

**Workshop 2:
Treating the Entire Lipid Profile**

Workshop Learning Objectives

Upon completion of this workshop, participants will be able to:

- Explain Reverse Cholesterol Transport (RCT)
- Use the [Reprint 1] and [Reprint 2] reprints to confidently explain:
 - The need for CV risk reduction in addition to that provided by statin therapy alone
 - The need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG
 - The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies

Overview

- This workshop begins with a review of the clinical presentations with respect to treating all three key lipid parameters, LDL-C, HDL-C and TG. Working in triad table teams, the participants apply this knowledge to complete the RCT Work Mat.
- In the following activity, participants identify key data in the [Reprint 1] and [Reprint 2] reprints to support:
 - The need for CV risk reduction in addition to that provided by statin therapy alone
 - The need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG
 - The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies
- Participants role-play using the reprints as a support tool.

Facilitator Notes

The workshop facilitator provides direction and feedback to participants at their assigned tables regarding the above activities.

Room Design

The workshop takes place in rooms with round tables and 2 triad teams at each table (6 people). There will be PowerPoint projection equipment and a screen in the front of each workshop room.

Workshop Materials

- Facilitator's Guide
- Participant's Guide
- PowerPoint slide set for Workshop 2
- Key Messages Worksheet (Appendix)
- RCT schematic work mat (Appendix)
- Workshop 2 Observer Checklist (Appendix)

Workshop 2: Treating the Entire Lipid Profile

Topic	Time	Activity
Introduction	2 Minutes	<ul style="list-style-type: none"> • Facilitator welcomes the participants, reviews the workshop objectives
Review Clinical Presentations	5 Minutes	<ul style="list-style-type: none"> • Facilitator reviews the key learnings from the general sessions with respect to: <ul style="list-style-type: none"> – The need for CV risk reduction in addition to that provided by statin therapy alone – The need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG – The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies
RCT Review	5 Minutes	<ul style="list-style-type: none"> • Facilitator reviews the Reverse Cholesterol Transport (RCT) process
RCT Schematic Activity	30 Minutes	<ul style="list-style-type: none"> • Facilitator divides the participants in table triads to work and complete the RCT Schematic Work Mats (15 min) • Teams share their schematic layouts for feedback (10 min) • Facilitator invites volunteers to verbalize an explanation of RCT (5 min)
[Reprint 1] and [Reprint 2] Reprint Activity	60 Minutes	<ul style="list-style-type: none"> • Facilitator divides the room into four teams and introduces the activity (5 min) <ul style="list-style-type: none"> – First and third teams review the [Reprint 1] Reprint first and the [Reprint 2] Reprint second – Second and fourth teams review the [Reprint 2] Reprint first and the [Reprint 1] Reprint second • Participants review the reprints (30 min), identifying key data to support the rationale for: <ul style="list-style-type: none"> – The need for CV risk reduction in addition to that provided by statin therapy alone – The need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG – The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies • Facilitator selects random teams to take turns presenting their findings (25 min)

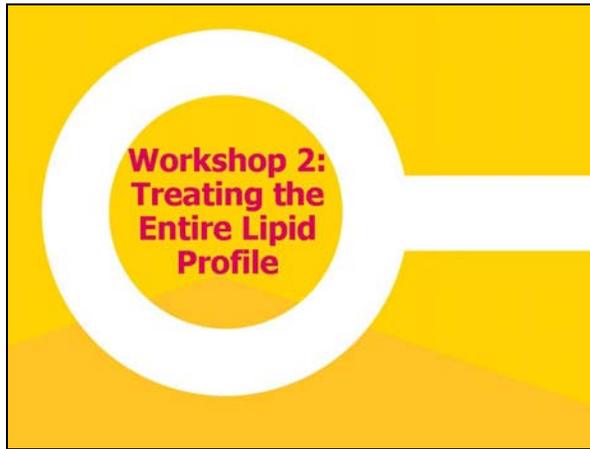
Workshop 2: Treating the Entire Lipid Profile

Topic	Time	Activity
Role-Play With Reprints	45 Minutes	<ul style="list-style-type: none">• Facilitator directs participants to work in triads, to practice verbalizing all three core messages with support from the reprints (20 min)• Facilitator calls on volunteers to verbalize the core messages and supporting statements as if speaking with a physician, solicits feedback from the group (25 min)
Conclusion	3 Minutes	<ul style="list-style-type: none">• Facilitator debriefs the group, thanks the participants and closes the workshop
TOTAL TIME	150 Minutes	

