pre-biotics (non-digestible food ingredients that may benefit the host by selectively stimulating bacteria in the colon).

Probiotics may maintain or restore gut micro-ecology during or after antibiotic treatment by competition for nutrients, inhibition of epithelial adherence of pathogens, lowering colonic pH favoring the growth of non-pathogenic species, stimulation of immunity, and production of antimicrobial substances.

This systematic review and meta-analysis evaluated and updated the available evidence on live probiotics that included the genera *Lactobacillus, Bifidobacterium, Saccharomomyces, Streptococccus, Enterococcus, and/or Bacillus*, alone or in combination, for the prevention and treatment of AAD.

STUDY

1. Selected parallel randomized controlled trials (**RCT**) that compared probiotics use as an adjunct (a supplement) to antibiotics vs. a concurrent control group receiving no treatment, placebo, or a different probiotic or pre-biotic dose.
2. Included antibiotic-treated patients of all ages regardless of the indication and the underlying symptoms. The probiotics were used for prevention and treatment (mainly prevention) of AAD.
3. Used the original study-definition of diarrhea ranging from uncomplicated to severe.
4. Used *Lactobacillus* alone or in combination with other genera.
5. The primary outcome was the number of participants with diarrhea in each treatment group.

RESULTS

1. A total of 82 RCTs met inclusion criteria. Most trials (52/82) enrolled adults.
2. The clinical indication for the antibiotic use varied; 24/82 concerned treatment of *H pylori.* Sixteen trials reported use of a single antibiotic (eg, amoxicillin, azithromycin, clarithromycin).
3. Only two trials were identified that explicitly investigated probiotics for treatment of AAD rather than for prevention. All remaining RCTS used probiotics given at inception of antibiotic therapy to prevent AAD.
4. Most RCTs included a modest number of patients (mean = 93). Most probiotics contained *Lactobacilli* alone or with other genera.
5. The quality of the trials was low. Questions about conflict of interest and bias remained.
6. Efficacy: 63 RCTs reported the number of participants with diarrhea, and the number randomized to both groups. Most trials did not show a statistical advantage for probiotic use. However, across 63 RCTs (N = 11 811) probiotic use was associated with a lower relative risk (**RR**) of developing AAD compared with the control groups. (RR = 0.58; Number needed to treat = 13.)
7. Seventeen RCTs used *Lactobacillus* only. The pooled RR of AAD was 0.65. (NNT = 14) For 15 RCTs using yeast-based probiotics (*Saccharomyces*) the pooled RR of AAD was 0.48 (NNT = 10). One study concluded that no specific species or combination of species of probiotics showed substantial superiority over the others.
8. There was no statistically significant difference in associations between different age groups.
9. In 24 RCTs, hospitalized patients were included. Adjunct probiotic preventive treatment was associated with a statistically significant lower risk of AAD. (RR = 0.55; NNT = 10). The duration of antibiotic treatment (1 to 14 days) did not influence the results.
10. Trials that reported incidence of AAD after cessation of antibiotic therapy reported that the number of patients experiencing AAD was lower in those who received probiotics. (RR = 0.44)
11. Severe AAD and *Clostridium difficile* infections were less common in the probiotic group.
12, Only 19 RCTs reported on possible adverse effects of probiotics. No adverse effects were reported, and the probiotics were considered safe.

DISCUSSION

1. The principal finding of this study is that use of probiotics as adjunct therapy reduces the

risk of AAD with a pooled RR of 0.58. (NNT = 13)

2. The results were consistent across a number of subgroups.
3. The main limitations of the study are unexplained heterogeneity, poor documentation of probiotic strains, and lack of assessment of probiotic-specific adverse effects.
4. *Lactobacillus*, either alone or in combination, was the chief organism studied. (Most documented interventions used blends of genera.)
5. No systematic differences in results were identified across trials using different age groups, clinical inductions, duration of antibiotic use, and type of probiotics.
6. AAD does not occur in the majority of patients and when it occurs, it is usually self-limited.
7. Only a small number of trials targeted elderly persons. More data on this group is needed.
8. Some antibiotics are more likely to cause AAD, but the included trials rarely specified the antibiotic used.
9. Additional questions: What is the optimum dose of probiotics ? What is the comparative effectiveness of different probiotics?

