PRACTICAL POINTERS

FOR

PRIMARY CARE MEDICINE

ABSTRACTED MONTHLY FROM THE JOURNALS

A Free Public-service Publication

OCTOBER 2014

JAMA, NEJM, BMJ, LANCET
JAMA 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

29th YEAR OF PUBLICATION

Practical Pointers is published every month on the internet as a public service.

The complete content of all issues for the past 10 years can be accessed at

www.practicalpointers.org

It is also 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

I hope you will find *Practical Pointers* interesting and helpful.

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

The editor thanks

Lois M. James for proof reading

Matthew Ramirez for internet application

10-1 EVALUATION AND TREATMENT OF OLDER PATIENTS WITH HYPERCHOLESTEROLEMIA: Literature Search "Clinical Review and Education"

Decision-making for administration of statins for older people is complex, with little evidence to support or refute benefit.

This article presents 3 case scenarios to illustrate this situation.

1) An older patient not taking statins who develops cardiac problems:

Mr. S An 89-year old man living independently had an acute myocardial infarction at age 70. During the past 2 years, he experienced chest pain on exertion. Medications included aspirin, dipyridamole, metroprolol, isosorbide, and sublingual nitroglycerine as needed.

His LDL-cholesterol is 104 (under the reference level of 115, but above 100, the level recommended for initiation treatment in the guidelines of Finland.).

The patient's physician did not recommend statins because he believed the LDL-c was sufficiently low and because of the patient's age.

Two months later the patient suffered an acute myocardial infarction and heart failure. An angiogram revealed extensive 3-vessel, CAD. Intervention for the CAD was considered too high risk and he received conservative care. He died 2 months later.

2) An older patient with good physical and cognitive function receiving statins:

Mr. J A 92-year old living independently had a history of hypercholesterolemia. Thirty years ago he developed clinically significant CAD and received a multivessel coronary artery bypass. A statin was started.

Now he remains active and independent. His medications are atorvastatin, ramipril, and aspirin.

3) An older patient receiving statins who has poor physical and cognitive function:

Mrs. P An 86 year old woman had a history of hypertension, hypercholesterolemia, and type-2 diabetes. Alzheimer disease was diagnosed 3 years ago and she was admitted to a nursing home. Her Mini-Mental State Examination score was 11 of 30.

She has been taking 12 different medications, including simvastatin and aspirin.

Her overall clinical state is stable. Her memory is failing, but she is alert and physically active without specific symptoms.

Her geriatrician, a respected physician, has no plans to change her medications.

Features of Old Age:

The 3 scenarios are increasingly common in societies in which the oldest old are rapidly increasing. In the U.S., an 80-year old man has an average life expectancy about 8 years, a woman has about 10 years. Overall, functioning and quality-of life in the very elderly is improving.

Atherosclerotic cardiovascular disease is less common in young people now than in the past, resulting in a large population of older individuals with complications of the disease. ASCVD may be under reported in people older than 80. Dementia and frailty follow without the traditional clinical manifestations of myocardial infarcts and stroke. This broadens the scope of prevention and treatment.

Individuals over 80 are physiologically heterogeneous, ranging from incapacitated nursing home residents to marathon runners. This heterogeneity must be taken into account when preventive therapies for chronic disease are considered. Chronological age is often given greater weight than physiological age. Risk factors for ASCVD do not predict outcomes n the elderly as well as they do in younger individuals. Frailty may exacerbate the adverse effects of therapy. Polypharmacy may result in drug interactions. Musculo-skeletal function, pain, and adverse cognitive effects of therapies (not restricted to statins) are more severe in older individuals. These factors predispose to reduced physical activity, sarcopenia, and falls.

Cardiovascular prevention may be ineffective if it is started too late.

It is difficult to predict which older patients will benefit from preventive therapy.

When assessing older patients for primary prevention, life expectancy, and the patient's overall health status must be considered in addition to ASCVD risk.

Hypercholesterolemia Effect on ASHD:

There is an established and graded association between serum cholesterol and risk of ASVCVD.

Hypercholesterolemia exists when total-c is over 200, corresponding to an LDL-c of 115. Although triglycerides and low HDL-c are risk factors in both young and old, they are not targets for drug therapy.

LDL-c is the main driver (predisposing factor) of the atherosclerotic process in the arterial wall. Statins induce plaque regression when LDL-c is lowered to less than 100.