Facilitator's Guide Icon Legend

Icon	What does this icon stand for?
	<p>1. <i>SHOW slide or DELIVER a presentation.</i></p>
	<p>2. <i>CONDUCT a group/room discussion.</i></p>
	<p>3. <i>INSTRUCT participants to begin an interactive table activity.</i></p>
	<p>4. <i>INSTRUCT participants to begin a role-play.</i></p>
	<p>5. <i>ASK participants to verbalize to the rest of the room.</i></p>
	<p>6. <i>Indicates timing for the various activities and reminds the Facilitator to be aware of the time allocated for that activity.</i></p>
	<p>7. <i>ASK participants if they have any questions.</i></p>

Introduction
2 Minutes



- WELCOME the participants to this workshop



Workshop Objectives

At the end of this workshop, you will be able to:

- Explain Reverse Cholesterol Transport (RCT)
- Use the Chapman and Nordestgaard reprints to explain:
 - The need for CV risk reduction in addition to that provided by statin therapy alone
 - The need to treat all three lipid parameters, LDL-C, HDL-C and TGs
 - The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies

- REVIEW the learning objectives
- *At the end of this workshop, you will be able to:*
 - Explain the Reverse Cholesterol Transport process
 - Use the [Reprint 1] and [Reprint 2] reprints to explain:
 - The need for CV risk reduction in addition to that provided by statin therapy alone
 - The need to treat all three lipid parameters, LDL-C, HDL-C and TGs
 - The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies

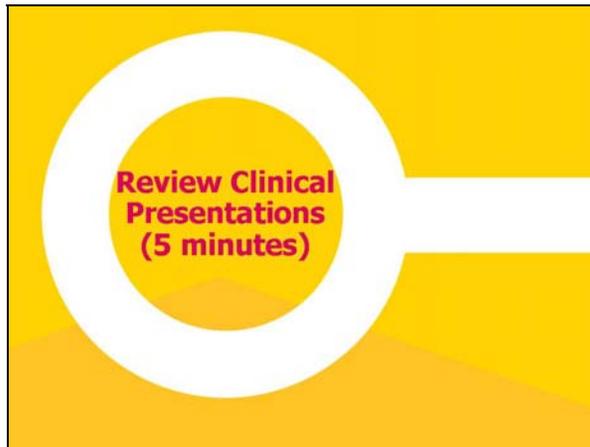


Workshop Format

- Introduction
- Review Clinical Presentations
- RCT Review (Reverse Cholesterol Transport)
- RCT Schematic Activity
- Chapman & Nordestgaard Reprint Activity
- Role-Play With Reprints
- Conclusion

- REVIEW the workshop format:
 - Review Clinical Presentations
 - EXPLAIN that this workshop will begin with a review of the clinical presentations that support treating all three key lipid parameters, LDL-C, HDL-C and TG
 - RCT Review (Reverse Cholesterol Transport)
 - RCT Schematic Activity
 - To test your understanding of RCT
 - [Reprint 1] and [Reprint 2] Reprint Activity
 - Two selling tools that help you explain the 3 key messages
 - Role-Play With Reprints
 - Put your knowledge into practice through role-playing with use of the two reprints
 - TRANSITION to Review Clinical Presentations

Review Clinical Presentations
5 Minutes



- REVIEW the key learnings from the general session with respect to a need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG



Substantial Risk of CHD Events Remains for Many Patients on Statin Therapy

Trial (N)	Statin treatment	Clinical events ^a	
		Risk reduction vs placebo	Remaining risk
WOSCOPS ^b (6595)	Pravastatin 40 mg	31%	69%
AFCAPS/TexCAPS ^c (6605)	Lovastatin 20 or 40 mg	37%	63%
ASCOT-LLA ^d (10,305)	Atorvastatin 10 mg	36%	64%
4S ^e (4444)	Simvastatin 20 mg	26%	74%
CARE ^f (4159)	Pravastatin 40 mg	24%	76%
LIPID ^g (9014)	Pravastatin 40 mg	24%	76%
HPS ^h (20,536)	Simvastatin 40 mg	27%	73%
PROSPER ⁱ (5804)	Pravastatin 40 mg	19%	81%

