PRACTICAL POINTERS

FOR

PRIMARY CARE MEDICINE

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

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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 review of the current literature and his 25-year publication of Practical Pointers.

2) The main **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.

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HIGHLIGHTS AND *EDITORIAL COMMENTS* JULY 2011

When Treatment Is Valued Over Care

7-1 IMPROVING CARE AT THE END OF LIFE

Three short anecdotal articles in this issue of Archives describe encounters with 3 elderly patients with medical emergencies.

The first patient was a 62 year old woman. She was a 40-pack-year smoker; had a history of intravenous drug use and was presently on methadone. Also poorly controlled diabetes, hepatitis C, end-stage renal disease on hemodialysis, asthma, multiple abdominal surgeries, and an ostomy following complicated cholecystectomy.

Over the past 5 months, she was admitted twice to reverse a fistula, once for urosepsis, once for hyperkalemia.

Her final admission to the hospital emergency department (**ED**) was for a high grade small bowel obstruction.

The attending ED physician noted she appeared much older than her stated age. She was in severe respiratory distress. Her breathing became more labored, and her oxygen level and BP dropped. Her pulse raced at 130.

She was informed about the intended treatment and she consented. She was sedated and a ventilation tube and central line were passed.

Finally, the critical care team arrived and whisked her off to the intensive care unit.

The physician knew that any other ED physician would do the same. But she wondered if she had done the right thing—what was best for the patient. While she may have survived, her quality-of-life would remain poor, and she would continue to suffer. She had been managed from one crisis to another without any serious discussion about her wishes or her prognosis.

In the hospital, she developed overwhelming sepsis and multiorgan failure.

One day before her death, the surgical and intensive care team communicated her poor prognosis to the family, and she was given a do-not-resuscitate order and weaned from the ventilator.

This presents an ethical problem. How far should the medical profession and hospitals go to preserve a suffering life for which prognosis appears dismal? How far should society go in paying for such treatment?

The patient presented herself to the ED. The intended treatment was explained to her. Did she fully understand? But she agreed to the stated treatment. She expressed her autonomy. Apparently she had decision-making capability.

Should the ED physician make any decision to overrule her autonomy?

This is an example of paying excellent attention to the disease, and not paying attention to the patient with the disease. Certainly, decisions should have been made long ago about end-of-life care.

Would Hospice have been helpful?

Her family was finally contacted and, apparently having health-care power of attorney, was able to make the decision to stop interventions. Why was the family involved so late in the course of the disease?

The second patient was a 90 year old female, a 19-year nursing home resident with advanced dementia. She had very little awareness of her surroundings. And little enjoyment of life.

She developed gangrene of the feet.

Her physician contacted her niece and nephew, who had co-powers of attorney and discussed treatment options.

They agreed that only supportive comfort measures should be implemented.

The physician went on vacation for 2 weeks. On returning he learned that the nursing home administrators and nurses had obtained permission from the substitute physician to send the patient several times by ambulance to the hospital for wound care.

The nursing home administration felt they could not risk an investigation claiming that they could have done more for the patient.

The futile trips to the hospital involved uncomfortable transfer and painful debridement, with no change in the inevitable outcome of death.

The case of this elderly woman who was treated aggressively against the wishes of her power-of-attorney demonstrates the harm that can be done in an environment that values treatment over care.

This is an example of lack of communication. The holders of the health care power of attorney had clear authority to decide about transport to the hospital and other treatments. Their decision was ignored by the substitute physician and the nursing home administration.

Firm decisions about continuing care should be reiterated from time to time. Clear instructions should be placed in a prominent place in the chart for all to see.

Many problems are best avoided, and can be avoided.

The third patient was an 80-year old man who came by ambulance vomiting blood. He was visibly uncomfortable and very pale. His undershirt was covered with coffee-ground emesis. The ED physician had to decide quickly how to treat him. Should he be intubated to protect his airway? Does the patient have a health-care proxy and advanced directive?

At this point, a middle-aged man arrived—the patient's son. He explained that his father had Alzheimer dementia and that he had his father's power of attorney. His father would not want a breathing tube. He had directed comfort care only.

The physician was relieved and proceeded to ease the patient's nausea and his pain and discomfort, and to transfuse with blood if necessary. They decided to call the patient's doctor to inform him of the patient's condition, And to call the family and tell them to come quickly.

His daughter and two grandsons arrived.

After sedation and intravenous fluids and transfusion with packed red cells, the elderly man's color returned. After a transfusion, the patient was back to baseline and was discharged the next day.

This is a good example of family support.

There was a striking difference between this patient's care and that of the preceding patient's due to careful predetermination of health care power of attorney, and advanced directives.

The commentators add:

It is widely asserted that more medical care (more tests and procedures) results in better outcomes. But there is mounting evidence to suggest otherwise.

