

Dear Reader,

We are grateful to present you the 7th issue of “The State of the Heart”, which explores the clinical evidence supporting the new understandings and happenings in the field of cardiology.

In India, the epidemiological transition from predominantly infectious disease conditions to non-communicable diseases has occurred over a rather succinct period of time. Despite wide heterogeneity in the prevalence of cardiovascular risk factors across different regions, CVD has emerged as the leading cause of death in all parts of India, including poorer states and rural areas. In this research driven time, management of these disorders is also constantly evolving towards the betterment whether it's pharmacological or non-pharmacological.

Being a healthcare custodian of the society, clinicians are constantly thriving to be abreast with the novel understandings of disease and its management. In this context, this is our initiative to provide you a compiled and to the point information.

Present booklet comprises of recent and latest deeds in the field of cardiovascular diseases like dyslipidemia, coronary artery disease, heart failure and its management. We hope that it will facilitate increased cooperation and innovation, and enthuse commitment to prevent these life-threatening and disabling disorders and providing the best possible care for people who suffer from these conditions.

Editor in chief

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Editorial Board:

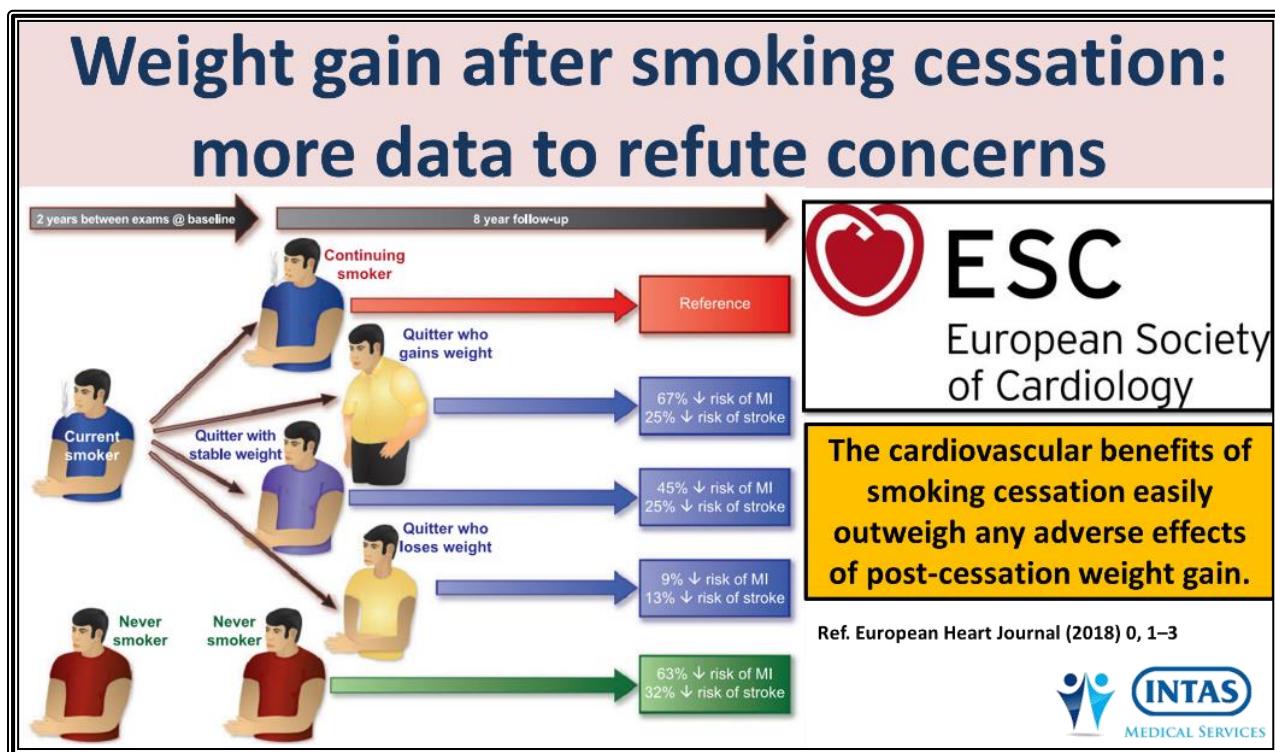
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1. Weight gain after smoking cessation: more data to refute concerns



Is it ever dangerous for an individual to quit smoking? Given that cigarette smoking is the main avoidable cause of mortality worldwide with an annual death toll of more than 6 million people, This is a provocative question. After all, the health benefits of stopping smoking are multiple, substantial and proven beyond doubt. Overall, smoking cessation decreases morbidity and mortality and increases life expectancy by 10 years or more. It is an essential component of both primary and secondary cardiovascular disease prevention. Few, if any, health behavior changes or medical interventions have such a large potential benefit on health and survival. So how could stopping smoking be hazardous?

In summary, the study of Kim et al. provides additional reassurance that the cardiovascular benefits of smoking cessation easily outweigh any adverse effects of post-cessation weight gain. Furthermore, it extends the generalizability of the finding to an Asian population with a different underlying prevalence of obesity. Smokers and health care providers can be reassured about the safety of smoking cessation, even when weight gain occurs. Few interventions in primary and secondary prevention other than quitting smoking have the potential to reduce the risk of cardiovascular disease by half within a few years. Health care providers have a clear responsibility to advise all smokers to quit, and to routinely offer them the behavioral support and pharmacologic assistance that they need to succeed.