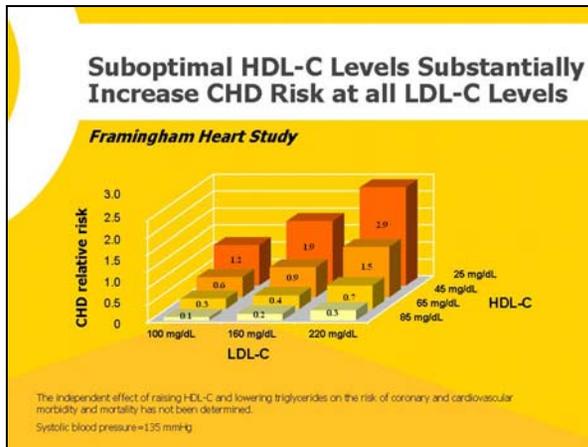
- EXPLAIN that since 1994, 8 placebo-controlled trials that enrolled a total of 67,462 patients with dyslipidemia have evaluated the efficacy of statin therapy for the primary or secondary prevention of CHD events.
- In these trials, LDL-C reductions ranging from 25% to 35% corresponded with relative risk reductions of 24% to 40% for CHD death or non-fatal myocardial infarction.
- While such risk reductions represent clear progress over prior therapies, it is clear that a substantial risk (approximately 60%–80%) of CHD events remains.
- This seems to indicate a need for intervention that is more comprehensive than reducing LDL-C alone.



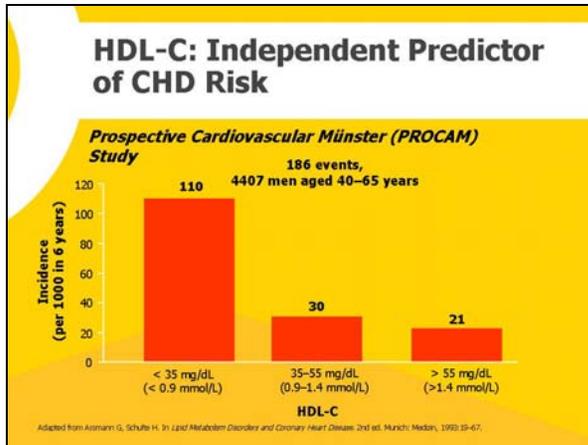
The Need to Treat Beyond LDL-C

- Intensive lipid lowering with high-dose statin therapy has improved clinical outcomes, confirming that “lower is better”
 - But remaining CHD risk may still be as high as 60%–80%
- Development of new approaches should target the broad lipoprotein profile, eg, HDL-C + triglycerides

- As shown in the previous slide, large placebo-controlled trials have demonstrated that statins may reduce the risk for primary or secondary CHD events by 20% to 40%.
- Furthermore, intensive lipid lowering with high-dose statin therapy improves clinical outcomes compared with less intensive statin therapy.
 - This confirms that “lower is better” with respect to LDL-C concentrations.
 - However, these trials suggest that the remaining risk for CHD events remains as high as 60% to 80% in some statin-treated patients.
- Therefore, it seems reasonable to conclude that further progress against CHD disease requires a different approach.
- Researchers have proposed that new approaches should target non-LDL-C parameters, such as HDL-C and triglycerides.



- The Framingham Heart Study was one of the first epidemiologic studies to demonstrate the association between increased CHD risk and suboptimal HDL-C levels.
- This landmark trial examined HDL-C and LDL-C levels in relation to CHD risk in a large cohort of men 50 to 70 years of age.
- The relative risk of CHD events increased markedly with decreasing HDL-C concentration at every level of LDL-C concentration.
- Conversely, as LDL-C increased, the most dramatic increases in CHD risk were evident within the lowest HDL-C categories: 0.6 mmol/L (25 mg/dL) and 1.2 mmol/L (45 mg/dL)



- The Prospective Cardiovascular Münster (PROCAM) study provided evidence of an inverse correlation between CHD risk and plasma HDL-C.
- The greatest risk was seen in individuals who had HDL-C levels below 0.9 mmol/L (35 mg/dL)
 - 110 of 186 CHD events occurred in this group within the 6-year observation period of the study.
- The risk was lower by nearly three quarters among individuals who had higher HDL-C concentrations of 0.9 to 1.4 mmol/L (35–55 mg/dL)
- The CHD risk was lower by nearly half again among individuals who had HDL-C levels above 1.4 mmol/L (55 mg/dL) compared to levels of 0.9 to 1.4 mmol/L (35–55 mg/dL).