There is no evidence that any current treatment can reduce LDL-c too much. Combinations of some developing drugs with statins have reduced LDL-c levels to less than 50. So far, very low levels have not been associated with any specific harm.

In addition to being influenced by LDL-c, ASCVD events such as acute myocardial infarction and stroke are influenced by other risk factors such as smoking, hypertension, and diabetes.

The Cholesterol Paradox of Old Age:

The association between higher cholesterol levels and ASCVD risk is attenuated in old age.

Levels may decrease in old age because of frailty or presence of comorbid conditions. An apparent increase in mortality asssociatd with low cholesterol levels in the elderly may be due to changes in cholesterol metabolism, malnutrition, frailty, and chronic disease. After adjustment for chronic disease, the positive association between cholesterol levels and increased death from CVD in patients mean age 79 was restored during a 5-year follow-up.

Although the relative difference in risk related to cholesterol levels decreases with old age in comparison to younger age, the absolute effect of cholesterol levels on CAD mortality rates are much greater when people get older. Among 80-89 year old individuals, the annual CAD mortality rate increased 10-fold compared with 40-49 year olds for each 39 mg increase in total cholesterol levels.

The confusing relationship of the association between cholesterol levels and mortality for the very old results in uncertainty regarding benefits of hypercholesterolemia drug treatment for healthy very old patients. For the present, the decisions about drug lowering for the very old must be based on observational studies and extrapolations from the RCTs in younger people.

Treating Hypercholesterolemia in the Very Old. Evidence from Statin Trials:

Statin use for primary prevention among 80-year olds is increasing. One U.S. survey reported use was 29% in persons age 80-84;, 24% in age 85-89; and 14% in those older than 90. These older patients will have had a long-term, probably irreversible "cholesterol burden" in their arteries. However, because, in some RCTs, ASCVD was reduced in 75-80 year olds, the AHA guideline supports continuing statin use beyond age 75 in persons already taking a statin. The guideline also supports starting a moderate-intensity statin in patients age 75-82 with clinical ASCVD.

The time to benefit from statins may be less than 2 years, well within the general life expectancy of 80-year olds.

Observational studies and RCTs, in which the upper baseline limit has been age 82, demonstrate benefits of starting statins for secondary prevention in patients with ASCVD .

Benefits of statins in primary preventions in older patients with diabetes are not known.

It is important to consider a patient's personal preferences, life expectancy, frailty, comorbid conditions, and treatment lag time to benefit.

Effect of Frailty:

Although lacking in universal definition, frailty is considered a geriatric condition characterized by reduced physiological reserve and increased predisposition to even minor stress. Clinically, it can be defined by a frailty index—a combination of weakness, slowness, exhaustion, inactivity. It is common, recognizable in 10% of people over age 70 and increasing with age. Frail individuals are more susceptible to adverse effects of drugs and have a reductions in efficacy of treatments—for example in treatment of hypertension.

Adverse Effects of Statins in Older Patients:

Frail old individuals with co-morbidity may be more prone to adverse effects. Because individuals with significant co-morbidities have been excluded from trials, the spectrum of adverse events is not known.

Well-documented, established adverse effects: muscle toxicity, effects on live enzymes, and risk of diabetes. Cognitive and neurological symptoms have been reported, but there is no consistent evidence of a causal relationship.

For older patients, the muscle-related effects are particularly important. They range from pain without elevated creatine kinase to rhabdomyalysis. Large RCTs reported frequency of symptoms of pain with increased creatine kinase >10 times normal were 11 per 100 000 person-years and with rhabdomyalysis is 3 per 100 000 person-years. Milder symptoms (myalgia and cramps without elevated creatinine kinase) are common, but a true causal relationship is difficult to establish.

There is concern that statins could promote sarcopenia and predispose to frailty, falls, and morbidity, especially in nursing home patients. However, most studies have not included people over age 80 or the frailest individuals.

The general conclusion from community-living older people is that statin treatment has no general deleterious effects on frailty or physical function. At the individual level—especially in patients already frail and with polypharmacy—it is important to provide close follow-up for possible adverse effects and be vigilant to drug interactions, dehydration, and co-morbidity in which risk of adverse effects increases.

Elevations of hepatic transaminases usually resolve after dose reduction or discontinuation.

The clinical significance of statin-related diabetes is not known in older patients who may not have had time to develop complications.

There is a higher risk for drug interactions in old people because of polypharmacy.

