Recommendations for clinical practice. The major strengths of this study are that patient selection and treatment are driven by clinical presentation rather than endoscopic diagnosis, and that the measured outcomes are patient-oriented. The study shows that patients presenting with heartburn have a small but probably clinically significant benefit from ranitidine. Given the small overall benefit and the high cost of ranitidine, comparison with antacids and lifestyle changes is also warranted.

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RISK FACTORS FOR HIP FRACTURES

TITLE: Risk factors for hip fracture in white women
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Clinical question. Which risk factors are associated with hip fractures in white women 65 years and older?

Background. The lifetime risk for hip fracture in white women is close to 20%. Risk factors for hip fracture have been identified in previous studies, including lower body weight, inactivity, and use of sedatives, caffeine, and tobacco. However, the studies that identified these risk factors were thought by the authors above to be flawed in design. According to them, the prospective study reported here is unusual in that many potential risk factors were included, as well as bone density measurements.

Population studied. The study population consisted of 9516 white women who were at least 65 years of age and had been recruited by mail in four different areas of the country between 1986 and 1988. Black women (because of their low incidence of hip fracture), women with a previous hip fracture, and women with bilateral hip replacement were excluded. During the study period, 192 participants had a hip fracture, 585 died, and 92 were lost to follow-up.

Study design and validity. Study participants were questioned and examined in an outpatient clinic. They were interviewed regarding medical history, medications, exercise, daily activity, and estimation of calcium and caffeine intake. Examination included anthropometry, neuromuscular function and strength, mini-mental status examination, visual and orthostatic testing, and calcaneal bone density measurement. Patients were contacted every 4 months for ascertainment of hip fracture (confirmed by review of the radiographs) and followed for an average of 4.1 years. We are not given the response rate of the women recruited for the study and, therefore, cannot judge whether this group is representative of all white women over age 65 or whether it suffers from significant selection bias. For example, women with more risk factors or a family history of osteoporosis might be more likely to volunteer for the study.

Outcomes measured. Risk factors for hip fracture were identified with regression analysis statistics. The estimate of risk used was relative risk (RR) with 95% confidence interval (CI). A risk factor with an RR of 1.0 or those with a CI that includes 1.0 are considered unlikely to be related to the outcome, which, in this case, is hip fracture. In addition, the authors were especially interested in whether some of the more significant risk factors were independent of the bone density measurements.

Results. Sixteen independent risk factors for hip fracture were identified. Those with an RR of 1.5 or greater included age, history of maternal hip fracture, self-rated poor health, previous hyperthyroidism, current use of long-acting benzodiazepines, current use of anticonvulsant drugs, on feet less than 4 hours per day, inability to rise from chair without using arms, poor depth perception, resting pulse rate greater than 80, and decreased calcaneal bone density. Factors that seemed protective (RR less than 1.0) included increase in weight since age 25 and walking for exercise. The incidence of hip fractures was directly related to the number of risk factors present. The hip fracture incidence rate among women with five or more risk factors and low bone density was 27 times greater than among women with fewer than three risk factors and normal bone density.

Some commonly believed risk factors, such as fair hair color, northern European ancestry, and earlier natural menopause, were not found to be significant. Although current smoking was not an independent risk factor, it still was associated with hip fracture. Estrogen therapy seemed to be protective in those women without a history of osteoporosis or fracture, but the CI was wide (RR=0.3; CI=0.1 to 1.1). Based on a single self-reported assessment during the study, calcium intake was not found to be related to hip fracture.

Recommendations for clinical practice. Many of the risk factors identified in this study were found in previous studies. Each of the risk factors was of moderate value alone; however, the more risk factors in one woman, the greater the risk of hip fracture. Therefore, patients who have risk factors they cannot change (eg, decreased bone density, history of maternal hip fracture, history of hyperthyroidism) should be counseled to minimize the risk of hip fracture, specifically by increasing physical activity and avoiding use of tobacco and long-acting sedatives. Other risk factors for hip fracture, such as problems with impaired vision and increased pulse rate, also should be addressed.

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PROSTATE CANCER SCREENING

TITLE: Prostate cancer screening: a decision analysis
AUTHORS: Cantor SB, Spann SJ, Volk RJ, Cardenas MP, Warren MM
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Clinical question. Is it beneficial to screen men age 50 and older for prostate cancer with digital rectal examination (DRE), transrectal ultrasound (TRUS), and prostate-specific antigen (PSA)?

Background. Screening asymptomatic men for prostate cancer is a controversial practice. Screening advocates cite better survival rates in men with early stage prostate cancer, and doubters point to the lack of either convincing epidemiological data or a controlled trial showing improvement in morbidity or mortality. A definitive controlled trial would take years to complete and may never be done. In the face of imperfect information, decision analysis is a quantitative analytic method used to determine the optimal clinical strategy. The decision process is modeled using probabilities of health states and outcomes gleaned from existing scientific literature, combined with preferences for outcomes, commonly called *utilities.*[1,2] In this review, I have used the critique format proposed by the Evidence-Based Medicine Working Group to evaluate this prostate cancer screening decision analysis.[3]

Study design and validity. **Were all important strategies and outcomes included?** No. The authors confine their model to a single screening strategy: digital rectal examination and PSA, followed by biopsy for a suspected nodule or positive PSA (10 ng/mL or greater). If the DRE is negative and the PSA is indeterminate (4 to 10 ng/mL), transrectal ultrasound and the predicted PSA (PSA level divided by estimated prostate volume, or PSA density) would be performed to determine if a biopsy is indicated. This analysis is superior to previous analyses in that an annual screening strategy is examined. However, a newer screening strategy based on yearly rate of change of age-specific PSA, called *PSA velocity*, is not included.

Was an explicit and sensible process used to identify, select, and combine the evidence into probabilities? Yes. Extensive documentation of the probabilities of disease states and outcomes are given. A strength of this analysis was the use of prostate cancer prevalence of *clinically detectable lesions* rather than detection of microscopic disease, which is probably of little biologic consequence. Because 5-year survival rates for treated prostate cancer are based on National Cancer Institute data from 1973–1986, these estimates may not be accurate for 1995.

Were the utilities obtained in an explicit and sensible way from credible sources? Yes. Ten male patients who were in their 50s and free of prostate disease and their spouses were interviewed using a time-trade-off method to determine quality-adjusted life years for living with the complications of treatment: incontinence, impotence, urethral stricture, rectal injury, and gynecomastia. A previous prostate cancer screening decision analysis has been criticized for using physicians' preferences to determine utilities.[4] Using patients is an improvement, but 10 is still a small number, and men in their 60s and 70s were not included.

Was the potential impact of any uncertainty in the evidence determined? Yes. Sensitivity analyses were performed to determine if varying the probability and utility parameters in the model affected the preferred strategy.

Results. **In the baseline analysis, does one strategy result in a clinically important gain for patients? If not, is the result a toss-up?** The preferred strategy favored no screening by a slim margin—about 6 quality-adjusted months. When adverse outcomes of treatment were ignored, screening was the favored strategy, yielding an advantage of 6 unadjusted months. This sounds like a toss-up to me, though patient preference clearly plays a role. Varying the probabilities of disease states and outcomes in the sensitivity analyses did not change the preferred strategy.

How strong is the evidence used in the analysis? In general, the analysis is based on fairly good data. The sensitivities and specificities of PSA, DRE, TRUS, and