



2017

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Recommended Citation

Adams, Brian, "The Effect of Statins in Primary Prevention on All-Cause Mortality" (2017). *Physician Assistant Scholarly Project Posters*. 29.

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The Effect of Statins in Primary Prevention on All-Cause Mortality

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Abstract

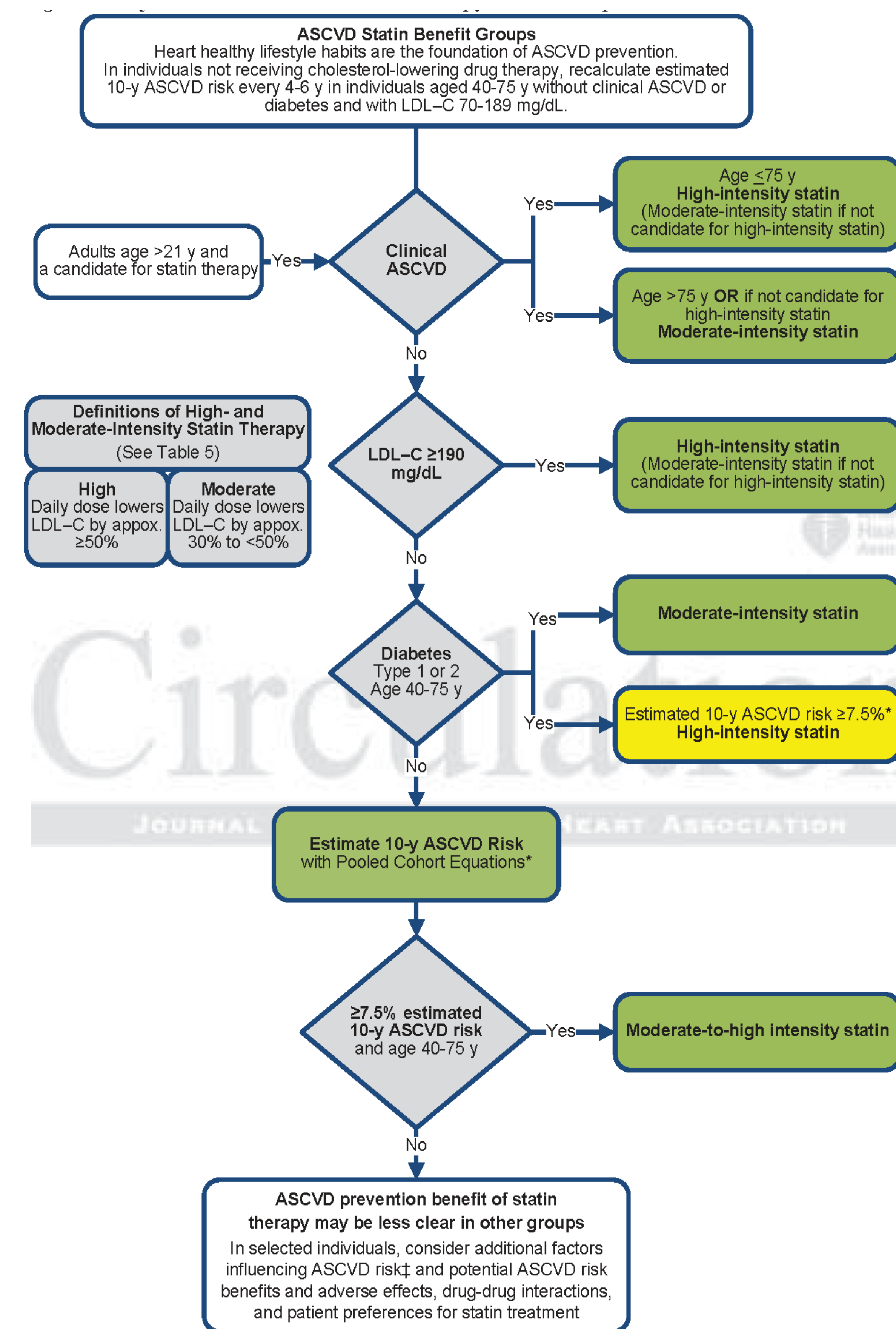
During routine yearly physicals, primary care providers often evaluate serum laboratory lipid levels. Many of these patients have no past medical history of cardiovascular events related to atherosclerotic disease. Some patients do not have secondary risk factors, such as diabetes mellitus or smoking history.