Managing Hypercholesterolemia in People Older than 80 years:

In older people, it is important to consider possible secondary causes of hypercholesterolemia—liver or kidney disease, hypothyroidism, or use of antipsychotic drugs.

Non-pharmacologic therapy should be considered to reduce risk—smoking cessation, sodium reduction, avoidance of obesity, and increased physical activity.

Threats to quality of life and personal and cultural preferences must be recognized. In older people, recommending less fat or red meat may lead to an accelerated sarcopenia and frailty.

Plant stanol/sterols products may reduce cholesterol absorption and lower levels by 10% or 17%.

Statins:

The AHA guidelines recommend a moderate-intensity (but not high-intensity) statin for patients over age 75 who have clinically evident ASCVD—e.g., atorvastatin 10 mg, fluvastatin 20-80 mg, lovastatin 20-40, simvastatin 20-40.

Development of fragility should be closely monitored irrespective of statin treatment.

There is interest in potential "pleiotherapeutic" effects of statins not related to ASCVD. These include better recovery from serious infections or trauma, reduced incidence or better outcomes, and fewer complications of surgery or certain cancers. There is no RCT evidence to support these claims.

Other Drugs:

Non-statin drugs for hypercholesterolemia include ezetimib (inhibits cholesterol absorption) which can be combined with statins or used alone especially in statin-resistant patients. Fibrates or niacin, alone or combined, can be used in select cases of combined hyperlipidemia and hyper-triglyceridemia. There are no outcome studies in patients older than 80. These drugs have adverse effects that limit use.

When to Discontinue Statin Therapy: Adverse Effects Threatening Physical and Mental Function:

It is mandatory to consider statin discontinuation if there are adverse effects impairing quality of life that cannot be managed by dose reduction or change of statin type. However, it is possible to successfully re-challenge patients older than 75 after adverse effects. Drug interactions, polypharmacy, frailty and co-morbidity predispose to serious effects. It is important to note that co-morbidity and frailty are not indications for palliative care, nor is treatment in a nursing home considered palliative care. Not using a statin for these reasons is not appropriate.

Quality of life of even the most vulnerable patients can be better preserved if an ASCVD is avoided with statins.

Transitioning to End-of –Life Care:

In older patients, determination of life expectancy is not always straightforward. Predictive tools such as the Multidimensional Prognostic Index have been validated in older persons having a variety of clinical conditions.

When the decision is made to pursue only palliative care, ASCVD preventive treatment should be discontinued, irrespective of chronological age.

Recommendations for Mr. S, Mr. K, and Mrs. P:

Clinical features of these patients have not been studies by RCTs. It is important to distinguish patients already using a statin when they turn 80 (i.e., started at an age where there is RCT evidence of benefit) from those who initiate a statin after age 80.

In secondary prevention, benefits outweigh the risk of serious adverse events. In primary prevention, each patient's characteristics predisposing to adverse events (frailty, co-morbidities, other medications) as well as quality of life should be considered.

Shared decision-making is very important in old age. Personal preferences vary.

For Mr. S, an 80-year old, statin therapy should have been started 10 to 20 years earlier. In this patient, ASCVD was far enough advanced that statins would not be beneficial.

Mr. J, a 90-year old, should continue statin therapy unless unmanageable adverse effects occur or his clinical conditions deteriorate sufficiently to require initiation of palliative care.

Mrs. P. the 86-year old, is nearing the stage where the statin could be discontinued, but currently her calculated 10-year mortality is only 3.6% (Estimated Prognosis for Elders Tool), so

it is reasonable to continue statin therapy because the benefits of statin therapy are expected to continue within this time frame.

Clinical Bottom Line:

Populations older than 80 comprise an increased patient segment in which hypercholesterolemia and risk of CV disease are prevalent.

Ideally, treatment of hypercholesterolemia (usually with a statin) in high risk individuals should be started before age 79.

Older people are a heterogeneous group both clinically and functionally.

Decisions to start statins in older individuals should be made individually and are not supported by high-quality evidence.

JAMA September 17, 2014; 1136-44 Review article, First author Timo E Strandberg, University of Helsinki, Finland.

I enjoyed this article. It presents a number of practical points for primary care—not only in the elderly, but for younger patients as well.

Prolonging preventive therapies into old age presents ethical question, as well as medical applications. A determining factor is the individual patient's personal wishes, hopefully expressed before the infirmities of old age prevent decision-making. For Mrs. P, the elderly lady with cognitive disability, I believe many individuals in the same state would opt to discontinue preventive therapy. She is looking forward to an increasing burden of dementia. Certainly, few clinicians would start statins in this patient.

