Cardiovascular Risk Factors

(Assessment and Modification)

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Disclosures

NONE

Estimation of Cardiac Risk

Why do we bother to estimate the risk of a first cardiovascular event?

Best tool we currently have to individualize treatment

Helps gauge the potential treatment benefit against the risks of treatment

Helps reduce cost of disease management

BEST FOR THE PATIENT

Because it can make a difference:

In the INTERHEART study of patients from 52 countries, nine changeable risk factors accounted for the vast majority (90%) of the risk for a first MI. These included smoking, dyslipidemia, hypertension, diabetes, abdominal obesity, psychosocial factors (eg, depression, perceived stress, life events), daily consumption of fruits and vegetables, regular alcohol consumption, and regular physical activity. (notice that Genetics and economics were not assessed)

Who Gets Screened?

> 20 years without established CVD or Equivalent every three to five years

Patients With CVD or Equivalent should not get risk screening - They should be treated with appropriate secondary prevention.

When do we stop screening?

The age at which we should stop doing primary risk factor screening is not established however, many of the validated risk models have only included patients up to age 79

The decision to stop periodic risk assessment should be made along with the patient based on things such as their functional status, life expectancy, and desire to modify those risks.

Which Screening tool is Best??

Why can you plug in the same patient data into 2 different models and get different risk scores???

Different Variables were used to calculate risk

Different patient populations were used to calculate risk

The events being studied were different (different outcomes) were researched and looked at.

No single risk model will be appropriate for all patients all of the time:

The choice to use a specific risk model should be based on specific characteristics (eg, age, gender, ethnicity).

A brief overview of risk estimator tools

History to Current

Framingham

The original Framingham risk score was developed in 1998 from a mostly European descent / Caucasian population.

VARIABLES USED:

- Age
- Gender
- Total or LDL cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Diabetes mellitus (yes or no)
- Current smoking (yes or no)

VARIABLES USED:
- Blood pressure treatment (yes or no)
- Family history of CVD (yes or no)

WHAT WAS EVALUATED?
- CHD death
- Nonfatal MI
- Unstable angina
- Stable angina

ATP III hard CHD risk score (2002)

The Third Adult Treatment Panel (ATP III) adapted the Framingham model for use in their recommendations to screen for and treat dyslipidemia. Those modifications include elimination of diabetes from the algorithm, since it was considered to be a CHD equivalent; along with other adjustments.

VARIABLES USED:

- Age
- Gender
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Blood pressure treatment (yes or no)
- Current smoking (yes or no)

VARIABLES NOT USED:
- Diabetes mellitus (yes or no)
- Family history of CVD (yes or no)

WHAT WAS EVALUATED?
- CHD death
- Nonfatal MI

SCORE CVD death risk score (2003)

Used data gathered from more than 200,000 patients studied in 12 European countries. The economic regions of europe were able to be calculated to determine their impact on CVD and outcomes. SCORE differs from other risk models in these important ways:

1. Estimates the 10-year risk of any first fatal atherosclerotic event (eg, stroke or ruptured abdominal aneurysm),

2. Estimates cardiovascular disease mortality as well as

3. Geographic impact on outcomes

VARIABLES USED:

- Age
- Gender
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Current smoking (yes or no)
- Region of Europe (high risk or low risk region)

VARIABLES NOT USED:

- Blood pressure treatment (yes or no)
- Diabetes mellitus (yes or no)
- Family history of CVD (yes or no)

WHAT WAS EVALUATED?

- Cardiovascular disease death (including CHD, arrhythmia, HF, stroke, aortic aneurysm, and peripheral vascular disease)

QRISK and QRISK2

Evaluated the difference in ethnicity in England/Wales. Included risk predictors used in the modified Framingham/ATP III model, as well as ethnicity, socioeconomic status, family history, and other medical variables such as chronic renal disease, atrial fibrillation, and rheumatoid arthritis.