Risk of harm is inherent in all tests and procedures. Discomfort is associated with much end-of-life care. New evidence suggests that treating patients' pain and other symptoms is associated with improvement in physical status and may even lengthen survival.

Though most patients prefer to die at home, many die in hospitals, often hooked up to tubes and lines in intensive care, uncomfortable and unable to communicate. Far fewer live through the end stage of life having their pain and other symptoms treated, and able to speak and communicate with loved ones.

It is worth pausing for a moment to consider how health care providers can treat more patients like the old man and fewer like the old women.

As a health care provider, it is necessary to be receptive and accessible, to have expertise in pain and symptom management, and to respond to the wishes of the patient and the family. As a patient, it is vital

to have strong social support, especially a reliable, local officially-designated individual who knows how to navigate the health care bureaucracy and can serve as advocate.

Many may believe that supportive and comfort care is appropriate for elderly patients and those with severe dementia, but not for younger persons with normal cognition.

In the opinion of one commentator, it is not age or cognitive function that determines whether we should provide comfort care rather than aggressive care, but each individual patient's goals after a realistic discussion of the prognosis and quality-of- life**.**

This illustrates an important aspect of primary care. Clinicians should ask elderly patients if they have a health-care power of attorney, and if they have prepared advance directives. This data should be prominently placed in the office record. If it is not, the *patients should be reminded of its importance.*

I believe that, in addition to the written directive, elderly patients should verbally express their wishes at family gatherings, and let it be understood that one person will have the authority to make substitute decisions if and when they may become necessary. This will help to avoid possible dissention in the family.

Archives Internal Medicine July 11, 2011; 171: 1200-02 "Perspective"
"At The End Of Life, Sometimes Less Is More" commentary first author Corita Gruzen, Mt Sinai School of Medicine, New York
"Improving Care at the End of Life" commentary first author Corita Gruzen, Mt Sinai School of Medicine, New York
"Honoring Patients' Wishes for Less Health Care" commentary by Phillip Wickenden Bale, T J Samson Hospital, Glasgow, KY

Adversely Affects Home Life And Practice.

7-2 WORK/HOME CONFLICT AMONG ACADEMIC INTERNAL MEDICINE PHYSICIANS: " Physician Burnout"

Work/home conflict may have a central role in physician-burnout.

A previous study found that 3 factors were independently associated with burnout: hours worked per week; experiencing a work/home conflict; and how the work/home conflict was resolved.

This study was designed to validate the importance of these factors in relation to physician burnout, and to explore whether they are related to internal medicine physicians in a large academic center.

The study used only 2 questions to survey burnout in a group of 465 general and subspecialty internists:

1) Do you feel burnout from your work at least weekly?

2) Have you become more callous toward people since taking this job?

The mean hours of work per week = 64. About 1/3 (31%) experienced burnout at least once a week. Over ¾ (78%) experienced conflict between work and home over the past 3 weeks. The conflict was resolved in favor of work 57% of the time.

About 10% became more callous toward people.

Physician burnout was common, and related to hours of work and work/home conflict.

Given the high prevalence and the well-established negative personal and professional consequences of burnout, the observed associations between hours worked and home/work conflicts suggest possible targets for action.

I believe burnout is more common than most physicians would admit. We are a conscientious bunch of high achievers and hard workers.

Burnout undoubtedly adversely affects the physician-patient relationships as well as home life.

The prevalence of burnout among physicians is common. I suspect it is also common among patients.

Both high work load and resultant work/home conflict led to burnout. I suspect the latter was more important. However, the conflict was most often resolved in favor of work. I wonder how long the conflict remained resolved.

This is an important aspect of primary care practice. Clinicians should think about the possibility of self-burnout. They should also address the possibility that some patients also experience burnout.

Steps can be taken to avoid it and to prevent it.

Several inventories are available on the internet to judge burnout.

http://www.mindtools.com/stress/Brn/BurnoutSelfTest.htm

The Hepatic Manifestation Of The Metabolic Syndrome.

7-3 HOW BIG A PROBLEM IS NON-ALCOHOLIC FATTY LIVER DISEASE?

The authors based these comments on an extensive search of the current literature. The many studies in progress will add to our understanding. Much uncertainty remains.

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of liver diseases (in the absence of excessive alcohol consumption):

Steatosis: Simple fatty infiltration

Non-alcoholic steatohepatitis (NASH): Fatty infiltration + inflammation

Fibrosis

Cirrhosis

Liver cancer

Simple steatosis has not been associated with liver-related morbidity. NASH may lead to progressive liver fibrosis, cirrhosis, and liver cancer.