I believe it was Osler who said that "Pneumonia is the old man's friend". Now we may better declare that "ASCVD is the old person's friend."

Primary care clinicians will increasingly encounter aging patients. I believe too many elderly receive tests, procedures, and medications that are no longer helpful and might actually be harmful. I recall seeing a very old, bed-ridden, terminally ill patient who was still taking daily medication for osteoporosis.

==========

10-2 FOLLOW-UP OF BLOOD PRESSURE LOWERING AND GLUCOSE CONTROL IN TYPE-2 DIABETES

The original ADVANCE trial was conducted in 215 centers in 20 countries. Beginning in 2002, randomized 11 140 patients (mean age 66) with type-2 diabetes and at least one other risk factor for CVD into 2 groups for 4.5 years.

1) Blood pressure control trial:

Randomized to a single daily fixed dose of perindopril (an ACE inhibitor) + indapamide (a thiazide-like drug) [P-I] vs placebo.

At baseline, mean BP was 145/80.

Mean reduction in BP was 5.6/2.2.

Over 4.5 years, compared with placebo, the P-I group had a reduced risk of the primary composite outcome of major macrovascular or microvascular events and death.

Patients in the active treatment group experienced a reduction in death from any cause (7.3% vs 8.5%), death from CVD (3.8% vs 4.6%), myocardial infarction (2.9% vs 3.0%), and stroke (3.8% vs 3.9%)

Hazard ratios (treatment vs placebo) for death from any cause, death from cardiovascular disease, myocardial infarction, and major macrovascular events were all less than 1.00, but only the first 2 were significant.

2) Intensive glucose control trial:

Randomized to gliclazide (a sulfonylurea) or to standard glucose control for 5 years, after which patients were returned to usual care.

Baseline HbA1c was 7.5%. Targeted to an HbA1c of 6.5% or lower. Mean reduction was 0.67%, lowering HbA1c to 6.83%.

Intensive glucose control was associated with a reduction in risk of major macrovascular and microvascular events, primarily due to reduction in nephropathy.

There was no clear preventive or harmful effects of intensive control with respect to death from major macrovascular events.

Post-trial follow-up

The present study (ADVANCE-ON) is a 6-year observational post-trial follow-up study of the preceding trial.

Survivors of the trial were invited to participate in follow-up which began in 2008..

Two primary outcomes were pre-specified: death from any cause, and major macrovascular events.

1) BP trial follow-up:

About 20%of patients remained off BP therapy.

The mean difference in BP in the randomized trial (5.6/2.2) ws no longer evident at 6 months. Little difference in BP remained between the former treated and placebo groups.

Among the P-I group; there remained a significant, but attenuated, cumulative benefit with respect to death from any cause that extended to the end of follow-up.

2) Glucose-control grop:

Use of sulfonylureas declined over follow-up.

The mean difference in HbA1c of 0.67% was no longer evident. HbA1c returned to 7.4% in both groups.

There was no cumulative benefit with respect to death from any cause or major macrovascular events or severe diabetes-related eye disease. There was a significant cumulative benefit on end-stage renal disease (- 46%), although relatively few events were recorded.

DISCUSSION

After following the current cohort for a total of 10 years, including the original trial period and the post-trial study, there were attenuated but still significant reductions in the rates of death from any cause and from cardiovascular causes resulting from the 4.5 year period of BP-lowering treatment with P-I.

The cumulative reductions in mortality in the P-I group can be ascribed largely to a carrying forward of the effects observed during the randomized treatment. It is possible that with longer post-trial follow-up, these effects might be further dissipated. This emphasizes the importance of continuing BP-lowering medications.

In contrast, there were no significant benefits with respect to mortality, macrovascular events, or microvascular events resulting from the period of intensive glucose control except for a reduction in end-stage renal disease, but not with serious eye complications.

In the trial, the original benefits of intensive glucose control were primarily due to reductions in new, or worsening, nephropathy. However, the numbers of events were very small and should be interpreted with caution.

This study did not observe any long-term beneficial effects of earlier periods of intensive glucose control.

Conclusion:

Among patients with long-standing type-2 diabetes, BP-lowering with P-I for an average of 4.5 years resulted in an attenuated but significant long-term benefit with respect to death from any cause and from cardiovascular causes.

Intensive glucose control for an average of 5 years did not provide any long-term benefits with regard to death or major macrovascular events.