VARIABLES USED:

- Age and Gender
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Blood pressure treatment (yes or no)
- Current smoking (yes or no)
- Family history of CVD in first degree relative aged <60 years (yes or no)
- Region of United Kingdom (score based on levels of unemployment, overcrowding, car ownership, home ownership)
- Body mass index (kg/m2)

VARIABLES NOT USED:

- Diabetes mellitus (yes or no)

WHAT WAS EVALUATED?

- CHD death
- Nonfatal MI
- Coronary insufficiency or angina
- Coronary revascularization
- Fatal or nonfatal stroke
- Transient ischemic attack
- Intermittent claudication

Reynolds CVD risk score for women (2007)

Developed from a prospective cohort of nearly 25,000 American women without diabetes. The main difference between Reynolds score and other risk scores are (Family History and high-sensitivity C-reactive protein (hs-CRP)

VARIABLES USED:

- Age
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Diabetes mellitus assessed by hemoglobin A1c (percent)
- Current smoking (yes or no)
- Parental history of MI before age 60 years (yes or no)
- Serum hs-CRP (mg/L)

VARIABLES NOT USED:

- Blood pressure treatment (yes or no)

WHAT WAS EVALUATED?

- Cardiovascular death
- Nonfatal MI
- Nonfatal stroke
- Coronary revascularization

Framingham General CVD risk score (2008)

This revision included more manifestations of clinical atherosclerosis such as stroke, transient ischemic attack, claudication and heart failure. The risk scores were much higher with this risk score than the others due to more outcome's being measured.

VARIABLES USED:

- Age
- Gender
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Blood pressure treatment (yes or no)
- Diabetes mellitus (yes or no)
- Current smoking (yes or no)

VARIABLES NOT USED:

- Family history of CVD was not included

WHAT WAS EVALUATED?

- CHD death
- Nonfatal MI
- Coronary insufficiency or angina
- Fatal or nonfatal ischemic or hemorrhagic stroke
- Transient ischemic attack
- Intermittent claudication
- HF

Reynolds CVD risk score for men (2008)

Developed from a prospective cohort of over 10,000 American men without diabetes and like the Reynolds score for women, also included family history of MI and hs-CRP as variables, but unlike the Reynolds risk score for women, hemoglobin A1c level was not included.

VARIABLES USED:

- Age
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Current smoking (yes or no)
- Parental history of MI before age 60 years (yes or no)
- Serum hs-CRP (mg/L)

VARIABLES NOT USED:

- Diabetes mellitus (yes or no)
- Blood pressure treatment (yes or no)

WHAT WAS EVALUATED?

- Cardiovascular death
- Nonfatal MI
- Nonfatal stroke
- Coronary revascularization

ACC/AHA pooled cohort hard CVD risk calculator (2013)