Previous cardiovascular events provide stronger indications for the use of HMG-CoA reductase inhibitors (statins). In the absence of these, the provider may turn to current guidelines, in this case the 2013 the American College of Cardiology and the American Heart Association published the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults.

There is however, controversy, even within the evidence to this guideline, about the effect of statins in primary prevention with respect to the reduction that they have on all-cause mortality. There are many factors that could influence the use of statin therapy for primary prevention. These could include non-fatal myocardial infarction, non-fatal cerebral vascular accident, among others. One of the biggest factors is all-cause mortality.

A review of the evidence cited for these guidelines demonstrates that the majority of the clinical trials did not show a reduction in all-cause mortality, in primary prevention. It is important to understand that this evidence comes directly from the same evidence that the ACC/AHA used to create the primary prevention guidelines.

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults – PRIMARY PREVENTION



Research Question

Does the use of statins, in the **primary prevention** setting, without additional risk factors, affect **all-cause mortality**?

The answer is that a review of the evidence used in the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults, the Cholesterol Treatment Trialists' (CTT), demonstrates more evidence that not that statin therapy does not reduce the risk of all-cause mortality.

Statement of the Problem

ALL-CAUSE MORTALITY in PRIMARY PREVENTION

- Without factoring in any other data sets, evidence is controversial.
- By only focusing on one specific factor, the hope is to paint a clear picture of that factor, thereby facilitating a better decision making process.
- All-cause mortality is one of the end points that is most easily tracked without interruption needed.

Literature Review

JUPITER – “Rosuvastatin also **significantly** reduced the incidence of death from any cause.”

AFCAPS/TexCAPS – “Rates for overall mortality, cardiovascular mortality, noncardiovascular mortality, and fatal cancer were low, and there were **no** treatment group **differences**.”

CARDS – “We recorded a 27% **fall** in all-cause mortality in patients allocated atorvastatin.”

WOSCOPS- “treating 1000 middle-aged ... pravastatin for five years will result in ... **2 fewer deaths** from other causes than would be expected in the absence of treatment.”

4D- “Atorvastatin had **no significant effect** on the individual components of the primary end point.”

ALERT- “Total mortality and graft loss did **not differ significantly** between groups.”

ALLHAT-LLT – “All-cause mortality **was similar** for the 2 groups.”

ASCOT-LLA – “All-cause mortality was **non-significantly reduced**”

ASPEN – “Composite end point reductions were **not statistically significant**.”

AURORA – “Rosuvastatin had **no benefit** in any subgroup examined, including patients with diabetes”

MEGA – “Although treatment with pravastatin was associated with lower total mortality than with diet alone, this result was **not significant**”