NEJM October 8, 2014;371:1392-406 First author S Zoungas, George Institute for Global Health, Camptown, Austria

Supported by the National Health and Medical Research council of Australia and others.

This is discouraging.

What is the message for primary care?

Control of BP in high-risk patents (with diabetes + other CVD risk factors) in late middle-age is beneficial. It should be continued past 5 years.

It is very difficult to achieve beneficial HBA1c lowering. Target levels were not reached in this cohort. Benefits from modest lowering were small. Treatment should continue beyond 5 years, but we still do not know if longer treatment will be beneficial.

It is hard for patients and clinicians to persist in treatment.

==========

10-3 ANALYSIS REVEALS INCREASE IN HOSPITALIZATIONS AMONG OLDER PATIENTS PRESCRIBED OPIOIDS: "Medical News and Perspectives"

The Agency for Healthcare Research and Quality reports trends in hospitalizations of adults related to use of prescription opioid pain killers (not illicit drugs) during 1992 to 2012.

It found that the biggest jump in the rate of such hospitalizations in that period was in people age 85 and older, followed close behind by 65 to 84-year olds, and 45 to 64 year olds.

Compared with other payers, Medicare experienced the biggest annual increase—from 51 per 100 000 in 1993 to 265 per 100 000 in 2012.

This is a situation where there is an over-reliance on opioids, particularly for long-term conditions. It is an important public health issue.

As people age they are more likely to have chronic pain and are less likely to abuse prescription painkillers. They are more likely to experience adverse effects from opioids. At the equivalent dose, elders are much more likely to experience falls, liver impairment, cardiac toxicity, and, particularly, cognitive impairment.

In part, the increase in opioid-related hospitalizations could be related to increase in diagnosis.

Whether the increase in opioid prescriptions for the elderly is appropriate or not is difficult to ascertain. There may be situations when opioids are prescribed too soon, when other analgesics or physiotherapy could have been tried.

Several factors have combined to fuel the increase in opioid prescribing:

A great push to make pain the "fifth vital sign"

Medical educators are advising treating pain in all patients.

Increasing concern about safety of other pain medications—acetaminophen, NSAIDS, and Cox-2 inhibitors.

The American Geriatrics Society (2009) guidelines might have encouraged pain control. "All patients with moderate to severe pain, pain related to functional impairment, or diminished quality of life due to pain [should] be considered for opioid therapy". Non-selective NSAIDS and COX-2 selective inhibitors "may be considered rarely, with caution, in highly selected individuals".

This is a significant departure from the 2002 guidelines.

Monitoring older patients who are prescribed opioids is important. But we tend not to be suspicious of elderly patients who request pain medications.

Old patients are more sensitive to opioids and the dose is sort of a guess. There is not a lot of long-term data. There has been inadequate testing of opioids in old people. For what type of pain should they be used? By what means of administration?

The rate of adverse events varies depending on the opioid and the duration of treatment.

Many clinicians prescribe too much opioid treatment when non-opioids would be effective. Some clinicians avoid opioids entirely.

It is important to go low and very slow.

Little is known about the relative safety of various opioids for treating non-cancer pain in adults.

As baby boomers age, overuse of opioids is expected to increase. With their history of experimental drug use, they may be more likely to seek and abuse opioids.

JAMA October 22, 2014; 1621-23 Commentary by Rita Rubin, JAMA staff

=====

This is not a study. It is a collection of commentaries by various experts interested in opioids.

It points out an important clinical dilemma.

Primary care clinicians must relieve pain as much as possible. But they must also judge the adverse effects, which may be disabling in elderly patients.

Clinicians should know the elderly patients and their families well enough to trust their judgment about opioid use. Illicit use by families and friends is common.

The dose and frequency of prescriptions should be closely monitored and recorded. The patient should be told that, if they run out of the opioid too soon, it will not be renewed until the proper time. The family should be told to guard and carefully oversee the patient's usage.

Other analgesics should be prescribed as substitutes.

==========

Is It Time To Abandon Pap Testing?

10-4 HUMAN PAPILLOMA VIRUS TESTING FOR PRIMARY CERVICAL CANCER: Editorial

Since the Pap test entered clinical practice in the 1950s, cervical cancer (CC) incidence and mortality have markedly declined. Historically, Pap testing was conducted annually, and continued indefinitely. In general, all abnormalities were treated aggressively by excision or ablation, and annual testing was resumed.