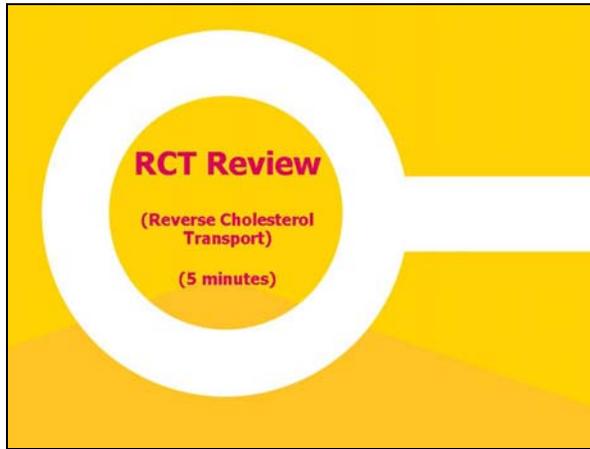
**Nicotinic Acid and Atherosclerosis:
A Positive Effect on Clinical Outcomes**

Randomized Controlled Clinical Trials of Nicotinic Acid and Effect on HDL and Clinical Outcomes

Source Clinical outcome studies	Special Agent(s)	Patients Receiving Treatment, No./Total (%)	Increase in HDL-C Levels, %	Follow-up Duration, y	Outcomes*
CDP	Niacin	1119/8341 (13.4)	NR	6	Decreased (27%) nonfatal MI
CDP follow-up	Niacin	1119/8341 (13.4)	NR	15	Decreased (11%) death
Stockholm	Niacin + clofibrate	279/555 (50.3)	NR	5	Decreased (26%) death; Decreased (36%) CAD death
HATS	Niacin + simvastatin	38/160 (23.8)	26	3	Decreased (90%) first death, MI, stroke, or revascularization
AFREGS	Niacin + gemfibrozil + cholestyramine	71/143 (49.7)	36	2.5	Decreased (13%) composite clinical outcome of angina, MI, TIA, stroke, death, and cardiovascular procedures; Decreased local coronary stenosis (secondary outcome)

- The Coronary Drug Project (CDP), Stockholm Ischemic Heart Disease Secondary Prevention Study (Stockholm), HDL Atherosclerosis Treatment Study (HATS), and Armed Forces Regression Study (AFREGS) studied nicotinic acid (niacin) within their respective protocols
- The results of these clinical outcome studies and the effect on HDL-C levels are described in this table.

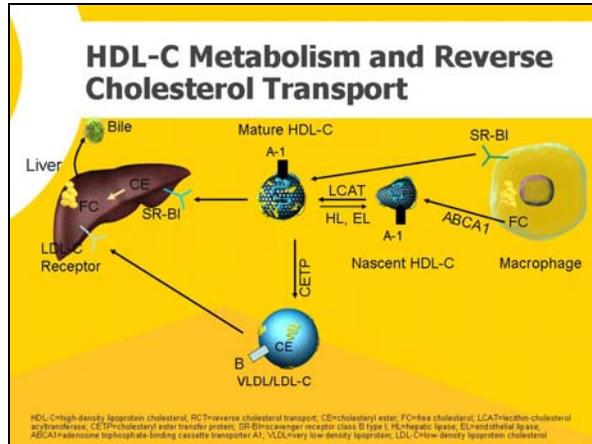
RCT Review
5 Minutes



- TRANSITION to the RCT Review (Reverse Cholesterol Transport)