CONCLUSION

Adjunct probiotic administration is associated with lower risk for AAD. This generalized conclusion likely obscures heterogeneity of effectiveness among the patients, the antibiotics, and the probiotic strains and blends.

JAMA May 9, 2012; 307: 1850- 60 "Clinical Review" Original investigation, first author Susanne Hempel, RAND Health, Santa Monica, California

==========

Associated With An Increased Risk Of Total Mortality, CHD Mortality, And AF

5-3 SUBCLINICAL HYPERTHYROIDISM AND THE RISK OF CORONARY HEART DISEASE AND MORTALITY

Subclinical hyper-thyroidism (**sc-hyper-t**) is defined by a low thyrotropin (TSH) level and normal concentrations of free thyroxine (FT4) and triiodothyronine (T3). It has been associated with several biological effects on the cardiovascular system such as increased heart rate, left ventricular mass, carotid intimal-medial thickness, and plasma fibrinogen levels.

No large randomized controlled trials have examined the effects of treatment of sc-hyper-t on clinically relevant outcomes. A consensus statement and recent guidelines advocate treatment, particularly in patients with TSH levels lower than 0.10 mIU/L to avoid long-term complications.

This study assessed the risks of total mortality, CHD mortality, and atrial fibrillation (**AF**) associated with endogenous sc-hyper-t.

STUDY

1. A systematic literature search included longitudinal cohort studies reporting participants with lower TSH levels and normal FT4, vs.euthyroid controls. None were taking thyroid-altering medications.
2. Included individual data on 52 674 participants pooled from 10 cohorts. CHD events were analyzed in 22 437 participants; AF in 8711 participants. Median age= 59; 58% women; median duration of follow-up = 8.8 years.
3. Used a uniform cutoff level for sc-hyper-t based on expert consensus and current guidelines. Defined sc-hyper-t as a second generation, more accurate, TSH level lower than 0.45 mIU/L with normal FT4 levels; euthyroidism as TSH between 0.45 and 4.49.
4. Sc-hyper-t was further categorized as levels of TSH below 0.10, and levels of 0.10 to 0.44.

RESULTS

1. Total participants = 52 674; 50 486 were euthyroid; 1866 (4.2%) had endogenous sc-hyper-t, and 0.15% had TSH <0.10.
2. During follow-up, 8577 died; including 1896 participants who died from CHD; 3653 of 22 437 had CHD events; 795 of 8711 developed incident AF.
3. Risks (hazard ratios [**HR**]) were consistently greater in the sc-hyper-t groups. However, absolute risks were small. Stroke and cancer mortality did not differ.

	HR for sc-hyper-t vs euthyroid	Risks per 1000-person0years
Total mortality	1.24	+3.6
CHD mortality	1.29	+0.6
CHD events	1.21	+3.2
Incident AF	1.68	+4.6