Developed from several large studies. It is the first risk model to include data from large populations of both Caucasian and African-American patients.
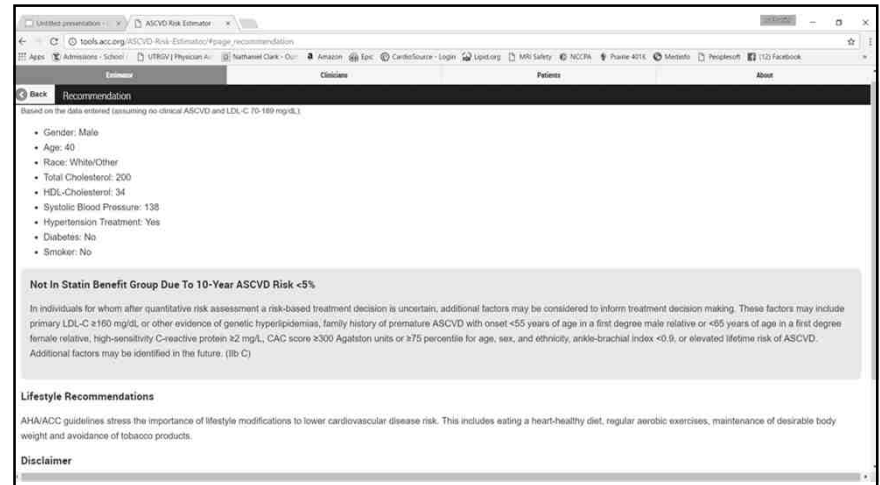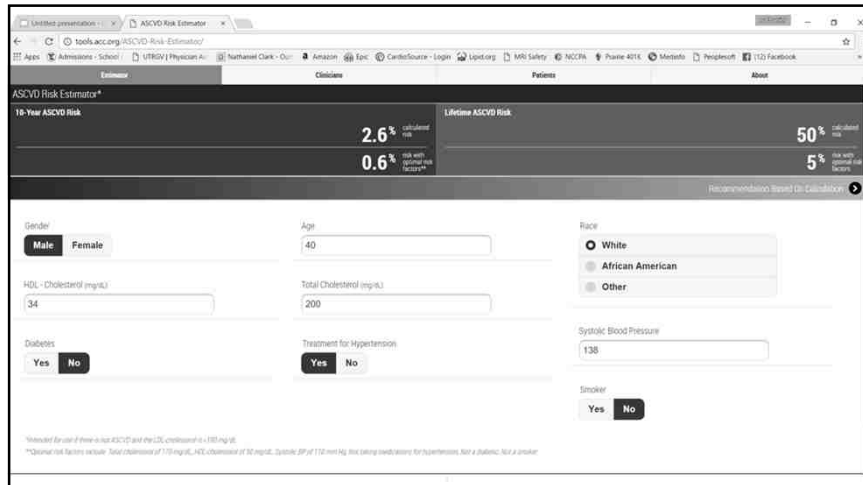
VARIABLES USED:

- Age
- Gender
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Blood pressure treatment (yes or no)
- Diabetes mellitus (yes or no)
- Current smoking (yes or no)

VARIABLES NOT USED:

- Family history of CVD (yes or no)

WHAT WAS EVALUATED?

- CHD death
- Nonfatal MI
- Fatal stroke
- Nonfatal stroke

JBS3 (Joint British Societies) risk score (2014)

Based on statistical Modeling and *"consensus recommendations"* but has not been externally validated. It is Based on the QRISK lifetime Cardiovascular calculator and allows for the estimate of **"heart age"** and the assessment of risk over longer time frames (30, 50 years).

VARIABLES USED:

- Age / Gender / Ethnicity
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Systolic blood pressure (mmHg)
- Blood pressure treatment (yes or no)
- Diabetes mellitus (yes or no)
- Current smoking (yes or no)
- Family history of CVD in first degree relative aged <60
- Chronic kidney disease / Atrial fibrillation / Rheumatoid arthritis
- Region of United Kingdom (score based on levels of unemployment, overcrowding, car ownership, home ownership)
- Body mass index (kg/m2)

WHAT IS BEING ASSESSED FOR?

- CHD death
- Nonfatal MI
- Coronary insufficiency or angina
- Coronary revascularization
- Fatal or nonfatal stroke
- Transient ischemic attack
- Intermittent claudication

MESA risk score (2015)

The Multi-Ethnic Study of Atherosclerosis (MESA) is a 2015 risk score that was validated in two separate prospective cohort groups. This risk model also includes multiple ethnic backgrounds and also uses coronary artery calcium score to further classify the patients.

VARIABLES USED:

- Age / Gender / Diabetes mellitus (yes or no)
- Ethnicity (non-Hispanic white, Chinese American African American, Hispanic)
- Total cholesterol (mg/dL)
- HDL cholesterol (mg/dL)
- Lipid lowering treatment (yes or no)
- Systolic blood pressure (mmHg)
- Blood pressure treatment (yes or no)
- Current smoking (yes or no)
- Family history of myocardial infarction at any age
- Coronary artery calcium score

VARIABLES NOT USED:

- Family history of CVD other than myocardial infarction

WHAT WAS EVALUATED?