2. Risk Factors of Sudden Cardiac Death (SCA) in the Young Multiple-Year Community-Wide Assessment

Risk Factors of Sudden Cardiac Death(SCA) in the Young Multiple-Year Community-Wide Assessment

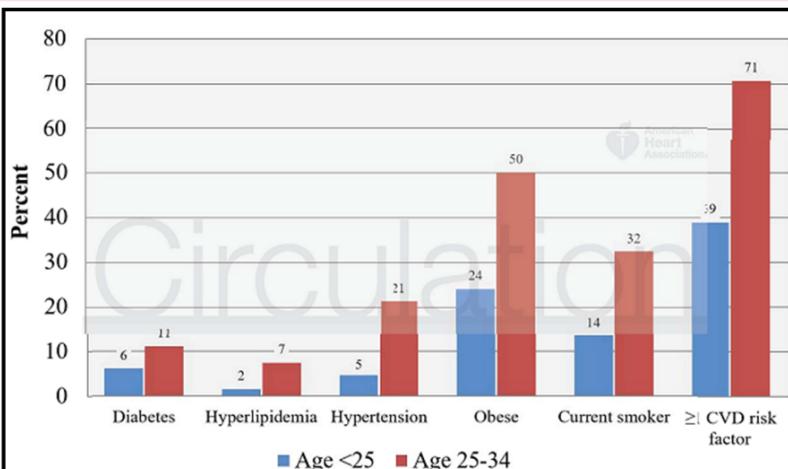


Fig. Prevalence of established cardiovascular risk factors in young subjects who suffered SCA

SCA between the ages of 5 and 34 years (2002–2015) catchment population ≈1 million



Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

SCA occurred without warning symptoms, Standard cardiovascular risk factors were found in over half of patients, suggesting the potential role of public health approaches that screen for cardiovascular risk factors at earlier ages.

Ref. Circulation. 2018;137:1561-1570



Background: Prevention of sudden cardiac arrest (SCA) in the young remains a largely unsolved public health problem, and sports activity is an established trigger. Although the presence of standard cardiovascular risk factors in the young can link to future morbidity and mortality in adulthood, the potential contribution of these risk factors to SCA in the young has not been evaluated.

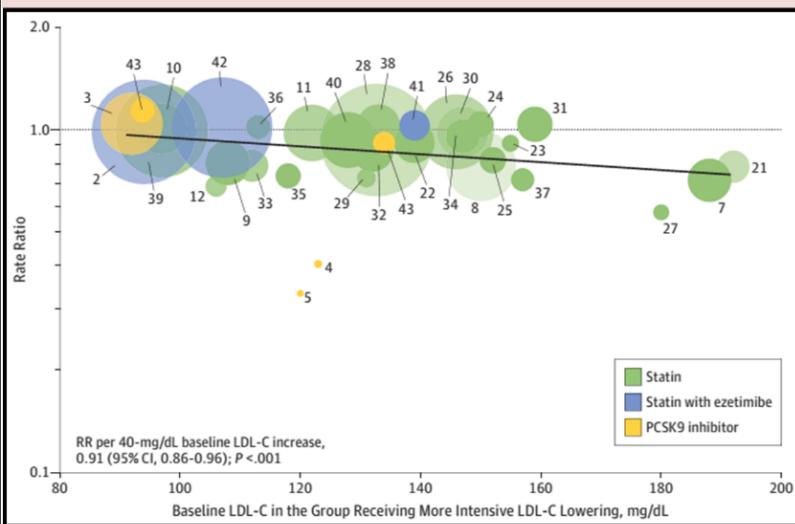
Methods: They prospectively ascertained subjects who experienced SCA between the ages of 5 and 34 years in the Portland, Oregon, metropolitan area (2002–2015, catchment population ≈1 million). Specifically evaluated the association of standard cardiovascular risk factors and SCA, and sports as a trigger for SCA in the young.

Results: Of 3775 SCAs in all age groups, 186 (5%) occurred in the young (mean age 25.9±6.8, 67% male). In SCA in the young, overall prevalence of warning signs before SCA was low (29%), and 26 (14%) were associated with sports as a trigger. The remainder (n=160) occurred in other settings categorized as nonsports. Sports-related SCAs accounted for 39% of SCAs in patients aged ≤18, 13% of SCAs in patients aged 19 to 25, and 7% of SCAs in patients aged 25 to 34. Sports-related SCA cases were more likely to present with shockable rhythms, and survival from cardiac arrest was 2.5-fold higher in sports-related versus nonsports SCA (28% versus 11%; P=0.05). Overall, the most common SCA-related conditions were sudden arrhythmic death syndrome (31%), coronary artery disease (22%), and hypertrophic cardiomyopathy (14%).

Conclusions: Sports was a trigger of SCA in a minority of cases, and, in most patients, SCA occurred without warning symptoms. Standard cardiovascular risk factors were found in over half of patients, suggesting the potential role of public health approaches that screen for cardiovascular risk factors at earlier ages.

3. Does the magnitude of reductions in CV mortality after LDL-C lowering depend on the baseline LDL-C level?

Does the magnitude of reductions in CV mortality after LDL-C lowering depend on the baseline LDL-C level?



In this meta-analysis of 34 randomized clinical trials that included 270 288 participants

Answer is Yes

More intensive LDL-C-lowering therapy was associated with a progressive reduction in total mortality with higher baseline LDL-C

Ref. JAMA. 2018;319(15):1566-1579.

Fig. Meta-regression Analysis of All-cause Mortality by Baseline LDL-C Level (34 RCTs)



OBJECTIVE:

To evaluate whether baseline LDL-C level is associated with total and cardiovascular mortality risk reductions.

DATA SOURCES AND STUDY SELECTION:

Electronic databases (Cochrane, MEDLINE, EMBASE, TCTMD, ClinicalTrials.gov, major congress proceedings) were searched through February 2, 2018, to identify randomized clinical trials of statins, ezetimibe, and PCSK9-inhibiting monoclonal antibodies.

DATA EXTRACTION AND SYNTHESIS:

Two investigators abstracted data and appraised risks of bias. Intervention groups were categorized as "more intensive" (more potent pharmacologic intervention) or "less intensive" (less potent, placebo, or control group).

MAIN OUTCOMES AND MEASURES:

The coprimary end points were total mortality and cardiovascular mortality. Random-effects meta-regression and meta-analyses evaluated associations between baseline LDL-C level and reductions in mortality end points and secondary end points including major adverse cardiac events (MACE).