NASH is strongly associated with obesity, insulin resistance, type-2 diabetes (DM-2) , and dyslipidemia. It may be considered the hepatic manifestation of the metabolic syndrome.

NAFLD has become the most common cause of abnormal liver biochemistry.

But despite substantial clinical and basic research, the true prevalence of NAFLD and NASH in communities and the likely future disease burden remains unclear.

Diagnosis:

NASH is often asymptomatic. It is often first discovered by incidental routine biochemical abnormalities (often mild increases in aminotransferase levels).

NASH is probably underdiagnosed in patients with advanced liver disease, which is thought to be the underlying cause of a high % of cases where no specific cause is readily identified. ("cryptogenic cirrhosis").

Ultrasound provides a quantitative assessment of hepatic fat content. Sensitivity of ultrasound is limited, especially when steatohepatitis progresses.

Other than biopsy, no widely acceptable reliable method is available to differentiate simple steatosis from steatohepatitis in routine practice

Although biopsy remains the optimum investigation for assessing degree of inflammation and fibrosis, invasive tests are not appropriate in primary care practice.

Prognosis:

Only a minority of patients progress from steatosis to more advanced disease characterized by inflammation, fibrosis and subsequent cirrhosis and hepatocellular cancer. Studies suggest that about 5% with NASH develop complications of end-stage liver disease during a long follow-up.

Hepatic fibrosis may take years to progress. High quality data from prospective trials is limited, particularly in primary care settings. Currently, liver biopsy is the optimum investigation to assess the degree of inflammation and the extent of fibrosis as markers for liver-related morbidity.

About 1/3 of patients with NASH will exhibit progressive fibrosis.

A cohort study reported that NASH was associated with increased risk of liver-related death and double the *cardiovascular* risk over 14 years.

Treatment

Current treatment includes weight loss and amelioration of the metabolic syndrome by lifestyle interventions (diet and exercise).

Insufficient evidence is presently available to formulate authoritative and balanced treatment guidelines. No drugs are currently licensed specifically for treatment. Lifestyle changes are the mainstay of treatment. Trial evidence shows that weight reduction of > 7% maintained over 48 weeks is associated with significant reduction in histological evidence of NASH

As a marker of the metabolic syndrome, identification of NAFLD should prompt modification of cardiovascular risk factors.

I recall (in the "olden days") when I first started practice, we were puzzled by elevated aminotransferase levels in otherwise apparently healthy patients. We were equally puzzled by the occasional patient with cirrhosis who had no history of alcohol abuse.

The evidence of liver disease associated with DM-2 and obesity is important to primary care practice. We now have an additional talking point to try to convince patients to change lifestyles. I would add, an admonishing to stop alcohol consumption entirely, even though intake is modest.

When an obese patient with DM-2 or impaired fasting glucose presents in primary care, would it not be reasonable to assume that NAFLD is present (or will occur) and omit the burden and expense of other tests to confirm it. After all, the treatment would be the same in either case. The patient may reasonably be assured that their liver disease will improve with weight loss and diet control.

The concept that NAFLD is another manifestation of the metabolic syndrome expands treatment to lower risk of cardiovascular disease (BP and lipid control; physical activity).

According to my chef friend, pate de foie gras is prepared by restraining geese and force feeding them for 3 or 4 months. The disparity between energy intake and expenditure leads to massive growth of the liver due to fat accumulation. They say the pate prepared from the fat liver is delicious. I have never tasted it, and don't intend to. So could not NAFLD be termed the foie gras syndrome, or more provocatively, the pate de foie gras syndrome?

An Important Application For Primary Care Patients And For Public Health

7-4 SODIUM AND POTASSIUM INTAKE AND MORTALITY AMONG U.S. ADULTS

Examining the joint effects of Na and K intakes on CVD risk is particularly important because most of the US population consumes more Na and less K daily than is recommended.

This study reports an analysis between the estimated usual intakes of Na and K, as well as their ratio, with all-cause and CVD mortality.

The third National Health and Nutrition Examination Survey (NHANES III- 1988-1994) examined a nationally representative sample of non-institutionalized US adults (n = 12 267). Each survey participant completed a household interview and a 24-hour dietary recall. Determined the baseline 24-hour Na and K intake from the dietary recall and calculated the Na/K ratio. A linked mortality file (1988-2006)) determined mortality from CVD, IHD, and all-causes as related to the baseline Na and K intake and the Na/K ratio.

Estimates of usual daily intakes of Na, K, and the Na/K ratio and caloric intake at baseline: (means)

	Na (mg)	K (mg)	Na/K	Calories
Men	4323	3373	1.31	2697
Women	2518	2433	1.23	1785

Intake of Na was much higher than the recommended 1500 mg/d (5000 mg NaCl))

Intake of Na paralleled the caloric intake.