- CHD death
- Nonfatal MI
- Resuscitated cardiac arrest
- Coronary revascularization in patient with angina

CURRENT SCORE LIMITATIONS

Can identify high-risk persons, tend to falsely reassure people at low to moderate risk.

Many do not estimate a lifetime risk, which might be substantially higher cause more aggressive treatment in marginal patients.

Some tools have been found to overestimate 10-year risk of CVD.

During the last 18 years many of the risk factors significance has changed (obesity, diet, lifestyle,etc…) and many of the tools are ill equipped to evaluate those changes.

Some risk models do not include patient important CVD outcomes such as stroke, HF, or development of symptomatic peripheral artery disease.

Lifetime risk can help guide treatment options long term that a 10 year risk may not show although most risk scores look at 10 years.

The lifetime risk of CVD increased progressively with the number and intensity of risk factors.

Many risk factors are influenced by the time a patient has had them and the success of treatment however modification of those risk factors is not readily addressed with current tools. (previous history of smoking, family history, poor diet, etc…)

Additional Screening

Additional Screening Tools to help estimate CVD risk:

In patients whom risk assessment places the patient in a moderate risk or in whom the decision to escalate or deescalate treatment is not clearly defined then the following factors have been shown to help reclassify a patient's risk and further educate about escalating treatment:

Evaluation of family history

hs-CRP

coronary artery calcium score:

Significant re-modifier of risk and adjustment of treatment plan. (patients with poor genetics, patients with a calcium score of 0, risk assessment uncertain, Low 10 year risk/high lifetime risk, etc…) *(personal use in Dr. Google pts uncertain of taking statin)*

ankle-brachial index

Risk Factor Modification

Lifestyle Changes and Medications

Healthy Diet

Healthy diet — in multiple studies, individuals who self reported a healthy diet have had significantly lower risks of cardiovascular disease (CVD), including both coronary heart disease (CHD) and stroke. Components of a healthy diet include intakes of:

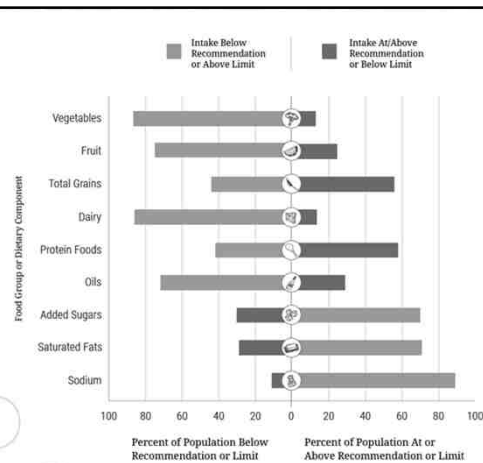Fruits and vegetables

Fiber, including cereals

Foods with a low glycemic index and low glycemic load

Monounsaturated fat rather than trans fatty acids or saturated fats

Omega-3 fatty acids (from fish, plant sources, or supplements)

Studies have consistently shown that diets high in vegetables and fruits, (Mediterranean diet, Ornish Diet, etc…) have a reduced risk of CVD

Please consider that some patients with other co-morbidities (DM, Celiac Dz, Wasting Syndrome, HIV, CKD, etc…) may have other dietary needs beyond primary cardiovascular prevention…..

HTN control

Hypertension is a well known risk factor for CVD, including morbidity and mortality from stroke, CHD, heart failure, and sudden death.

Generally defined as a systolic pressure ≥140 mmHg and/or diastolic pressure ≥90 mmHg. However, patients with systolic 120 to 139 mmHg and/or diastolic 80 to 89 mmHg are also at increased cardiovascular risk.