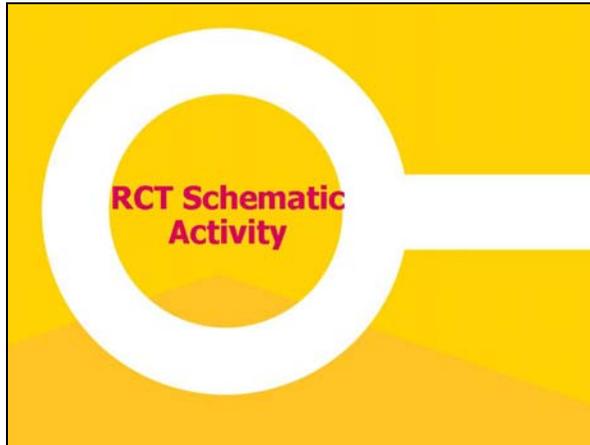


5 Minutes



- HDL-C mediates reverse cholesterol transport (RCT), in which cholesterol is transferred from peripheral tissues to the liver for disposal
- In RCT, lipid-poor apo A-1 promotes efflux of cellular-free cholesterol via the ABCA1 transporter
- HDL-FC can be esterified by LCAT to CE-forming mature HDL-C. In the direct pathway, CE and FC from HDL particles are selectively taken up by the liver via SR-BI
- Removal of free cholesterol from macrophages that form atheromas in arterial walls may slow or reverse the growth of the lesion.
- HDL-C can also deliver CEs to the liver via an indirect pathway, where CEs are passed to apo B-containing lipoproteins by cholesteryl ester transfer protein (CETP) and then cleared by hepatic LDL receptors
- In the indirect pathway, CEs carried by HDL-C are exchanged for triglycerides found on apo B-rich particles (LDL-C and very low-density lipoprotein [VLDL]) by CETP
- The subsequent uptake of apo B-containing lipoproteins rich in CEs by hepatic LDL receptors may be responsible for up to 50% of cholesterol uptake
- Triglyceride-rich HDL can then undergo hydrolysis by hepatic lipase and endothelial lipase to form small HDL that can re-enter the cholesterol transport process. As this figure shows, free cholesterol in the macrophages may be removed into nascent HDL particles through the action of the ATP-binding cassette protein 1, or ABC1.

RCT Schematic Activity
25 Minutes



- TRANSITION to the RCT Schematic Activity (25 minutes)



15 min

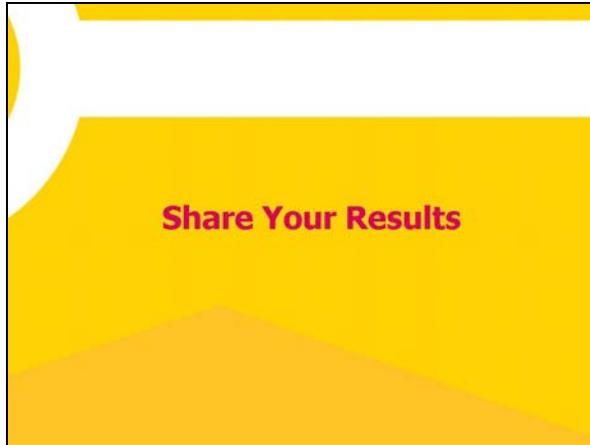
RCT Schematic Activity Instructions

- You will be divided into table triads to complete the RCT Schematic Workmat (15 min)
- You will be randomly selected to share your results and verbalize an explanation of RCT

- DIVIDE participants into table triads to complete the RCT Schematic Work Mats
- EXPLAIN that participants will be randomly selected to share results with the group and then verbalize an explanation of RCT
- KEEP time ANNOUNCING 5-minute intervals
- CONCLUDE the activity after 15 minutes



15 Minutes



- Randomly SELECT triads to share their schematic layouts
- ASK for feedback from other participants (10 min)
- Randomly SELECT individual participants to verbalize the RCT process to the group (5 min)
- CONCLUDE the verbalization activity after 5 minutes
- TRANSITION to the [Reprint 1] and [Reprint 2] Reprint Activity

[Reprint 1] and [Reprint 2] Reprint Activity
60 Minutes



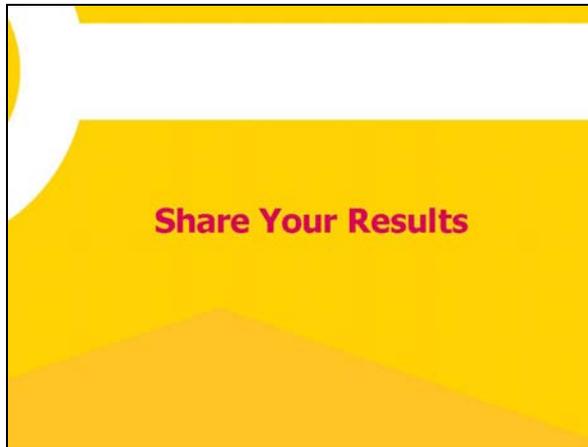
- INTRODUCE the [Reprint 1] and [Reprint 2] Reprint Activity



- REFER participants to the Key Messages Worksheet
 - POINT OUT the worksheet 2nd and 3rd columns (Supporting Clinical Reprints and Clinical Reprint Data Statements)
- DIVIDE the group into four teams
- EXPLAIN the activity:
 - Working in table triads, participants review the [Reprint 1] and [Reprint 2] reprints
 - Identify key data to support:
 - The need for CV risk reduction in addition to that provided by statin therapy alone
 - The need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG
 - The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies
 - Note the reprint name in column 2
 - Summarize the supporting data in column 3 and note its location in the reprint
 - The 1st and 3rd teams will review the [Reprint 1] Reprint first and the [Reprint 2] Reprint second (15 min each reprint)
 - The 2nd and 4th teams will review the [Reprint 2] Reprint first and the [Reprint 1] Reprint second (15 min each reprint)
- KEEP time, ANNOUNCING 5 minute intervals