Intake of K was much lower than the recommended "adequate" 4700 mg/d

The Na/K ratio remained much higher than 1.00

Over a mean follow-up of 14.8 years (170 110 person-years) there were 2270 all-cause deaths, including 825 CVD and 443 IHD deaths

Hazard ratios (**HR**) of usual intakes of Na/K ratio for *all cause mortality*;

Quartiles--lowest to highest)

Na/K ratio	0.98	1.17	1.33	1.57
HR	1.00	1.13	1.25	1.46

Higher Na intake was associated with *higher* all-cause mortality. (HR = 1.20 for each 1000 mg per day.)

Higher K intake was associated with a *lower* all-cause mortality (HR = 0.80 for each 1000 mg per day.

HR of Na/K ratio for *CVD and IHD mortality*

Na/K ratio	0.98	1.17	1.33	1.57

CVD mortality	1.00	1.13	1.25	1.46
IHD mortality	1.00	1.28	1.51	2.15

Higher Na/K ratio was significantly associated with increased risk of death from CVD and IHD.

In this nationally representative sample of adults followed for about 15 years, there was a significant monotonic association between increased Na/K ratio and risk of mortality from CVD, IHD, and all-causes. The association was independent of sex, race-ethnicity, and other covariates.

High Na levels increase BP by stimulating endothelial cells, thickening and narrowing resistance arteries, and blocking nitric oxide synthesis. High K levels can counteract these effects by activating nitric oxide release. The opposing biological effects of Na and K may explain stronger associations of the Na/K ratio with CVD mortality than either Na or K intake alone.

Conclusion: In the general US population, a high Na/K ratio was associated with a significant increase in CVD mortality and all-cause mortality. High Na intake was associated with increased all-cause mortality.

The more you eat, the more Na you consume.

This may be another reason for the benefits of the Mediterranean diet, which is high in fruits and vegetables as well as oils and wine.

I was hoping that wine would contain a high level of K. But according to a Google search, it contains from 60 to 120 mg per 100 g. Not much, but every little bit helps. I doubt if wine contains any Na.

7-5 NEW TOOL TO GAUGE DEPRESSION REMISSION

How do primary care clinicians know when their patients with depression are in remission? The lack of symptoms alone may not be adequate to gauge remission.

Primary care physicians need more effective, practical tools to determine not only how patients do not feel, but how they do feel.

REMIT[1] consists of 5 questions asked about patient's feelings of happiness, contentment, resilience, and optimism. They enlarge upon global sense of feeling better. It is designed to be used along with the 9-item Patient Healthy Questionnaire (PHQ-9), which provides a score based on DSM-IV criteria for depression.

A study tested the questions in over 1000 patients being treated for depression in primary care. It used REMIT in conjunction with PHQ-8 (omitting a question about suicide). REMIT and PHQ-8 used together explained more about a patient's own sense of recovery than the PHQ-8 used alone.

The REMIT questions:

Do you feel happy?

Do you feel content?

Do you feel in control of your emotions?

Do you bounce back when things go wrong?

Does the future look dark to you?

Answers range in severity from 0 to 4 based on how the patient felt over the past 2 weeks. (0 is all of the time; 4 is none of the time)

JAMA July 21, 2011; 304: 363-64 "Medical News and Perspective" by Rebecca Voelker, JAMA Staff.

I included this brief article because primary care clinicians may fail to detect depression in many of their patients. I believe questionnaires are helpful.

A host of inventories and questionnaires addressing many health questions appear on the web. I accessed PHQ-9 at http://steppingup.washington.edu/key/documents/phq-9.pdf.

The first 2 questions: 1) Do you have little interest or pleasure in doing things?, 2) Do you feel down, depressed, or hopeless? Some authorities have stated that these 2 questions are a good, rapid screen for depression. This is the PHQ-2 screening test. A high score on both questions indicates the possibility of a depressive disorder of over 90%.

1. Remission Evaluation and Mood Inventory (REMIT) Gen Hosp Psychiatry 2011; 331:279-86 First author D E Neese, The Advisory Board Company, Washington DC

A Potential "Game Changer" For Primary Prevention Of Melanoma.

7-6 PREVENTION OF MELANOMA WITH REGULAR SUNSCREEN USE

Evidence from randomized controlled trials demonstrate that regular sunscreen use protects against cutaneous squamous cell carcinoma.

Up to now, there has been no randomized controlled trial (RCT) data on sunscreen prevention of melanoma. Case-control studies have yielded conflicting results.

Now a RCT from Australia provides evidence that regular use of sunscreens does prevent melanoma.

The trial entered 1621 adult subjects. Randomized to regular use of sunscreen vs discretionary use. Those randomized to regular use were given an unlimited supply of a broad spectrum sunscreen—sun

protective factor (SPF) of 16, and asked to apply it to the head, neck and hands every morning. Reapplication was advised after heavy sweating, bathing and long sun exposure.