(There is a linear progression in multiple studies showing the higher BP readings the higher the risk)

Blood Pressure Goal:

The goal blood pressure is usually <140 systolic as well as <90 mmHg diastolic, but higher risk patients have a lower goal, such as those with metabolic syndrome, diabetes, or proteinuric chronic kidney disease.

Pharmacological Options:

(Defer to the JNC 8 Guidelines)

Non-pharmacologic measures:

All patients with hypertension and prehypertension should practice nonpharmacologic therapeutic lifestyle changes, which include weight reduction, especially in overweight/obese patients, salt restriction, and avoidance of excess alcohol intake, regular exercise.

Exercise

Regular exercise has been shown to benefit patients in the following ways

Lower risk of premature death compared to sedentary patients

Lower risk of Breast and Colon Cancer

Reduced risk of Falls and Fractures (hip)

Can stave off the age related decrease in mental function

Lowers BP

Lowers Cholesterol

Can prevent or improve Type 2 Diabetes

People who are physically active for about 7 hours a week have a 40 percent lower risk of dying early than those who are active for less than 30 minutes a week.

Exercise

Recommendations:

moderate intensity exercise for 150 minutes a week or vigorous intensity exercise for 75 minutes a week

There has been positive benefit in long term patient outcomes for having 3 main focus of activity in a patient exercise program:

    i.   Aerobic Exercise (see above)

    ii.   Flexibility Training

    iii.   Strength Training

Weight Loss

In the United States and worldwide, obesity is quickly overtaking tobacco consumption as the major cause of preventable premature death.

Data from large prospective cohort studies have consistently shown that individuals with higher BMI's have an increase in morbidity and mortality from CHD, after proper adjustment for other risk factors.

The National Center for Health Statistics reports that over 40 percent of adults have metabolic syndrome (obesity, dyslipidemia, hypertension, and insulin resistance).

Weight Loss

Treatment:

Healthy Diet

Increased Exercise ("WALK WITH A DOC", "Silver Sneakers", etc…)

Set realistic Goals:

People at high risk of developing diabetes who are able to lose 5 percent of their body weight and maintain this weight will reduce their risk of developing diabetes by about 50 percent and reduce their blood pressure.

Slide 1 (Weight loss medications table)

Brand Name	Generic Name	Description	Controlled Substance?
Adipex-P	Phentermine	Appetite suppressant; anorectic	Yes, DEA schedule IV
Alli	Orlistat	Lipase inhibitor; inhibits fat absorption in the intestine	No, available over-the-counter (OTC)
Belviq, Belviq XR	Lorcaserin	Selective serotonin 2C receptor agonist; promotes a feeling of fullness or satiety	Yes, DEA schedule IV
Bontril PDM, Bontril SR	Phendimetrazine	Appetite suppressant; anorectic	Yes, DEA schedule III
Desoxyn	Methamphetamine	Appetite suppressant; use cautiously if prescribed for weight loss due to high potential for abuse, illegal distribution	Yes, DEA schedule II
Didrex	Benzphetamine	Appetite suppressant; anorectic	Yes, DEA schedule III
Diethylpropion	Diethylpropion	Appetite suppressant; anorectic	Yes, DEA schedule IV
Meridia	Sibutramine	Anorectic; withdrawn from US market in 2010 due to increased heart risk.	Not available
Qsymia	Phentermine and topiramate extended-release capsules	Combination appetite suppressant-anorectic; exact action of topiramate on weight loss is not known	Yes, DEA schedule IV
Suprenza	Phentermine	Appetite suppressant; anorectic	Yes, DEA schedule IV
Xenical	Orlistat	Lipase inhibitor; prescription form of Alli (OTC); higher dose than Alli; inhibits fat absorption in the intestine	No
Contrave	Bupropion hydrochloride-naltrexone hydrochloride	Increases metabolism, suppresses appetite, affects central reward center (proposed mechanism)	No
Saxenda	Liraglutide	GLP-1 may regulate areas of brain involved in appetite (proposed mechanism)	No

Slide 2

Aspirin Therapy

Is Aspirin Beneficial??

