

## Can We Cure Atherosclerosis?

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## What if you had a guide ...

- To guarantee you a longer life?
- To prevent heart disease, stroke?
- To feel stronger and healthier now and later?
- To provide a better quality of life as you invest in your relationships and life goals?



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American Heart Association | American Stroke Association  
 Learn and Live



→ Living Better with Life's Simple 7™

American Heart Association Living Better with Life's Simple 7 3

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## Life's Simple 7

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- Eat healthy
- Get active
- Control weight
- Don't smoke
- Control blood pressure
- Control blood sugar
- **Control cholesterol**



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## United States - Leading Causes of Death Prevented by Lowering Cholesterol

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1. Heart disease	9. Influenza, pneumonia
2. Cancer	10. Suicide
3. Chronic lung disease	11. Septicemia
4. Stroke	12. Chronic liver disease and cirrhosis
5. Accidents	13. Hypertension and related renal disease
6. Alzheimer's disease?	14. Parkinson's disease
7. Diabetes	15. Pneumonitis
8. Kidney diseases	

CDC

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## New cholesterol guideline

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- Treat blood cholesterol to reduce cardiovascular (CVD) risk
- Healthy lifestyle is foundation
- Drug therapy for people most likely to benefit
  - Statins are first line
  - "Nonstatins" may benefit some

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## Net benefit from statins



- Clear net benefit in 4 groups
  - Already have cardiovascular disease
  - Genetic high cholesterol  $\geq 190$  mg/dl
  - Diabetes age 40-75 years
  - $\geq 7.5\%$  10-year cardiovascular risk age 40-75 years

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## Who might need more cholesterol lowering?



- Already have cardiovascular disease
- Genetic high cholesterol  $\geq 190$  mg/dl
- Intolerant to statins

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## New cholesterol drugs in the pipeline



- PCSK-9 monoclonal antibodies most promising
- Lower LDL-cholesterol ("bad") 50-65% when added to statins
- Commonly  $\downarrow$  LDL-C levels  $< 50$  mg/dl
  - Often  $\downarrow$  LDL-C levels  $< 25$  mg/dl
  - Average untreated LDL-C is 130 mg/dl

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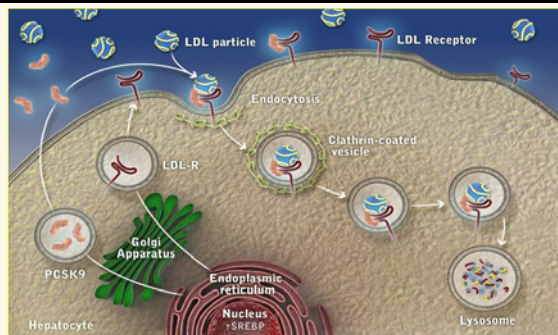
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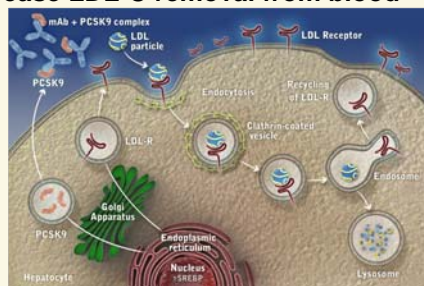
## LDL-receptor removes LDL-C from blood PCSK9 targets LDL-Receptor for breakdown



McKenney JM, et al. *J Am Coll Cardiol*. 2012;59:2344–2353

## PCSK9 antibodies block PCSK-9 Increase LDL-Receptor Expression

⇒ Increase LDL-C removal from blood

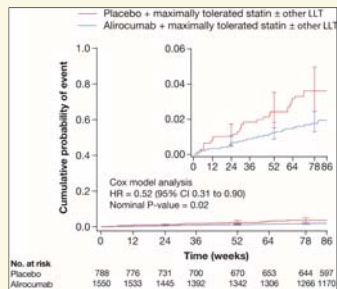


LDL, low-density lipoprotein; LDL-R, LDL receptor; mAbs, monoclonal antibodies; PCSK9, proprotein convertase subtilisin/kexin type 9; SREBP-2, sterol regulatory element-binding protein-2.  
Adapted from: Catapano AL, Papadopoulos N. *Atherosclerosis* 2013;228(1):18–28.