The trial lasted 5 years.

During a 10-year follow-up (after the initial 5 years) incidence of a new primary melanoma:

Regular daily use 11 cases among 812 persons

Discretionary use 22 cases among 804 persons.

A reduction of 50% (By my calculation, NNT for 5 years to prevent one melanoma = 74. Ed.)

The reduction in invasive melanoma was substantial:

Regular daily use 3 cases

Discretionary use 11 cases

Since exposure to ultraviolet radiation (UVR) is the only known modifiable cause of melanoma, this study is a potential "game changer" for primary prevention of melanoma.

In the US, this recommendation is particularly relevant to those who live in relatively high ambient UVR locations such as Florida, California, and Arizona.

The US Preventive Services Task Force suggests that counseling can increase sun-protective behavior and decrease indoor tanning.

If sunscreens are used every day, they can be time consuming and expensive. Costs may be reduced by wearing wide-brimmed hats, long sleeves, and long pants.

Over 68 000 new cases of melanoma occurred in the US in 2010. Effective use of sunscreens can reduce the risk.

The full abstract presents detailed directions for application of the sunscreen. I believe many individuals would not comply and consider the protocol too burdensome as well as too costly. The protocol from Australia is much simpler.

If my calculations about the NNT are correct, the one in 74 chance of avoiding melanoma would convince many individuals to use sunscreen regularly.

FULL ABSTRACTS JULY 2011

Adversely Affects Home Life And Practice.

7-2 WORK/HOME CONFLICT AMONG ACADEMIC INTERNAL MEDICINE PHYSICIANS:

" Physician Burnout"

Work/home conflict may have a central role in physician-burnout.

In a recent comprehensive evaluation of a wide variety of personal and professional factors hypothesized to contribute to burnout in American surgeons, 3 factors were independently associated with burnout: hours worked per week; experiencing a work/home conflict; and how the work/home conflict was resolved.

The present study was designed to validate the importance of these factors in relation to physician burnout, and to explore whether they are related to internal medicine physicians in a large academic center.

STUDY

1. In 2009, all faculty members in the Mayo Clinic Department of Medicine received a survey of items pertaining to demographics, work characteristics, and experience of work/home conflict, and how the conflict was resolved.
2. This study used only 2 questions to survey burnout in a group of 465 general and subspecialty internists:
   1) Do you feel burnout from your work at least weekly?
   2) Have you become more callous toward people since taking this job?
   (Both questions have a high likelihood of agreement with larger inventories that assess burnout.)

RESULTS

1. Hours (mean) worked per week 64
2. About 1/3 (31%) experienced burnout at least once a week.
3. Over ¾ (78%) experienced conflict between work and home over the past 3 weeks.
4. How was the conflict resolved?
   In favor of work 57%
   In favor of home responsibilities 8%
   Able to resolve in a manner meeting both responsibilities 35%
5. About 10% became more callous toward people.

DISCUSSION

1. This group of physicians was working long hours under pressure.
2. Physician burnout was common, and related to hours of work and work/home conflict,
3. Given the high prevalence and the well-established negative personal and professional consequences of burnout, the observed associations between hours worked and home/work conflicts suggest possible targets for action.

Archives Internal Medicine July 11, 2011; 171: 1207-09 First author Liselotte N Dyrby Mayo Clinic, Rochester, Minn.

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The Hepatic Manifestation Of The Metabolic Syndrome.

7-3 HOW BIG A PROBLEM IS NON-ALCOHOLIC FATTY LIVER DISEASE?

The authors based these comments on an extensive search of the current literature. The many studies in progress will add to our understanding. Much uncertainty remains.

Non-alcoholic fatty liver disease (NAFLD) represents a spectrum of liver diseases (in the absence of excessive alcohol consumption):

Steatosis: Simple fatty infiltration

Non-alcoholic steatohepatitis (NASH): Fatty infiltration + inflammation

Fibrosis

Cirrhosis

Liver cancer

Simple steatosis has not been associated with liver-related morbidity. NASH may lead to progressive liver fibrosis, cirrhosis, and liver cancer.

NASH is strongly associated with obesity, insulin resistance, type-2 diabetes (DM-2) , and dyslipidemia. It may be considered the hepatic manifestation of the metabolic syndrome.

NAFLD is very common. One large study found NAFLD in 94% of obese persons (BMI > 30) and 67% of overweight persons (BMI > 25) and in 25% of normal weight persons. The overall prevalence of NAFLD in persons with DM-2 ranges from 40% to 70%.

NAFLD has become the most common cause of abnormal liver biochemistry.