RESULTS:

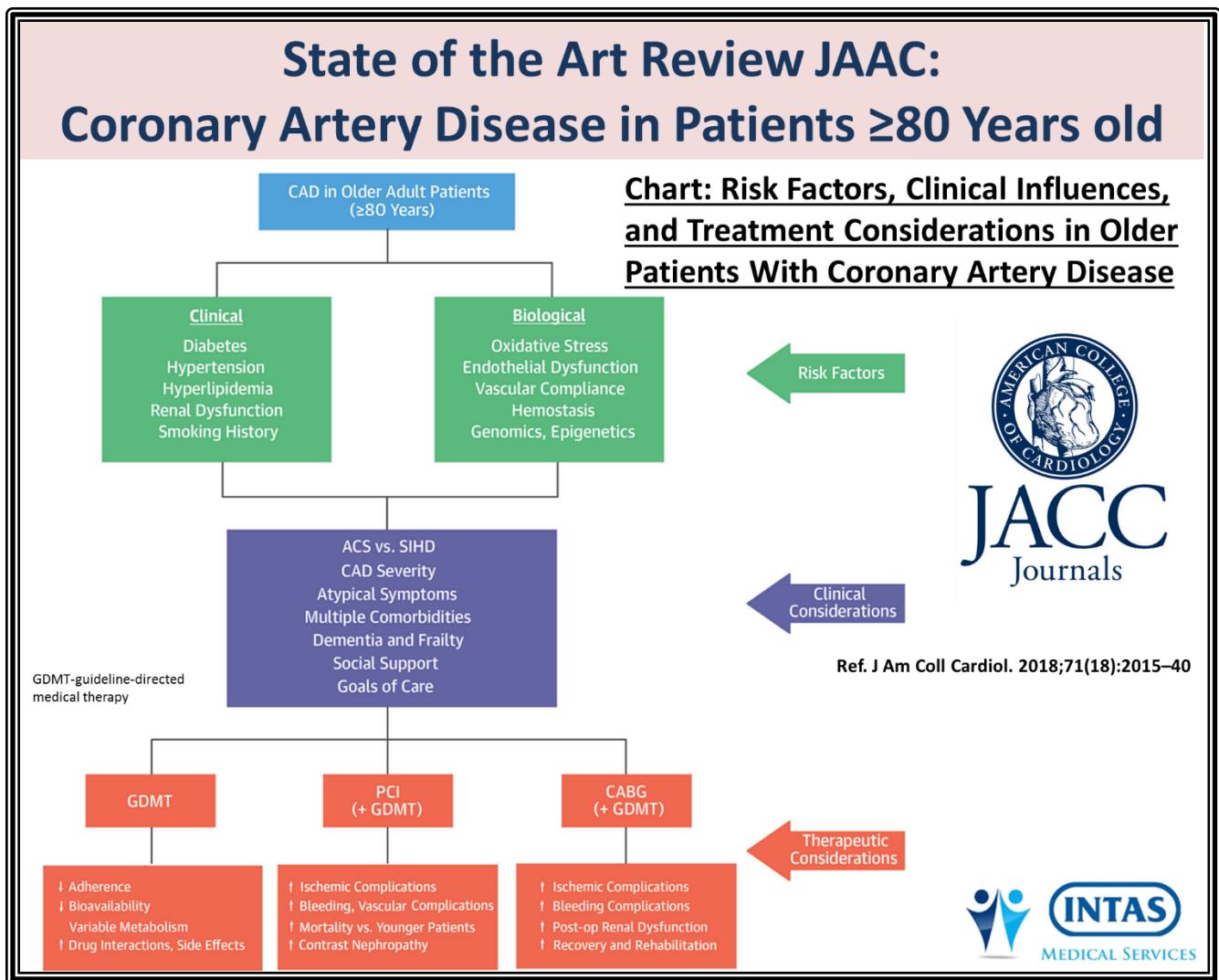
In 34 trials, 136 299 patients received more intensive and 133 989 received less intensive LDL-C lowering. All-cause mortality was lower for more vs less intensive therapy (7.08% vs 7.70%; rate ratio [RR], 0.92 [95% CI, 0.88 to 0.96]), but varied by baseline LDL-C level. Meta-regression showed more intensive LDL-C lowering was associated with greater reductions in all-cause mortality with higher baseline LDL-C levels (change in RRs per 40-mg/dL increase in baseline LDL-C, 0.91 [95% CI, 0.86 to 0.96]; $P = .001$; absolute risk difference [ARD], -1.05 incident cases per 1000 person-years [95% CI, -1.59 to -0.51]), but only when baseline LDL-C levels were 100 mg/dL or greater ($P < .001$ for interaction) in a meta-analysis.

Cardiovascular mortality was lower for more vs less intensive therapy (3.48% vs 4.07%; RR, 0.84 [95% CI, 0.79 to 0.89]) but varied by baseline LDL-C level. Meta-regression showed more intensive LDL-C lowering was associated with a greater reduction in cardiovascular mortality with higher baseline LDL-C levels (change in RRs per 40-mg/dL increase in baseline LDL-C, 0.86 [95% CI, 0.80 to 0.94]; $P < .001$; ARD, -1.0 incident cases per 1000 person-years [95% CI, -1.51 to -0.45]), but only when baseline LDL-C levels were 100 mg/dL or greater ($P < .001$ for interaction) in a meta-analysis. Trials with baseline LDL-C levels of 160 mg/dL or greater had the greatest reduction in all-cause mortality (RR, 0.72 [95% CI, 0.62 to 0.84]; $P < .001$; 4.3 fewer deaths per 1000 person-years) in a meta-analysis. More intensive LDL-C lowering was also associated with progressively greater risk reductions with higher baseline LDL-C level for myocardial infarction, revascularization, and MACE.

CONCLUSIONS AND RELEVANCE:

In these meta-analyses and meta-regressions, more intensive compared with less intensive LDL-C lowering was associated with a greater reduction in risk of total and cardiovascular mortality in trials of patients with higher baseline LDL-C levels. This association was not present when baseline LDL-C level was less than 100 mg/dL, suggesting that the greatest benefit from LDL-C-lowering therapy may occur for patients with higher baseline LDL-C levels.