Trials (CTT)	Number of patients	Women (%)	Diabetes (%)	Prior CHD (%)	Other vasc disease (%)	No prior vasc disease (%)
PROVE-IT	4162	911 (22%)	734 (18%)	4162 (100%)	328 (8%)	0
A to Z	4497	1100 (24%)	1059 (24%)	4497 (100%)	479 (11%)	0
TNT	10 001	1902 (19%)	1501 (15%)	10 001 (100%)	1537 (15%)	0
IDEAL	8888	1702 (19%)	1069 (12%)	8888 (100%)	971 (11%)	0
SEARCH	12 064	2052 (17%)	1267 (11%)	12 064 (100%)	1062 (9%)	0
SSSS	4444	827 (19%)	202 (5%)	4444 (100%)	126 (3%)	0
WOSCOPS	6595	0	76 (1%)	338 (5%)	193 (3%)	6096 (92%)
CARE	4159	576 (14%)	586 (14%)	4159 (100%)	0	0
Post-CABG	1351	102 (8%)	116 (9%)	1351 (100%)	37 (3%)	0
AFCAPS/TexCAPS	6605	997 (15%)	155 (2%)	10 (<1%)	9 (<1%)	6586 (>99%)
LIPID	9014	1516 (17%)	782 (9%)	9014 (100%)	905 (10%)	0
GISSI-P	4271	587 (14%)	582 (14%)	4271 (100%)	179 (4%)	0
LIPS	1677	271 (16%)	202 (12%)	1677 (100%)	142 (8%)	0
HPS	20 536	5082 (25%)	5963 (29%)	13 386 (65%)	8865 (43%)	3161 (15%)
PROSPER	5804	3000 (52%)	623 (11%)	1881 (32%)	1026 (18%)	3254 (56%)
ALLHAT-LLT	10 355	5051 (49%)	3638 (35%)	1188 (11%)	1788 (17%)	8037 (78%)
ASCOT-LLA	10 305	1942 (19%)	2527 (25%)	15 (<1%)	1435 (14%)	8860 (86%)
ALERT	2102	715 (34%)	396 (19%)	400 (19%)	241 (11%)	1702 (81%)
CARDS	2838	909 (32%)	2838 (100%)	9 (<1%)	97 (3%)	2738 (96%)
ALLIANCE	2442	434 (18%)	540 (22%)	2442 (100%)	162 (7%)	0
4D	1255	578 (46%)	1255 (100%)	630 (50%)	666 (53%)	344 (27%)
ASPEN	2410	811 (34%)	2410 (100%)	578 (24%)	302 (13%)	1663 (69%)
MEGA	8214	5547 (68%)	1686 (21%)	42 (<1%)	53 (<1%)	8119 (99%)
JUPITER	17 802	6801 (38%)	76 (<1%)	0	0	17 802 (100%)
GISSI-HF	4574	1032 (23%)	1196 (26%)	1797 (39%)	4574 (100%)	0
AURORA	2773	1050 (38%)	731 (26%)	659 (24%)	743 (27%)	1663 (60%)
Total (26 trials)	88075	32 210 (37%)	87 903 (99%)	25 920 (29%)	70 025 (80%)	0

(Cholesterol Treatment Trialists' (CTT) Collaboration et al., 2010)

Discussion

- 26 = Number of Cholesterol Treatment Trialists' (CTT)
- 11 = Number of Trials in CTTs that are actually PRIMARY PREVENTION
- 3 = Number of CTT's that show all cause mortality **REDUCTION**
- 8 = Number of CTT's that show **NO** all cause mortality reduction
- Eight out of eleven studies appears to be a wide margin of evidence supporting no effect on all-cause mortality in the primary prevention setting, with the use of statins.
- To come to a different conclusion would be to put more weight on the three positive studies, which would seem unlikely to be true given the evidence

Applicability to Clinical Practice

Cardiovascular disease would include strokes, myocardial infarctions, arrhythmias, peripheral arterial disease, or heart valve problems. An event from one of these conditions can have a profound effect on a patient's life, but not cause death. This is important to remember because the conclusion that statins do not reduce all-cause mortality in the primary prevention setting does not mean that statins will not protect against such cardiovascular events.

Although patients may end up living about the same amount of years, whether they take statins or not, it does not mean that they will have a better quality of life during those years. Where the research from this project can be useful in the clinical setting, especially primary care, is when patients have difficulty with the side effects of statins. Clinicians should discuss the risks and benefits to statin therapy before starting a regimen. This project will aid in that discussion.

References

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Acknowledgements

I would like to acknowledge the help of Julie Percival (statistics), Jeremy Hopkin, MD (clinical advisor), Douglas Callahan, DO (clinical advisor), Jay Metzger PA-C (faculty advisor). Most of all I would like to acknowledge my wonder wife and children for putting up with multiple conversations that I am sure did not interest them, and being so understanding for all the time away from them that this project took to complete.