Aspirin increases the risk of bleeding (particularly GI Bleed) in almost all patients.

The question is not if there is benefit or harm from aspirin therapy in patients who have not had CVD, but does the benefit outweigh the risk.

In secondary prevention the benefit is large, in Primary Prevention the benefit is smaller however in high risk patients the benefit may exist.

Slide 3

Aspirin Therapy

Safety:

A 2016 meta-analysis evaluated rates of major bleeding found in 10 primary prevention trials The following were noted:

Very low-dose aspirin use ($\leq$100 mg daily) increased the risk of major GI bleeding by more than 50% and hemorrhagic stroke by more than 25%

Advanced Age, male sex, and diabetes all increased the risk for major bleeding.

The absolute increase in risk increased as the baseline risk increased.

Benefit:

Generally in primary prevention the benefit does not outweigh the risk until the risk begins to exceed 6 to 10 percent in 10 years. (there are more detailed guidelines to help guide treatment from the United States Preventive Services Task Force (USPSTF))

Slide 4

Summary of Recommendations and Evidence

Population	Recommendation	Grade (What's This?)
Men, Age 45-79	The USPSTF recommends the use of aspirin for men age 45 to 79 years when the potential benefit due to a reduction in myocardial infarctions outweighs the potential harm due to an increase in gastrointestinal hemorrhage. See the Clinical Considerations section for discussion of benefits and harms.	A
Women, Age 55-79	The USPSTF recommends the use of aspirin for women age 55 to 79 years when the potential benefit of a reduction in ischemic strokes outweighs the potential harm of an increase in gastrointestinal hemorrhage. See the Clinical Considerations section for discussion of benefits and harms.	A
Men and Women, 80 Years and Older	The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of aspirin for cardiovascular disease prevention in men and women 80 years or older. See the Clinical Considerations section for suggestions for practice regarding the I statement.	I
Women Younger than 55 (Stroke), Men Younger than 45 (MI)	The USPSTF recommends against the use of aspirin for stroke prevention in women younger than 55 years and for myocardial infarction prevention in men younger than 45 years.	D

Lipid Lowering Therapy

PCSK9 inhibitors — Proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors have not been adequately evaluated in primary prevention in patients without familial hypercholesterolemia. Due to cost, the requirement for injections, and the lack of long-term safety data, combined with the lack of primary prevention data these would be considered only in select patient groups for primary prevention.

Statins — In contrast to other non-statin cholesterol medications, The following studies have shown benefit in primary prevention from using statin therapy:

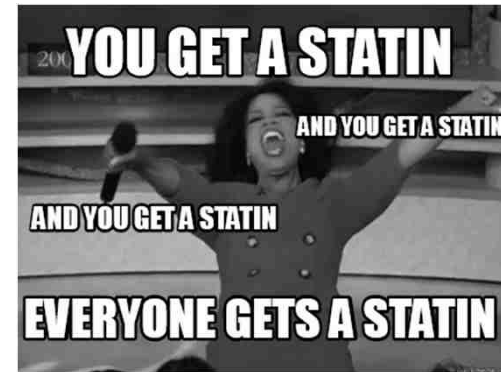The West of Scotland Coronary Prevention Study (WOSCOPS) evaluated pravastatin

The Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS) evaluated lovastatin

The ASCOT-LLA study looked at atorvastatin

The JUPITER trial evaluated rosuvastatin

These studies and others have shown a significant trend across multiple patient populations studied across doses and looking at various endpoints.

Who Gets A Statin????

Why STATIN's?

Reduce relative cardiovascular risk by approximately 20 to 30 percent regardless of baseline low-density lipoprotein cholesterol (LDL-C).

Have not been extensively evaluated in patients with very low baseline LDL-C levels (eg, below 70 mg/dL [1.8 mmol/L]), however most patients with high cardiovascular risk do not have those low LDL numbers.