4. State of the Art Review JAAC: Coronary Artery Disease in Patients ≥ 80 Years old



Coronary artery disease (CAD) is a major cause of morbidity and mortality in patients ≥ 80 years of age. Nonetheless, older patients have typically been under-represented in cardiovascular clinical trials. Understanding the pathophysiology, epidemiology, and optimal means of diagnosis and treatment of CAD in older adults is crucial to improving outcomes in this high-risk population. A patient-centered approach, taking into account health status, functional ability and frailty, cognitive skills, and patient preferences is essential when caring for older adults with CAD. The present systematic review focuses on the current knowledge base, gaps in understanding, and directions for future investigation pertaining to CAD in patients ≥ 80 years of age.

Appreciating the unique biological and disease oriented processes in older patients is essential to provide optimal care for CAD. A number of cellular and molecular processes contribute to the development

and progression of CAD in patients of advanced age, and may serve as future therapeutic targets. It is undisputed that older patients are at greater risk for adverse events and complications from nearly all pharmacological and procedural therapies, and contemporary treatments must be administered with a nuanced appreciation of the particular risks they may pose. Time and patience are often required to determine the most appropriate clinical course to meet the goals of care. For symptom relief, titration of antianginal therapy and close monitoring may alleviate the need for more invasive therapies. Understanding the personal and familial preferences and goals of each patient regarding quality of life and longevity is essential, and considering functional status should be a part of every therapeutic plan. Finally, the decision whether to perform increasingly invasive procedures must be individualized considering the potential risks and benefits.

5. Low adherence and higher discontinuation rate is a concern among Older Adults with Diabetes

BACKGROUND: Statins reduce the risk of cardiovascular disease in patients with diabetes. They examined the prevalence of statin use and assessed the long-term adherence and persistence among people aged ≥ 65 years with diabetes.

METHODS: Pharmaceutical Benefits Scheme data covering a 10% random sample of the Australian population were analysed. Among older adults with diabetes, the yearly prevalence of statin use was compared via Poisson regression modelling using 2006 as the reference year. A cohort of 7,400 new statin users (mean age 72.9 years; female 46.2%) was followed longitudinally. Adherence was assessed via the proportion of days covered

Low adherence and higher discontinuation rate is a concern among Older Adults with Diabetes

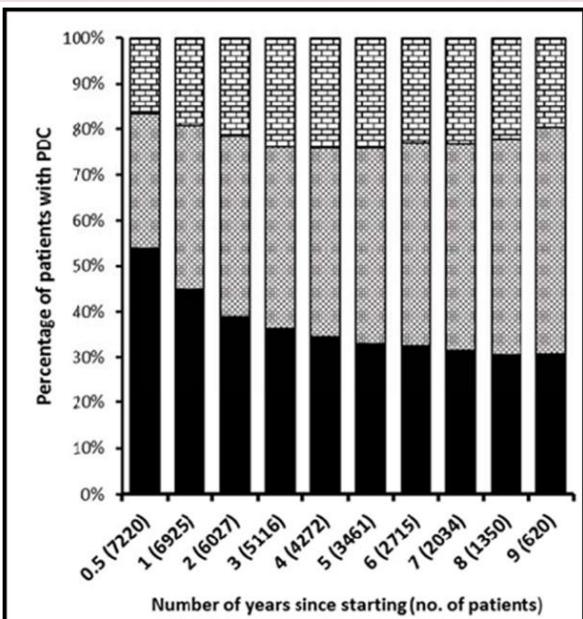
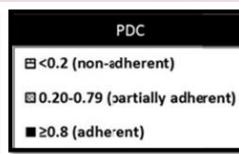


Fig. Proportion of adherence to statin in older adults with diabetes



The prevalence of statin use increased from 52.0% in 2006 to 71.2% in 2016



Ref., J Diabetes. 2018 Apr 15. doi: 10.1111/1753-0407.12769

Statin use has increased among older adults with diabetes. However, adherence is low and discontinuation is high.



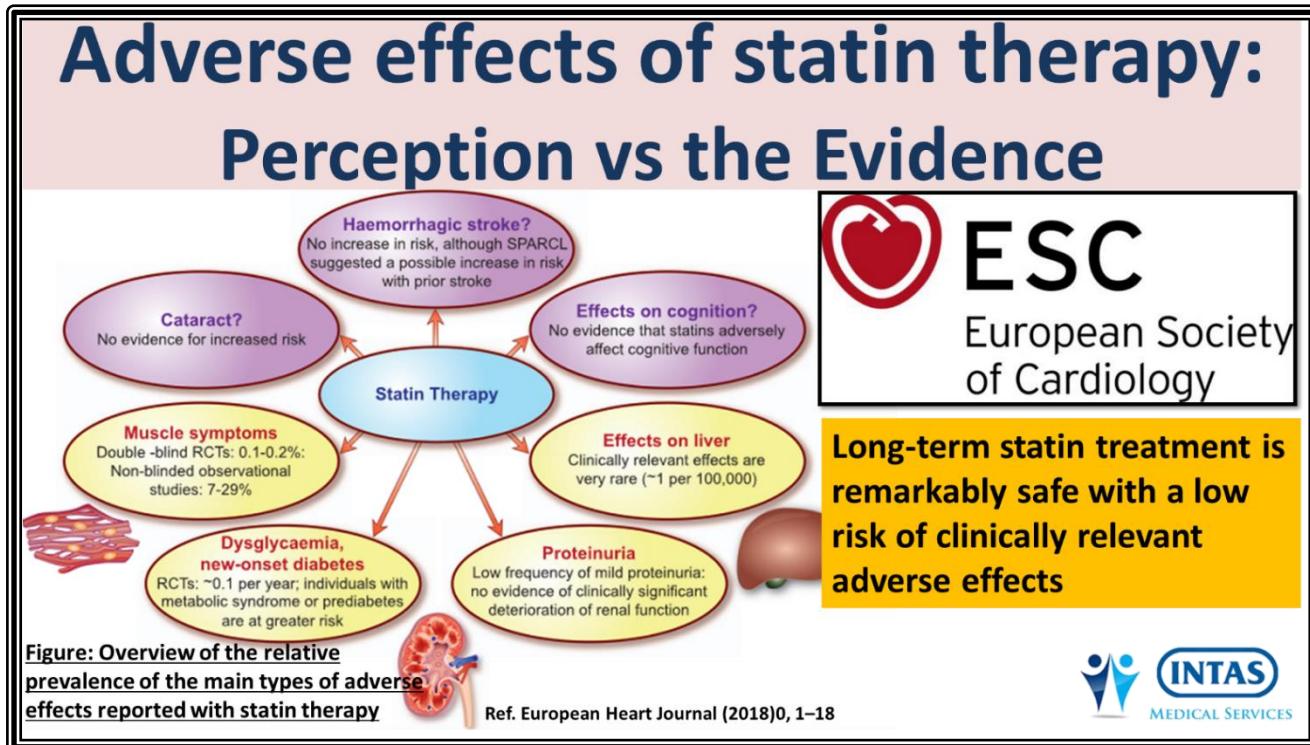
(PDC). Statin discontinuation was defined as the first ≥ 90 days without statin coverage.