## So far appear safe & Reduce cardiovascular events

### ODYSSEY LONG TERM

- Alirocumab 150 mg every 2 weeks
- Average 1.5 year follow-up
- 48% reduction cardiovascular events



Robinson JG et al. *N Engl J Med* 2015. DOI: 10.1056/NEJMoa1501031

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## PCSK-9 inhibitors

### Future directions

- “Stabilization” therapy – Clinical CVD
- Curing atherosclerosis – Primordial prevention

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## Atherosclerotic Cardiovascular Disease Progression Through the Lifespan

**CVD EVENTS**

- MI/Unstable angina
- Ischemic stroke/TIA
- Critical leg ischemia
- Intermittent claudication
- CV death

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## A new paradigm #1

### Plaque stabilization

**STABLE PLAQUE**

Stabilization/Regression  
PCSK-9 mAB  
Therapy

**CVD EVENTS**

- MI/Unstable angina
- Ischemic stroke/TIA
- Critical leg ischemia
- Intermittent claudication
- CV death

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## Plaque stabilization



- CVD patients = Large burden atherosclerosis
- PCSK-9 antibodies \$\$\$\$\$\$
- Very low LDL-C = Plaque regression/stabilization in most patients
- Treat 2-3 years with PCSK-9 antibodies
- CVD risk reduction over 5-10+ years
  - Large “Legacy Effect”

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## New paradigm #2: Cure atherosclerosis



- CVD remains the leading cause of death & major cause of morbidity in US & globally
- Population risk factor levels remain high
- If all forms of major CVD were eliminated, life expectancy could rise by almost 7 years
- CVD #1 cause of healthcare expenditures
  - Total CVD costs expected to triple by 2030 as US population ages

Go AS, et al. *Circulation* 2012; 127: e6-e245; Danesh G, et al. *PLoS Med* 2009;6:e1000058; Heidenreich P, Trogdon J, Khavjou O, et al. *Circulation*. 2011;123:933-944; Soti A. AHRQ statistical brief #331 [http://www.meps.ahrq.gov/mepsweb/data\\_files/publications/stat331/stat331.pdf](http://www.meps.ahrq.gov/mepsweb/data_files/publications/stat331/stat331.pdf)

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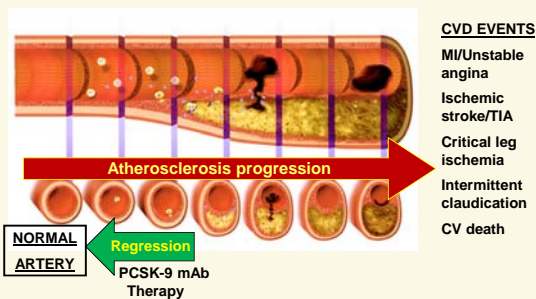
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## “Reverse” Atherosclerosis “Reset the (Vascular Aging) Clock”



Robinson JG, Gliddig SS. *JACC*. 2014;63(25, Part A):2779-2785

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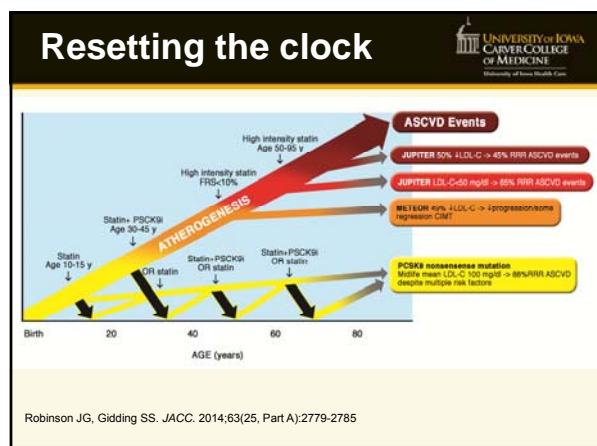
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## Conclusions

- Healthy lifestyle is the best way to prevent CVD
- For those with bad luck (genes), unable, or unwilling  $\Rightarrow$  Statin therapy prevents CVD & saves lives
- New cholesterol-lowering drugs may facilitate new prevention paradigms

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