As with most treatment's we strive to ensure that the benefit from treatment outweighs the risk:

Why STATIN's?

For Example:

If a patient with a 30 year old patient with a 10-year risk of a myocardial infarction of approximately 1 percent could expect to reduce this risk by 0.2 to 0.3 % from taking a statin daily for 10 years, would it be worth the cost, side effect, etc…

However, if a patient has a 10-year risk of a myocardial infarction of approximately 12 percent daily use of a statin would substantially change this patient's risk profile.

Thus the AHA/ACC 2013 Recommendations on Statin therapy:

LDL cholesterol ≥190 mg/dl
40 to 75 years of age and present diabetes and LDL cholesterol 70 to 189 mg/dl
40 to 75 years of age and risk score ≥7.5% and LDL cholesterol 70 to 189 mg/dl

Smoking Cessation!!!

Smoking Cessation

Five-step algorithm called the "5 As" (Ask, Advise, Assess, Assist, Arrange)

The best data shows that even approaching the subject with patients has benefit in smoking cessation. A combined approach addressing both nicotine addiction/craving as well as behavior modification has the greatest chances of success.

Support group from friends and family along with education about local and national assistance:

National toll-free number (1-800-QUIT-NOW)

With the changes to healthcare and demands of a busy schedule the best approach to smoking cessation is a team based approach: Utilize all staff and team members involved.

Celebrate victories:

Even small to moderate reduction in smoking cessation has been proven beneficial.

The goal however is total and complete cessation

Make the patient an advocate for change in their family as well.

Lifestyle Changes Work

A study looked at 20,000 Swedish men between 45 to 79 without cancer, CVD, or CVD equivalents who self reported following a healthy diet, moderate alcohol consumption, not smoking, being physically active, and having no abdominal obesity. During the 11-years of follow up, those men with a healthy lifestyle had an 86 percent lower risk for Heart Attack than those not following a healthy lifestyle.

An European study looked at more than 2,000 pts between 70 to 90 without cardiovascular disease (CVD) or cancer, who reported following a Mediterranean diet, being physically active, small to moderate alcohol intake daily, and/or not smoking. During the 10 years of follow-up those patient who followed all 4 healthy lifestyles had more than a 60% reduction in mortality compared to those who followed none or 1 healthy lifestyle choice.

References

https://www.uptodate.com/contents/estimation-of-cardiovascular-risk-in-an-individual-patient-without-known-cardiovascular-disease?source=search_result&search=Framingham%20risk%20score&selectedTitle=1~51

https://www.uptodate.com/contents/overview-of-smoking-cessation-management-in-adults/print?source=see_link

https://health.gov/dietaryguidelines/2015/guidelines/chapter-2/current-eating-patterns-in-the-united-states/#figure-2-1

https://www.drugs.com/article/prescription-weight-loss-drugs.html

http://content.onlinejacc.org/article.aspx?articleid=1879711&_ga=1.18941240.1087067141.1476469836

http://content.onlinejacc.org/article.aspx?articleid=1770219&_ga=1.269118577.1087067141.1476469836

https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/aspirin-for-the-prevention-of-cardiovascular-disease-preventive-medication

References cont.

http://imaging.onlinejacc.org/article.aspx?articleid=2555912&_ga=1.22225211.1087067141.1476469836

http://content.onlinejacc.org/article.aspx?articleid=1879710&_ga=1.64049071.1087067141.1476469836

https://www.uptodate.com/contents/benefits-and-risks-of-aspirin-in-secondary-and-primary-prevention-of-cardiovascular-disease?source=machineLearning&search=aspirin%20primary%20prevention&selectedTitle=1~150&sectionRank=2&anchor=H39#H39

https://www.uptodate.com/contents/treatment-of-lipids-including-hypercholesterolemia-in-primary-prevention?source=search_result&search=statin%20therapy%20primary%20prevention&selectedTitle=1~150#H5

http://www.aafp.org/afp/2014/1001/p503.html