However, over the past 20 years we have learned many things about CC. It is caused by a infection with "high risk"(subtypes 16 and 18) types of the human papilloma virus (HPV). But, HPV infection is prevalent in women who are sexually active, and most of these infections resolve spontaneously and do not lead to precancerous abnormalities.

There are risks of over-evaluation and treatment of HPV: pain, anxiety, costs.

In April 2014, the FDA approved a HPV test (Roche) for use for primary CC screening independent of Pap testing. It was approved for use in women age 25and older. The FDA approval stated that this HPV test is safe and effective as an alternative to the Pap test, or with co-testing with the Pap. Approval did not establish the HPV as the preferred screening method.

At present there are 3 other HVP tests approved by the FDA, but none are aproved for use independently of the Pap.

What do we know about primary HPV testing?

1) Randomized trials in Europe have shown improved sensitivity of primary screening with HPV compared with Pap in early detection of high-grade dysplasia, or with long-term detection of CC. HPV screening was associated with increased rates of colposcopy.

2) Over a median follow up of 6.5 years, primary HPV screening afforded a 60% to 70% greater protection against CC, compared with Pap.

3) In these studies, the cumulative rate of invasive CC was 8.7 per 100 000 in 5 years for women screened by HPV, and 36 per 100 000 screened by Pap.

4) The negative predictive value of a negative HPV test was greater than that of Pap.

However, when performed in different countries, and according to different evaluations and management strategies, markedly different costs for screening and for follow-up were reported.

It is still uncertain whether the HPV test will perform as well in routine practice as it did in RCTs.

In 2013, the WHO guidelines for preventing CC stated that a screening test with high diagnostic accuracy is not necessarily the test of choice in clinical practice.

Conclusion: the approval of the HPV test is an important step toward improving primary screening for CC. However, further data are needed about the actual benefits and costs and the impact on the use of colposcopy and other diagnostic tests.

It is not yet time to abandon the Pap test.

JANA Internal Medicine October 20, 2914; 1539-40 "Viewpoint" by Sarah Feldman, Brigham and Women's Hospital and Harvard Medical School, Boston,Mass

==========

Not yet an established practical point for primary care. This will be followed with great interest.

==========

10-5 USE OF HPV VACCINATION IN MALES AND FEMALES: JAMA Clinical Guidelines Synopsis

Types 16 and 18 cause about 70% of cervical cancers (CC). They are also associated with vulvar, vaginal, and oropharyngeal cancers. Types 6 and 11 cause approximately 90% of genital warts.

A recent study conducted in the US, Brazil and Mexico reported that, at mean age 25, 53% of women were infected with HPV, and 30% were infected with an oncogenic strain. A study in the U.S. reported a prevalence of 45% in women age 20-24.

About 22 000 cases of CC associated with types 16 and 18 occur every year in the U.S..

For the vaccine recommended for boys and men, and girls and women, efficacy data came from several RCTs. Vaccine efficacy ranged from 97% to 100% in the per-protocol analyses.

Harms of the vaccine appear to be minimal. There was concern that vaccination would lead to increased sexual activity among teens. One study reported no increase.

Most analyses have determined that HPV vaccination is cost effective in girls and young women. In boys and young men, cost effectiveness varies widely. The age targets for girls and women is 11-26 and for boys and men is 11-21.

Discussion: HPV vaccine appears to be highly effective and well tolerated. It is highly immunogenic. Trials with clinic endpoints show a reduction in genital condyloma and precancerous lesions such as cervical and vulvar intraepithelial neoplasia, and anal intraepithelial neoplasia in men. Effectiveness in reducing rates of CC has not yet been shown.

This guideline supports use of either quadrivalent or bivalent vaccine in women, but only the quadrivalent in men. For girls, the greater breadth of the quadrivalent would be preferred given its effectiveness against genital warts.

There is evidence that vaccination has positive effects on unvaccinated members of the population, through herd immunity.

The vaccine is administered in a 3-dose schedule, at 1 to 2 months after the first dose, and 6 months after the second dose.

Adherence to the vaccine remains low in the U.S. Rates of completion of the 3 doses are lower.

JAMA November 2014, "Clinical Review and Education" first author Adam S. Cifu, University of Chicago, IL This guideline was published by the Advisory Committee for Immunization Practices

==========

HPV infections are extraordinarily common. Will this vaccine reduce incidence of CC as much as the chicken pox vaccine will reduce the incidence of shingles?