RESULTS: The prevalence of statin use increased from 52.0% in 2006 to 71.2% in 2016 (age-and-sex-adjusted rate ratio [aRR] 1.37, 95% CI 1.33-1.41). No gender differences in statin use was observed, but the likelihood of being dispensed statin decreased with increasing age. Among the longitudinal cohort, the proportion adherent ($PDC \geq 0.80$) decreased from 54.0% at 6

months to 37.0% at 9 years. Over a mean follow-up of 4.9 years, 66.8% discontinued, including 42.7% who stopped their statin within the first year. No age or gender differences in statin discontinuation were evident.

CONCLUSIONS: Statin use has increased among older adults with diabetes. However, adherence is low and discontinuation is high. Further investigations into the factors associated with non-adherence or discontinuation of statins are important so as to optimise statin use towards achieving the intended cardiovascular benefits among older people with diabetes.

6. Adverse effects of statin therapy: Perception vs the Evidence



AIMS:

To objectively appraise evidence for possible adverse effects of long-term statin therapy on glucose homeostasis, cognitive, renal and hepatic function, and risk for haemorrhagic stroke or cataract.

METHODS AND RESULTS:

A literature search covering 2000-2017 was performed. The Panel critically appraised the data and agreed by consensus on the categorization of reported adverse effects. Randomized controlled trials (RCTs) and genetic studies show that statintherapy is associated with a modest increase in the risk of new-onset diabetes mellitus (about one per thousand patient-years), generally defined by laboratory findings (glycated haemoglobin ≥ 6.5); this risk is significantly higher in the metabolic syndrome or prediabetes. Statintreatment does not adversely affect cognitive function, even at very low levels of low-density lipoprotein cholesterol and is not associated with clinically significant deterioration of renal function, or development of cataract.

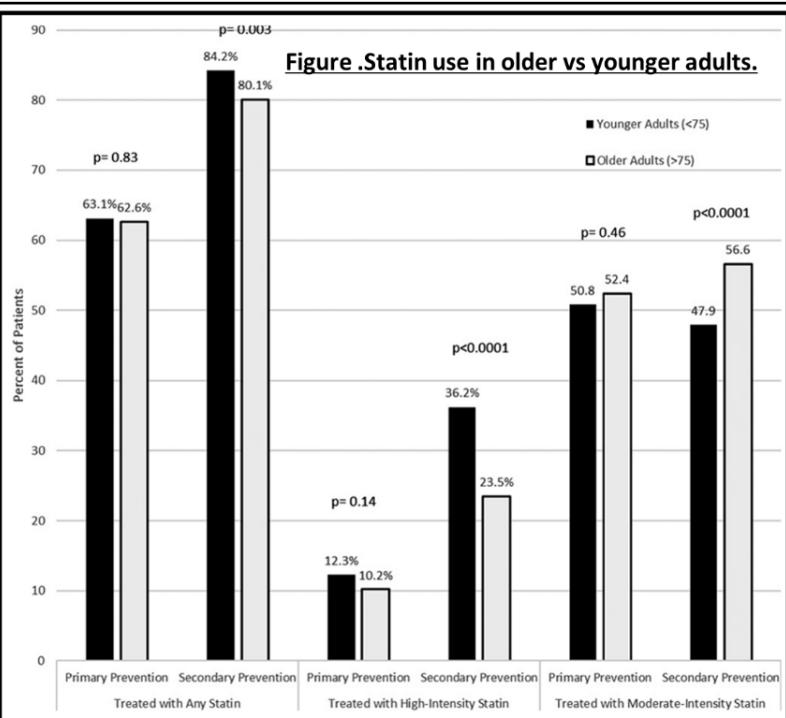
Transient increases in liver enzymes occur in 0.5-2% of patients taking statins but are not clinically relevant; idiosyncratic liver injury due to statins is very rare and causality difficult to prove.

The evidence base does not support an increased risk of haemorrhagic stroke in individuals without cerebrovascular disease; a small increase in risk was suggested by the Stroke Prevention by Aggressive Reduction of Cholesterol Levels study in subjects with prior stroke but has not been confirmed in the substantive evidence base of RCTs, cohort studies and case-control studies.

CONCLUSION:

Long-term statin treatment is remarkably safe with a low risk of clinically relevant adverse effects as defined above; statin-associated muscle symptoms were discussed in a previous Consensus Statement. Importantly, the established cardiovascular benefits of statin therapy far outweigh the risk of adverse effects.

7. Statin Use and Adverse Effects Among Adults >75 Years of Age: Insight from PALM registry



Statin Use and Adverse Effects Among Adults >75 Years of Age: Insight from PALM registry



Statins were similarly tolerated in older and younger adults but, older individuals less frequently received statin therapy and, in particular



Ref. J Am Heart Assoc. 2018;7:e008546.