Diagnosis:

Much of the population is at risk by being overweight, having insulin resistance, or both.

Many patients are not diagnosed, so the true prevalence of the disease and how many will develop liver-related morbidity is not known.

NASH is often asymptomatic. It is often first discovered by incidental routine biochemical abnormality (often mild increases in aminotransferase levels). Initially there is a relatively greater increase in alanine aminotransferase than in aspartate aminotransferase. With increasing hepatic fibrosis, alanine aminotransferase levels fall. Advanced steatohepatitis may be present in patients with relatively normal alanine aminotransferase levels. Hepatic fat content tends to diminish as cirrhosis develops. Thus, NASH is probably underdiagnosed in patients with advanced liver disease, which is thought to be the underlying cause of a high % of cases where no specific cause is readily identified. ("cryptogenic cirrhosis").

Ultrasound provides a quantitative assessment of hepatic fat content. Sensitivity of ultrasound is limited, especially when steatohepatitis progresses.

MRI has been proposed as a non-invasive quantification of liver fat and inflammation.

Other than biopsy, no widely acceptable reliable method is available to differentiate simple steatosis from steatohepatitis in routine practice.

As NASH is strongly associated with insulin resistance, it may be appropriate to assess patients with insulin resistance for advanced liver disease with biochemical liver tests and ultrasound. But, no imaging modality is ideal, and aminotransferases are not highly sensitive.

When abnormalities are found, other causes of liver dysfunction should be excluded (viral, autoimmune and metabolic). Although biopsy remains the optimum investigation for assessing degree of inflammation and fibrosis, invasive tests are not appropriate in primary care practice.

Prognosis:

Only a minority of patients progress from steatosis to more advanced disease characterized by inflammation, fibrosis and subsequent cirrhosis and hepatocellular cancer. Studies suggest that about 5% with NASH develop complications of end-stage liver disease during a long follow-up. Some prognosis is probably based on genetic and environmental factors.

Independent risk factors for progression are: Age > 45, obesity, and the presence of diabetes. Those that do progress often present late in the natural course of the disease and have subsequent liver-related morbidity.

Hepatic fibrosis may take years to progress. High quality data from prospective trials is limited, particularly in primary care settings. Currently, liver biopsy is the optimum investigation to assess the degree of inflammation and the extent of fibrosis as markers for liver-related morbidity.

NASH has a fibrotic potential similar to that of hepatitis C.

About 1/3 of patients with NASH will exhibit progressive fibrosis.

A cohort study reported that NASH was associated with increased risk of liver-related death and double the *cardiovascular* risk over 14 years.

Treatment

Current treatment includes weight loss and amelioration of the metabolic syndrome by lifestyle interventions (diet and exercise).

Insufficient evidence is presently available to formulate authoritative and balanced treatment guidelines. No drugs are currently licensed specifically for treatment. Lifestyle changes are the mainstay of treatment. Trial evidence shows that weight reduction of > 7% maintained over 48 weeks is associated with significant reduction in histological evidence of NASH.

What should we do in the light of uncertainty?

Identification of patients with NAFLD will change patient management:

Provide greater impetus for modification of diet and lifestyle.

Guide drug selection in patients with insulin resistance or diabetes. Trial evidence indicated that oral glitazone antidiabetic agents (pioglitazone) may alleviate steatohepatitis, although this has not been translated into reduced fibrosis.

As a marker of the metabolic syndrome, identification of NAFLD should prompt modification of *cardiovascular* risk factors.

Uncertainties remain:

The prevalence of NAFLD and NASH in an unselected general population.

The risk of liver-related morbidity in the general population with NAFLD and NASH.

The optimum method for identifying NASH in the community.

Clinically relevant, economical, and patient-acceptable non-invasive techniques for differentiating steatosis from NASH to identify those at greatest risk for liver-related complications.

Strategies to facilitate sustainable modification of lifestyles to achieve weight loss and control the metabolic syndrome.

Effective drug treatments directed at the liver to control steatosis and prevent fibrosis progression.

BMJ July 23, 2011; 343: 201-04 (BMJ2011;343:d3897) "Practice" "Uncertainty Page" a review article. first author Quentin M Anstee, Newcastle University, Newcastle upon Tyne, UK ,

A brief related article follows (p204 BMJ 2011;343:d446)

"Non-alcoholic Fatty Liver Disease in Children" first author C Ronny, Department of Health, Birmingham, UK.

NAFLD is now one of the most common reasons for referral for chronic liver disease in children and young people in the developed world.

It is also related to obesity and DM-2, but may also present as an inherited disorder.

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An Important Application For Primary Care Patients And For Public Health

7-4 SODIUM AND POTASSIUM INTAKE AND MORTALITY AMONG U.S. ADULTS

Individuals with high sodium or low potassium intakes have increased risk for hypertension.