4. CHD events and incident AF (but not other outcomes) were significantly greater in those with lower TSH levels

   A. TSH 0.10 to 0.44 HR

	CHD mortality	Incident AF
	1.24	1.63
B. TSH lower than 0.10		
	1.84	2.54

5 The population-attributable risk was 0.7% for total mortality, and 6.2% for incident AF.

DISCUSSION

1. In this analysis of all available prospective cohorts, based on individual participant data, sc-hyper-t was associated with increased risk of total mortality, CHD mortality, and incident AF.
2. CHD mortality and incidence of AF (but not other outcomes) were significantly greater in participants with TSH levels lower than 0.10 mIU/L than in those with levels 0.10 to 0.44.
3. Risks did not differ significantly by age, sex, or preexisting CVD, and were similar after further adjustment for CVD risk factors.
4. Some individual studies reported increased risk of AF especially in elderly patients, and those with TSH lower than 0.10.
5. The study did not have any information on the etiology of endogenous sc-hyper-t.
6. Recent guidelines suggest that treatment of sc-hyper-t should be strongly considered in all individuals age 65 and older with TSH levels below 0.10. And treatment should be considered in individuals age 65 and over with TSH levels 0.10-0.44.
7. However, findings based on observational data should be interpreted with caution in clinical practice. No clinical trials have assessed whether treatment results in improvement of CVD outcomes.
8. Because the study included data on a limited number of younger men and premenopausal women, generalization to younger adults is limited.

CONCLUSION

Endogenous sc-hyper-t is associated with an increased risk of total mortality, CHD mortality, and AF, with higher risks in those with TSH levels below 0.10 mIU/L

The study is observational and cannot assess whether the risks associated with sc-hyper-t are lowered by treatment.

Archives Internal Medicine May 28, 2012 by the Thyroid Study Collaboration, first author Tinh-Hai Collet, University of Lausanne, Lausanne Switzerland.

==========

5-5 CHOOSING WISELY: ***Helping Physicians And Patients Make Smart Decisions About Their Care***

"Five Things Physicians and Patients Should Question"

Lists of DO and DO NOT recommendations from 9 prestigious societies:

American Academy of: Allergy, Asthma, and Immunology; Family Physicians. American College of Cardiology; Physicians; Radiology. American Society of Nephrology; Nuclear Cardiology. American Gastroenterological Associating.

I downloaded the lists from the web site (www.choosingwisely.org) and selected recommendations applicable to Primary Care Medicine.

The last two were published previously. (See *Practical Pointers* August 2011)

Individual clinical judgment can overrule any of the recommendations.

Don't diagnose or manage asthma without spirometry.

Clinicians often rely solely upon symptoms when diagnosing and managing asthma, but these symptoms may be misleading and be from alternate causes. Therefore spirometry is essential to confirm the diagnosis in those patients who can perform this procedure. Recent guidelines highlight spirometry's value in stratifying disease severity and monitoring control. History and physical exam alone may over- or under-estimate asthma control. Beyond the increased costs of care, repercussions of misdiagnosing asthma include delaying a correct diagnosis and treatment.

Don't do imaging for low back pain within the first six weeks, unless red flags are present.

Red flags include, but are not limited to, severe or progressive neurological deficits or when serious underlying conditions such as osteomyelitis are suspected. Imaging of the lower spine before six weeks does not improve outcomes, but does increase costs. Low back pain is the fifth most common reason for all physician visits.

Don't use dual-energy x-ray absorptiometry (DEXA) screening for osteoporosis in women younger than 65 or men younger than 70 with no risk factors.

DEXA is not cost effective in younger, low-risk patients, but is cost effective in older patients.

Don't order annual electrocardiograms (EKGs) or any other cardiac screening for low-risk patients without symptoms.

There is little evidence that detection of coronary artery stenosis in asymptomatic patients at low risk for coronary heart disease improves health outcomes. False-positive tests are likely to lead to harm through unnecessary invasive procedures, over-treatment and misdiagnosis. Potential harms of this routine annual screening exceed the potential benefit.

Don't perform Pap smears on women younger than 21 or who have had a hysterectomy for non-cancer disease.

Most observed abnormalities in adolescents regress spontaneously, therefore Pap smears for this age group can lead to unnecessary anxiety, additional testing and cost. Pap smears are not helpful in women after hysterectomy (for non-cancer disease) and there is little evidence for improved outcomes.

Don't obtain screening exercise electrocardiogram testing in individuals who are asymptomatic and at low risk for coronary heart disease.

In asymptomatic individuals at low risk for coronary heart disease (10-year risk <10%) screening for coronary heart disease with exercise electrocardiography does not improve patient outcomes.

In the evaluation of simple syncope and a normal neurological examination, don't obtain brain imaging studies (CT or MRI).