Background: Current statin use and symptoms among older adults in routine community practice have not been well characterized since the release of the 2013 American College of Cardiology/American Heart Association guideline.

Methods and Results: They compared statin use and dosing between adults >75 and ≤75 years old who were eligible for primary or secondary prevention statin use without considering guideline-recommended age criteria. The patients were treated at 138 US practices in the Patient and Provider Assessment of Lipid Management (PALM) registry in 2015. Patient surveys also evaluated reported symptoms while taking statins.

Multivariable logistic regression models examined the association between older age and statin use and dosing. Among 6717 people enrolled, 1704 (25%) were >75 years old. For primary prevention, use of any statin or high-dose statin did not vary by age group: any statin, 62.6% in those >75 years old versus 63.1% in those ≤75 years old ($P=0.83$); high-dose statin, 10.2% versus 12.3% in the same groups ($P=0.14$). For secondary prevention, older patients were slightly less likely to receive any statin (80.1% versus 84.2% [$P=0.003$]; adjusted odds ratio, 0.81; 95% confidence interval, 0.66–1.01 [$P=0.06$]), but were much less likely to receive a high-intensity

statin (23.5% versus 36.2% [$P<0.0001$]; adjusted odds ratio, 0.54; 95% confidence interval, 0.45–0.65 [$P=0.0001$]). Among current statin users, older patients were slightly less likely to report any symptoms (41.3% versus 46.6%; $P=0.003$) or myalgias (27.3% versus 33.3%; $P<0.001$).

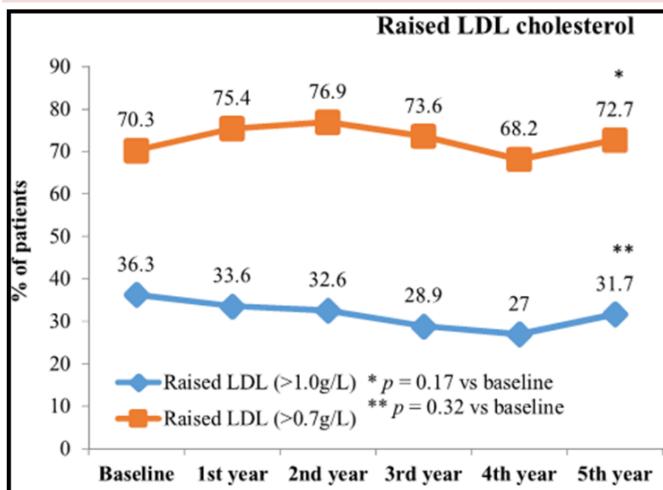
Conclusions: Overall use of statins was similar for primary prevention in those aged >75 years versus younger patients, yet older patients were less likely to receive high-intensity statins for secondary prevention. Statins appear to be similarly tolerated in older and younger adults.

8.>70% Indian CAD patients have their LDL above 100 mg/dl throughout 5 years : CLARIFY registry

Objective: Present paper describes trends in prevalence and control of cardiovascular risk factors and clinical outcomes at 5-years for CLARIFY Indian cohort compared with rest of the world (ROW).

Method: CLARIFY is an international, prospective-observational, longitudinal cohort study in stable coronary artery disease outpatients. The 5-year data of both cohorts were compared, and

>70% Indian CAD patients have their LDL above 100 mg/dl throughout 5 years : CLARIFY registry



- Five year results of CLARIFY India show varying trends in the prevalence of CV risk factors.
- The incidence rates of HR >70 bpm, HbA1c >7%, and raised blood pressure decreased significantly while,
- overweight and obesity remained same and raised LDL cholesterol (>1.0 g/L) showed no reduction

Ref. Indian Heart Journal. 2018; <https://doi.org/10.1016/j.ijh.2018.04.003>



Figure: Trends in risk factor distribution in Indian patients over 5 year period

evaluated.

Results: In Indian cohort, the angina prevalence declined significantly. There are few favorable changes in the pattern of receiving guideline-recommended therapy over 5 years, and the Indian cohort exhibited significantly lower adverse clinical outcomes than ROW.

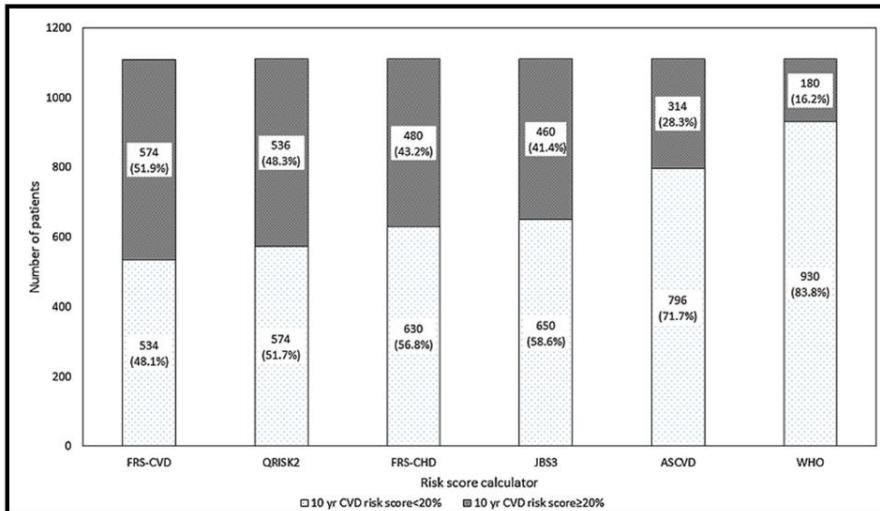
Conclusion: The 5-year trend of CLARIFY India registry indicate varying trends in prevalence and control of cardiovascular risk factors, the need for approaches to improve control of all modifiable risk factors, and increase in long-term use of essential primary and secondary prevention medications in clinical practice as emphasized in the latest Indian guidelines for management of stable CAD.

9. Comparison of different CV risk score calculators for CV risk prediction and guideline recommended statin uses

Objective: The accuracy of various 10-year cardiovascular disease (CVD) risk calculators in Indians may not be the same as in other populations. Present study was conducted to compare the various calculators for CVD risk assessment and statin eligibility according to different guidelines.