The observed associations between sodium (**Na**) and potassium **(K)** intake and cardiovascular disease (**CVD**) incidence and mortality have been inconsistent.

Recently several studies suggest that the ratio of sodium to potassium intake is a more important risk factor for hypertension and CVD than each alone.

Examining the joint effects of Na and K intakes on CVD risk is particularly important because most of the US population consumes more Na and less K daily than is recommended.

This study reports an analysis between the estimated usual intakes of Na and K, as well as their ratio, with all-cause and CVD mortality.

STUDY

1. The third National Health and Nutrition Examination Survey (NHANES III- 1988-1994) examined a nationally representative sample of non-institutionalized US adults (n = 12 267). Each survey participant completed a household interview and a 24-hour dietary recall.
2. Determined the baseline 24-hour Na and K intake from the dietary recall and calculated the Na/K ratio.
3. A linked mortality file (1988-2006)) determined mortality from CVD, IHD, and all-causes as related to the baseline Na and K intake and the Na/K ratio.

RESULTS

1. Estimates of usual daily intakes of Na, K, and the Na/K ratio and caloric intake at baseline: (means)

	Na (mg)	K (mg)	Na/K	Calories

Men	4323	3373	1.31	2697
Women	2518	2433	1.23	1785

Intake of Na was much higher than the recommended 1500 mg/d (5000 mg NaCl))

Intake of Na paralleled the caloric intake.

Intake of K was much lower than the recommended 4700 mg/d [1]

The Na/K ratio remained much higher than 1.00

2. Over a mean follow-up of 14.8 years (170 110 person-years) there were 2270 all-cause deaths, including 825 CVD and 443 IHD deaths.

(The distinction between CVD and IHD was based on the coding at the time of death .Ed.)

3. Hazard ratios (**HR**) of usual intakes of Na and K and the Na/K ratio for *all cause mortality*;:

(Quartiles (lowest to highest)

	Q1	Q2	Q3	Q4
Usual Na intake (mg/d)	2176	3040	3864	5176
HR	1.00	1.17	1.37	1.54
Usual K intake (mg/d)	1793	2476	3108	4069
HR	1.00	0.86	0.75	0.61
Na/K ratio	0.98	1.17	1.33	1.57
HR	1.00	1.13	1.25	1.46

Higher Na intake was associated with *higher* all-cause mortality. (HR = 1.20 for each 1000 mg per day.)

Higher K intake was associated with a *lower* all-cause mortality (HR = 0.80 for each 1000 mg per day.

3. The risk of all-cause death increased linearly with increasing Na/K ratio.

4. HR of usual Na and K intakes and Na/K ratio for *CVD and IHD mortality*

Usual Na intake (mg/d)	2176	3040	3864	5176
CVD mortality	No significant relationship			
IHD mortality	No significant relationship.			
Usual K intake (mg/d)	1793	2476	3108	4069
CVD mortality	1.00	0.75	0.58	0.39
IHD mortality	1.00	0.67	0.46	0.26

K intake was significantly inversely associated with risk of death from CVD and IHD.

Na/K ratio	0.98	1.17	1.33	1.57
CVD mortality	1.00	1.13	1.25	1.46

IHD mortality	1.00	1.28	1.51	2.15

Higher Na/K ratio was significantly associated with increased risk of death from CVD and IHD.

5. The increased risk for mortality associated with the Na/K ratio remained largely consistent across sex, race/ethnicity, BMI, hypertension status, physical activity, and educational level.

DISCUSSION

1. In this nationally representative sample of adults followed for about 15 years, there was a significant monotonic association between increased Na/K ratio and risk of mortality from CVD, IHD, and all-causes. The association was independent of sex, race-ethnicity, and other covariates.
2. Numerous studies have found that high Na or low K intakes were associated with increased risk of hypertension, with a stronger association observed for low K.
3. A meta-analysis of 19 cohorts, with 177 028 participants showed that higher salt (NaCl) intake was significantly associated with greater risk of stroke and CVD.
4. In a multi-center cross-sectional study of men across 16 countries, stroke mortality was strongly associated with a higher Na/K ratio.
5. High Na levels increase BP by stimulating endothelial cells, thickening and narrowing resistance arteries, and blocking nitric oxide synthesis. High K levels can counteract these effects by activating nitric oxide release. The opposing biological effects of Na and K may explain stronger associations of the Na/K ratio with CVD mortality than either Na or K intake alone.
6. Because Na is added to foods, especially prepared foods, whereas K is naturally present in most foods, a low Na/K ratio may be a marker of higher intake of plant foods, and low intake of processed foods. Cheeses, cooked meats, bread, soups, fast foods, pastries, and sugar products have higher Na/K ratio. Fruits, vegetables, dairy products, and hot beverages tend to have a lower ratio.
7. From a public health point of view, reduced Na intake accompanied by increased K could achieve greater health benefits than restricting Na alone.
8. The calculations of Na intake in the study did not include discretionary salt use. However, it is estimated that American adults consume an average of only 6% their daily intake of Na from table salt.