15 Minutes



- REFER to the answers in the Key Messages worksheet (located in the appendix)
- INSTRUCT team 1 to present their findings for the [Reprint 1] Reprint (15 min)
- After 7 minutes stop the first team presentation and INVITE team 3 to continue the presentation with their findings
 - INSTRUCT participants to highlight their reprints with any information they missed and contribute any information the presenting groups may have missed
- ASK teams 2 and 4 to provide any additional feedback
- REPEAT the process, instructing groups 2 and 4 to present the [Reprint 2] Reprint
- CONCLUDE the activity after 15 minutes
- TRANSITION to Role-Play

Role-Play With the Reprints 45 Minutes



- INTRODUCE the Role-Play with Reprints Activity



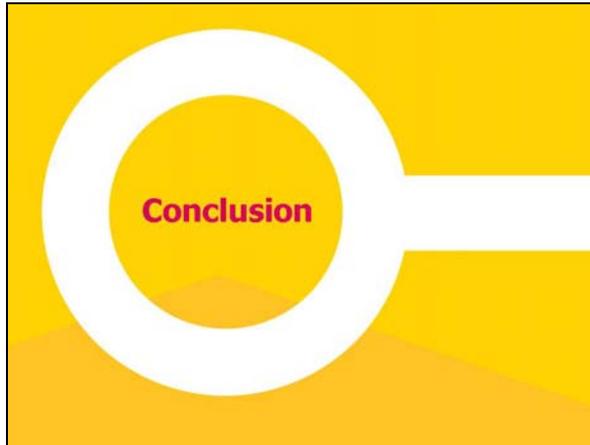
45 Minutes

Role-Play With Reprints

- Role-play sales call in triads
 - Participant delivers the 3 key messages, with support from reprint(s) (5 min)
 - “Observer” uses Observation Checklist to evaluate call & provide feedback (1 min)
- Switch roles and repeat 2 times

- CONDUCT a role-play using the Reprints as follows:
 - REFER participants to the Observer Checklist (appendix)
 - INSTRUCT participants to reform their triad teams
 - One participant plays the role of representative, one the physician, and one an observer
 - INSTRUCT participants to begin verbalizing a call using one or both Reprints (6 min)
 - “Observer” completes checklist and gives feedback (1 min)
 - ANNOUNCE time after 7 minutes
 - Facilitator circulates during role-plays to evaluate calls
- REPEAT process for remaining 2 rotations
 - DIRECT participants to switch roles
- KEEP time ANNOUNCING 10 minute intervals
- CALL ON volunteers to verbalize the key messages and supporting statements as if speaking with a physician (25 min)
 - GATHER feedback from the group

Conclusion 3 Minutes



- DEBRIEF the group and summarize key takeaways from the workshop (3 minutes)
 - EXPLAIN that we reviewed studies that support all key messages:
 - There is a need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG
 - There is a need for CV risk reduction in addition to that provided by statin therapy alone
 - The CV effect of niacin has been confirmed in numerous randomized, controlled clinical studies
- ASK if there are any questions about the workshop content
- CONCLUDE the workshop after addressing all questions and thank the participants

**Appendix:
Key Workshop Materials**

Observer Checklist for Workshop 2: Selling From the Reprints

Select the appropriate rating.	<u>O</u> bserved / <u>N</u> ot Observed	
Did the participant provide the citation? (title, author(s), journal and date)	O	N
Did the participant present all three key messages? <ul style="list-style-type: none"> – There is a need for CV risk reduction in addition to that provided by statin therapy alone – There is a need to measure and treat all three lipid parameters, LDL-C, HDL-C and TG – The CV effect of niacin has been confirmed in numerous randomized controlled clinical studies 	<input type="checkbox"/>	<input type="checkbox"/>
Did the participant support messages with relevant data from the [Reprint 1] reprint?	<input type="checkbox"/>	<input type="checkbox"/>
Did the participant support messages with relevant data from the [Reprint 2] reprint?	<input type="checkbox"/>	<input type="checkbox"/>
What went well in the discussion?		
What could have been improved?		