Methods: Consecutive 1110 patients who presented after their first myocardial infarction were

Comparison of different CV risk score calculators for CV risk prediction and guideline recommended statin uses



What was known

In Indians the 10 year CVD risk score calculators do not behave the same as in western population

What is new

For identification of high CVD risk group in Indians, FRS-CVD risk assessment model is most useful while for statin eligibility, NICE guideline use (using QRISK2) is most appropriate for our population.



Figure. 10-year dichotomized risk categorization of the patient population by various risk score calculators.
Ref. Indian Heart Journal 69 (2017) 458–463

included. Their CVD risk was calculated using Framingham Risk score- Coronary heart disease (FRS-CHD), Framingham Risk Score- Cardiovascular Disease (FRS-CVD), QRISK2, Joint British Society risk calculator 3 (JBS3), American College of Cardiology/American Heart Association (ACC/AHA), atherosclerotic cardiovascular disease (ASCVD) and WHO risk charts, assuming that they had presented one day before cardiac event for risk assessment. Eligibility for statin uses was also looked into using ACC/AHA, NICE and Canadian guidelines.

Results: FRS-CVD risk assessment model has performed the best as it could identify the highest number of patients (51.9%) to be at high CVD risk while WHO and ASCVD calculators have performed the worst (only 16.2% and 28.3% patients respectively were stratified into high CVD risk) considering 20% as cut off for high risk definition. QRISK2, JBS3 and FRS-CHD have performed

intermediately. Using NICE, ACC/AHA and Canadian guidelines; 76%, 69% and 44.6% patients respectively were found to be eligible for statin use.

Conclusion: FRS-CVD appears to be the most useful for CVD risk assessment in Indians, but the difference may be because FRS-CVD estimates risk for several additional outcomes as compared with other risk scores. For statin eligibility, however, NICE guideline use is the most appropriate.

10. Assessing Severity of Statin Side Effects: Fact Versus Fiction

Statins clearly help to lower the risk for future ASCVD events in patients at risk. In general, statins are very well tolerated and about 85-90% of patients report no side effects. However, there are a few side effects that tend to raise concern among patients when considering the need for one of these medications. Three of the most common concerns include muscle-related issues, new-onset diabetes and increased incidence of hemorrhagic stroke.

While the side effects of statins are important to keep in mind, overall, the benefits of lowering LDL with statins far outweigh the low likelihood of an adverse effect for the vast majority of adults at elevated risk for ASCVD. Fear of adverse effects should not prevent a healthcare provider from prescribing a statin, though it is important to be alert for a severe reaction to a statin and take it seriously. Providers should also be careful of factors that can increase the risk of side effects presenting in a patient, especially interacting medications. Ultimately, lowering LDL-C is

Assessing Severity of Statin Side Effects: Fact Versus Fiction



FACT
VS.
FICTION



JACC
Journals

- Statins clearly help to lower the risk for future ASCVD events in patients at risk. In general, statins are very well tolerated and about 85-90% of patients report no side effects.
- Fear of adverse effects should not prevent a healthcare provider from prescribing a statin

Ref. J Am Coll Cardiol. Apr 09, 2018 latest-in-cardiology/articles/2018/04/09/13/25/assessing-severity-of-statin-side-effects



incredibly important when it comes to improving heart health, and with only 55% of US adults needing cholesterol medicine currently taking it, statins are still a great way to prevent vascular events.

11. Time to Benefit is the new standard to measure the benefits of lipid-lowering drugs

Background: Time to benefit (TTB) in clinical trials of cholesterol-lowering drugs is important because it may provide a clue as to the potential mechanism of action of the drug, it is helpful in determining when to stop a trial for futility, and it may inform treatment decisions in subjects with a reduced life expectancy.

Objective: To compare TTB among clinical trials of cholesterol-lowering drugs.

Methods: They examined TTB in 24 trials of cholesterol-lowering drugs with positive outcomes. Benefit curves were constructed by subtracting the curve for placebo or comparator drug from the curve for active treatment.

Results: TTB ranged from 1-30 (mean 13.1) months, being shorter in trials of statins (n=17) compared to non-statins (n=7), 10.3 versus 20.0 months. Among statin trials, TTB was shorter

Time to Benefit is the new standard to measure the benefits of lipid-lowering drugs

Trial	Drug and statin dose (mg/day)	Comparator	Number in trial	Number of events	Baseline LDL-C (mg/dL)	LDL-C reduction (mg/dL)	Primary endpoint reduction (%)	Trial duration (years)	Estimated TTB (months)
Statins vs Placebo									
4S ¹	Simvastatin 20//40	Placebo	4444	855	189	64	34	5.4	12
JUPITER ²	Rosuvastatin 20	Placebo	17,802	393	108	54	44	1.9	3
MIRACL ³	Atorvastatin 80	Placebo	3086	497	124	52	16	0.3	1.5
WOSCOPS ⁴	Pravastatin 40	Placebo	6595	422	192	50	31	4.9	6
CARDS ⁵	Atorvastatin 10	Placebo	2838	210	116	46	37	3.9	6
HPS ⁶	Simvastatin 40	Placebo	20,536	2110	131	43	24	5.0	12
AFCAPS ⁷	Lovastatin 20/40	Placebo	6605	299	150	38	37	5.2	6
ASCOT-LLA ^{8,9}	Atorvastatin 10	Placebo	10,305	254	131	37	36	3.3	1
LIPID ¹⁰	Pravastatin 40	Placebo	9014	299	150	36	24	6.0	18
HOPE-3 ¹¹	Rosuvastatin 10	Placebo	12,705	539	128	35	24	5.6	30
CARE ¹²	Pravastatin 40	Placebo	4159	486	139	35	24	5.0	24
PROSPER ¹³	Pravastatin 40	Placebo	5804	881	147	50	15	3.2	18
MEGA ¹⁴	Pravastatin 10-20	None – open label	7832	167	156	23	33	5.3	6
SHARP ¹⁵	Ezetimibe/Simva 10/20	Placebo	9270	1145	107	33	17	4.9	12
High vs Low Dose									
PROVE-IT ¹⁶	Atorvastatin 80	Pravastatin 40	4162	1012	95	33	16	2.5	1
TNT ¹⁷	Atorvastatin 80	Atorvastatin 20	10,001	982	101	24	22	5.5	1
IDEAL ¹⁸	Atorvastatin 80	Simvastatin 20/40	8888	874	121	23	11	4.8	18
Non-Statin Drugs									
CPPT ²⁰	Cholestyramine	Placebo	3806	342	280	56	19	7.4	24
HHS ²¹	Gemfibrozil	Placebo	4081	140	189	16	34	5.0	24
VA-HIT ²²	Gemfibrozil	Placebo	2531	494	112	0	22	5.1	24
IMPROVE-IT ²³	Ezetimibe/Simva 10/20	Simvastatin	18,144	5314	69	16	6.4	7.4	14
FOURIER ²⁴	Evolocumab	Placebo	27,564	2907	92	62	15	2.2	12
ODYSSEY ²⁵	Alirocumab	Placebo	18,924	1995	87	54	15	2.8	12
REVEAL ²⁶	Anacetrapib	Placebo	30,449	3443	61	26**	9	4.1	30