In patients with witnessed syncope but with no suggestion of seizure and no report of other neurologic symptoms or signs, the likelihood of a central nervous system (CNS) cause of the event is extremely low and patient outcomes are not improved with brain imaging studies.

Don't obtain preoperative chest radiography in the absence of a clinical suspicion for intrathoracic pathology.

In the absence of cardiopulmonary symptoms, preoperative chest radiography rarely provides any meaningful changes in management or improved patient outcomes.

Don't do imaging for uncomplicated headache.

Imaging headache patients absent specific risk factors for structural disease is not likely to change management or improve outcome. Those patients with a significant likelihood of structural disease requiring immediate attention are detected by clinical screens that have been validated in many settings. Many studies and clinical practice guidelines concur. Also, incidental findings lead to additional medical procedures and expense that do not improve patient well-being.

For pharmacological treatment of patients with gastroesophageal reflux disease (GERD), long-term acid suppression therapy (proton pump inhibitors or histamine2 receptor antagonists) should be titrated to the lowest effective dose needed to achieve therapeutic goals.

The main identifiable risk associated with reducing or discontinuing acid suppression therapy is an increasesymptoburdenIt follows that the decision regarding the need for (and dosage of) maintenance therapy is driven by the impact of those residual symptoms on the patient's quality of life rather than as a disease control measure.

Do not repeat colorectal cancer screening (by any method) for 10 years after a high-quality colonoscopy is negative in average-risk individuals.

A screening colonoscopy every 10 years is the recommended interval for adults without increased risk for colorectal cancer, beginning at age 50 years. Published studies indicate the risk of cancer is low for 10 years after a high-quality colonoscopy fails to detect neoplasia in this population. Therefore, following a high-quality colonoscopy with normal results the next interval for any colorectal screening should be 10 years following that normal colonoscopy.

Do not repeat colonoscopy for at least five years for patients who have one or two small (< 1 cm) adenomatous polyps, without high-grade dysplasia, completely removed via a high-quality colonoscopy.

The timing of a follow-up surveillance colonoscopy should be determined based on the results of a previous high-quality colonoscopy. Evidence-based (published) guidelines provide recommendations that patients with one or two small tubular adenomas with low grade dysplasia have surveillance colonoscopy five to 10 years after initial polypectomy. "The precise timing within this interval should be based on other clinical factors (such as prior colonoscopy findings, family history, and the preferences of the patient and judgment of the physician)."

Avoid nonsteroidal anti-inflammatory drugs (NSAIDS) in individuals with hypertension or heart failure or CKD of all causes, including diabetes.

The use of NSAIDS, including cyclo-oxygenase type 2 (COX-2) inhibitors, for the pharmacological treatment of musculoskeletal pain can elevate blood pressure, make antihypertensive drugs less effective, cause fluid retention and worsen kidney function in these individuals. Other agents such as acetaminophen, tramadol or short-term use of narcotic analgesics may be safer than and as effective as NSAIDs.

Don’t perform cardiac imaging for patients who are at low risk.

Chest pain patients at low risk of cardiac death and myocardial infarction (based on history, physical exam, electrocardiograms and cardiac biomarkers) do not merit stress radionuclide myocardial perfusion imaging or stress echocardiography as an initial testing strategy if they have a normal electrocardiogram (without baseline ST-abnormalities, left ventricular hypertrophy, pre-excitation, bundle branch block, intra-ventricular conduction delay, paced rhythm or on digoxin therapy) and are able to exercise.

Do not obtain blood chemistry panels (eg, baseline metabolic panel) or urinalysis for screening asymptomatic healthy adults.

Only lipid screening yields significant numbers of positive results among asymptomatic patients.
Screen for type-2 diabetes in adults with hypertension. Source: USPSTF.

Use only generic statins when initiating long-term drug therapy

All statins are effective in lowering mortality, heart attacks, and stroke when dose is titrated to affect appropriate LDL-c reduction.