CONCLUSION

In the general US population, a high Na/K ratio was associated with a significant increase in CVD mortality and all-cause mortality. High Na intake was associated with increased all-cause mortality.

Archives Internal Medicine July 11, 2011; 171: 1183-91 Original investigation, first author Quanhe Yang, Center for Disease Control and Prevention, Atlanta, GA

1 More "Nutrition Facts" labels on foods now include K contents. If you calculate the recommended daily amount from the label, it is 3500 mg. Some authorities quote 4700 mg as an "adequate" amount**.**

An editorial in this issue of Archives (pp 1191-92), first author Lynn D Silver, New York Department of Health comments and expands on the article:

In 2010, the Institute of Medicine recommended that the FDA regulate Na in the food supply. Twenty eight major food companies have already made voluntary commitments to Na reduction. As food is processed, typically Na is added and K removed, reversing the Na/K ratio.

In Finland, after 18 years of regulatory measures to reduce Na, there has been a 1/3 decrease in Na intake with a reduction in hypertension and premature mortality from stroke and heart disease.

Potassium supplementation (eg, KCl tablets or shakers) has been suggested. However, major international guidelines have not recommended routine K supplementation. While K supplementation may be beneficial in many persons, a considerable number are at risk for hyperkalemia (those with diabetes, renal failure, heart failure, and those taking ACE inhibitors or spirinolactone).

The findings of the study have important implications for policy. It is crucial that we understand the interplay between K and Na in the diet and how to optimize intake.

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A Potential "Game Changer" For Primary Prevention Of Melanoma.

7-6 PREVENTION OF MELANOMA WITH REGULAR SUNSCREEN USE

Evidence from randomized controlled trials demonstrate that regular sunscreen use protects against cutaneous squamous cell carcinoma.

Up to now, there has been no randomized controlled trial (**RCT**) data on sunscreen prevention of melanoma. Case-control studies have yielded conflicting results.

Now a RCT from Australia provides evidence that regular use of sunscreens does prevent melanoma.

The trial entered 1621 adult subjects. Randomized to regular use of sunscreen vs discretionary use. Those randomized to regular use were given an unlimited supply of a broad spectrum sunscreen—sun protective factor (SPF) of 16, and asked to apply it to the head, neck and hands every morning. Reapplication was advised after heavy sweating, bathing and long sun exposure.

The trial lasted 5 years. The 2 groups were similar for known risk factors for melanoma: skin color, outdoor behavior, sun exposure, sunburn history, nevus density, a history of skin cancer at the start of the trial, and use of sun protection such as hats, and shade seeking.

During a 10-year follow up (after the initial 5 years) incidence of a new primary melanoma:

Regular daily use 11 cases among 812 persons

Discretionary use 22 cases among 804 persons.

A reduction of 50% *(By my calculation, NNT for 5 years to prevent one melanoma = 74. Ed.*)

The reduction in invasive melanoma was substantial:

Regular daily use 3 cases

Discretionary use 11 cases

Adherence to sunscreen application was estimated to be 75% daily among regular users. 25% of this group also applied the sunscreen to other parts of the body.

Since exposure to ultraviolet radiation (**UVR**) is the only known modifiable cause of melanoma, this study is a potential "game changer" for primary prevention of melanoma. Patients at high risk because of phenotypic characteristics (fair skin, freckling, tendency to sunburn, history of melanoma) who live in or visit sunny climates should routinely apply sunscreen before going outside.

In the US, this recommendation is particularly relevant to those who live in relatively high ambient UVR locations such as Florida, California, and Arizona. and those who frequently visit these areas.

The US Preventive Services Task Force suggests that counseling can increase sun-protective behavior and decrease indoor tanning. Counseling should include willingness to use sunscreen regularly.

Proper use of sunscreens: Before going out, apply two coats of about 1 teaspoon of sunscreen to head, neck and ears; front and back of trunk; each arm down to the hand and shoulder; each lower leg upper leg, and dorsum of the foot.

Reapply after sweating and after swimming.

If used every day, this can be time consuming and expensive. Costs may be reduced by wearing wide-brimmed hats, long sleeves, and long pants.

Over 68 000 new cases of melanoma occurred in the US in 2010. Effective use of sunscreens can reduce the risk.

JAMA July 20, 2011; 306: 302-03. "Commentary", first author June K Robinson, Northwestern University, Chicago, IL