Table: Analysis of TTB in 24 trials of cholesterol-lowering drugs with positive outcomes



- Time to benefit (TTB) is quite variable across trials of lipid-lowering drugs
- Among statin trials, TTB is shorter with atorvastatin than with other statins

Ref. Journal of Clinical Lipidology 2018

10.1016/j.jacl.2018.04.006



with atorvastatin (n=6) than in trials with other statins (n=11), 4.75 compared to 11.4 months.

Conclusions: TTB is variable among trials of cholesterol-lowering drugs, being shorter with statin compared to non-statin drugs. TTB is shorter with atorvastatin than with other statins. For trials of new cholesterol-lowering drugs, outcome curves that do not separate for up to 30 months do not preclude eventual benefit.

12. Statin use is associated with a decreased risk of osteoporosis in both genders

BACKGROUND:

Several observational cohort and meta-analytical studies in humans have shown that statin users have a lower risk of fractures or greater bone mineral densities (BMD) than nonusers. However, some studies including randomized clinical trials have the opposite results, particularly in Asian populations.

OBJECTIVE:

This study investigates the impacts of statins on new-onset osteoporosis in Taiwan.

METHODS:

In a nationwide retrospective population-based cohort study, 45,342 subjects aged between 50-

Statin use is associated with a decreased risk of osteoporosis in both genders

During the 13-year follow-up period, 16,146 of all enrolled subjects (10.03%) developed osteoporosis, including 3097 statin-users (6.83%) and 13,049 statin-non-users (11.29%).

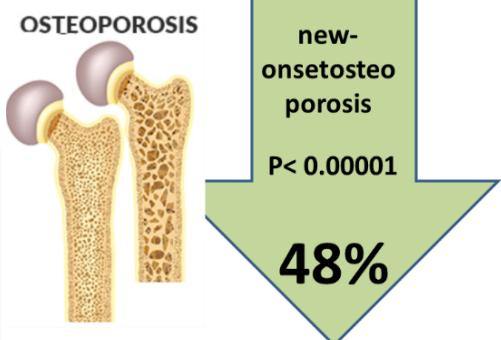
cDDDs level	n	HR (95% CI)	P value
cDDDs			
Non-users	115594	ref	-
<28 DDDs	6420	1.03(0.95–1.11)	0.47
28–90 DDDs	8858	0.84(0.78–0.90)	<0.0001
91–365 DDDs	13501	0.56(0.52–0.60)	<0.0001
≥366 DDDs	16563	0.23(0.21–0.25)	<0.0001

Model adjusted for age, sex, ALD, COPD, DM, Hyperthyroidism, Liver cirrhosis, CAD and HRT

Abbreviations: cDDD, cumulative defined daily dose

Table: Adjusted hazard ratio of statins cDDD for new-onsetosteoporosis

Ref. PLoS One. 2018 May 3;13(5):e0196713.



Statin use is associated with a decreased risk of osteoporosis in both genders. The osteo-protective effect of statins seemed to be more prominent with a dependency on the cumulative dosage and statin intensity.

90 years having received statin therapy (statin-users) since January 1 2001, and observed through December 31 2013 were selected from the National Health Insurance Research Database of Taiwan. Likewise, 115,594 patients had no statin therapy (statin-non-users) were included as controls in this study. Multivariable Cox proportional hazards analysis for drug exposures was employed to evaluate the association between statin treatment and new-onset of osteoporosis

risk. They also used the long-rank test to evaluate the difference of probability of osteoporosis-free survival.

RESULTS:

During the 13-year follow-up period, 16,146 of all enrolled subjects (10.03%) developed osteoporosis, including 3097 statin-users (6.83%) and 13,049 statin-non-users (11.29%). Overall, statin therapy reduced the risk of new-onset osteoporosis by 48% (adjusted hazard ratio [HR] 0.52; 95% CI 0.50 to 0.54). A dose-response relationship between statin treatment and the risk of new-onset osteoporosis was observed. The adjusted hazard ratios for new-onset osteoporosis were 0.84 (95% CI, 0.78 to 0.90), 0.56 (95% CI, 0.52 to 0.60) and 0.23 (95% CI, 0.21 to 0.25) when cumulative defined daily doses (cDDDs) ranged from 28 to 90, 91 to 365, and more than 365, respectively, relative to nonusers. Otherwise, high-potency statins (rosuvastatin and atorvastatin) and moderate-potency statin (simvastatin) seemed to have a potential protective effect for osteoporosis.

CONCLUSIONS:

In this population-based cohort study, they found that statin use is associated with a decreased risk of osteoporosis in both genders. The osteoprotective effect of statins seemed to be more prominent with a dependency on the cumulative dosage and statin intensity.

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