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11 CENTERS FOR MEDICARE AND MEDICAID SERVICES
12 MEDICARE EVIDENCE DEVELOPMENT & COVERAGE ADVISORY
13 COMMITTEE

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20 JULY 18, 2007

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22 CENTERS FOR MEDICARE AND MEDICAID SERVICES

23 7500 SECURITY BOULEVARD

24 BALTIMORE, MARYLAND

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1 PANELISTS
2
3 CHAIRPERSON
4 ALAN M. GARBER, M.D., PH.D.
5
6 VICE-CHAIR
7 ALEXANDER H. KRIST, M.D.
8
9 VOTING MEMBERS
10 CHAIM CHARYTAN, M.D.
11 A. MARK FENDRICK, M.D.
12 CAROLE REDDING FLAMM, M.D., M.P.H.
13 WILLIAM LEWIS, M.D.
14 WILLIAM H. MAISEL, M.D., M.P.H.
15 BARRY D. PRESSMAN, M.D.
16 SANFORD J. SCHWARTZ, M.D.
17 MARK SLAUGHTER, M.D.
18
19 HCFA LIAISON
20 STEVE E. PHURROUGH, M.D., M.P.A.
21 MARCEL SALIVE, M.D.
22
23
24
25

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1 PANELISTS (CONTINUED)

2

3 CONSUMER REPRESENTATIVE

4 LINDA A. BERGTHOLD, PH.D.

5

6 INDUSTRY REPRESENTATIVE

7 MICHAEL J. LACEY, M.SC.

8

9 GUEST EXPERT PANELISTS

10 MATTHEW S. EDWARDS, M.D.

11 STEPHEN C. TEXTOR, M.D.

12

13 EXECUTIVE SECRETARY

14 MICHELLE ATKINSON

15

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1 PANEL PROCEEDINGS
2 (THE MEETING WAS CALLED TO ORDER AT 8:05
3 A.M., WEDNESDAY, JULY 18, 2007.)
4 MS. ATKINSON: GOOD MORNING AND WELCOME
5 COMMITTEE CHAIRPERSON, MEMBERS AND GUESTS. I AM
6 MICHELLE ATKINSON, THE EXECUTIVE SECRETARY FOR THE
7 MEDICARE EVIDENCE DEVELOPMENT AND ADVISORY COMMITTEE.
8 THE COMMITTEE IS HERE TODAY TO DISCUSS THE EVIDENCE,
9 HEAR PRESENTATIONS AND PUBLIC COMMENT, AND MAKE
10 RECOMMENDATIONS CONCERNING PERCUTANEOUS TRANSLUMINAL
11 ANGIOPLASTY AND STENTING OF RENAL ARTERIES.
12 THE FOLLOWING ANNOUNCEMENT ADDRESSES
13 CONFLICT OF INTEREST ISSUES ASSOCIATED WITH THIS
14 MEETING AND IS MADE PART OF THE RECORD. THE CONFLICT
15 OF INTEREST STATUTES PROHIBIT SPECIAL GOVERNMENT
16 EMPLOYEES FROM PARTICIPATING IN MATTERS THAT COULD
17 AFFECT THEIR OR THEIR EMPLOYER'S FINANCIAL INTERESTS.
18 EACH MEMBER WILL BE ASKED TO DISCLOSE ANY FINANCIAL
19 CONFLICTS OF INTEREST DURING THEIR INTRODUCTION.
20 WE ASK IN THE INTEREST OF FAIRNESS THAT
21 ALL PERSONS MAKING STATEMENTS OR PRESENTATIONS ALSO
22 DISCLOSE ANY CURRENT OR PREVIOUS FINANCIAL
23 INVOLVEMENT IN ANY COMPANY THAT MANUFACTURES DEVICES
24 FOR RENAL ARTERY STENTING OR SURGERY FOR THE
25 TREATMENT OF RENAL ARTERY STENOSIS, DRUGS OR

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1 BIOLOGICS USED IN THE TREATMENT OF RENAL ARTERY
2 STENOSIS, OR OTHER TOOLS USED FOR DIAGNOSIS OR
3 TREATMENT OF RENAL ARTERY STENOSIS. THIS INCLUDES
4 DIRECT FINANCIAL INVESTMENTS, CONSULTING FEES AND
5 SIGNIFICANT INSTITUTIONAL SUPPORT. IF YOU HAVEN'T
6 ALREADY RECEIVED A DISCLOSURE STATEMENT, THEY ARE
7 AVAILABLE ON THE TABLE OUTSIDE OF THIS ROOM.
8 WE ASK THAT ALL PRESENTERS PLEASE ADHERE
9 TO THEIR TIME LIMITS. WE HAVE NUMEROUS PRESENTERS TO
10 HEAR FROM TODAY AND A VERY TIGHT AGENDA, AND,
11 THEREFORE, CANNOT ALLOW FOR EXTRA TIME. THERE IS A
12 TIMER AT THE PODIUM THAT YOU SHOULD FOLLOW. THE
13 LIGHT WILL BEGIN FLASHING WHEN THERE ARE TWO MINUTES
14 REMAINING AND THEN TURN RED WHEN YOUR TIME IS UP.
15 PLEASE NOTE THAT THERE IS A CHAIR FOR THE NEXT
16 SPEAKER, AND PLEASE PROCEED TO THAT CHAIR WHEN IT IS
17 YOUR TURN.
18 FOR THE RECORD, VOTING MEMBERS PRESENT FOR
19 TODAY'S MEETING ARE ALEX KRIST, CHAIM CHARYTAN, MARK
20 FENDRICK, CAROLE FLAMM, WILLIAM LEWIS, WILLIAM
21 MAISEL, BARRY PRESSMAN, SANDY SCHWARTZ, MARK
22 SLAUGHTER. A QUORUM IS PRESENT AND NO ONE HAS BEEN
23 RECUSED BECAUSE OF CONFLICTS OF INTEREST. THE ENTIRE
24 PANEL, INCLUDING THE NONVOTING MEMBERS, WILL
25 PARTICIPATE IN THE VOTING. THE VOTING SCORES WILL BE

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1 AVAILABLE ON OUR WEB SITE FOLLOWING THE MEETING. TWO
2 AVERAGES WILL BE CALCULATED, ONE FOR THE VOTING
3 MEMBERS AND ONE FOR THE ENTIRE PANEL.
4 I ASK THAT ALL PANEL MEMBERS PLEASE SPEAK
5 DIRECTLY INTO THE MIKES, AND YOU MAY HAVE TO MOVE
6 YOUR MIKES SINCE WE HAVE TO SHARE. NOW I WOULD LIKE
7 TO TURN THIS OVER TO DR. STEVE PHURROUGH.
8 DR. PHURROUGH: GOOD MORNING. I'M STEVE
9 PHURROUGH, THE DIRECTOR OF THE COVERAGE AND ANALYSIS
10 GROUP. LET ME THANK YOU FOR BEING PRESENT TODAY, AND
11 PARTICULAR THANKS TO THE PANEL MEMBERS FOR AGREEING
12 TO TAKE TIME OUT OF THEIR BUSY SCHEDULES TO BE PART
13 OF THIS MEETING TODAY.
14 OUR GOAL TODAY IS TO DISCUSS THE EVIDENCE
15 AROUND TREATMENT FOR RENAL ARTERY STENOSIS. WHILE WE
16 DO HAVE A PARTICULAR NCD LOOKING AT RENAL ARTERY
17 STENOSIS, THE GOAL OF THIS PARTICULAR MEETING IS NOT
18 TO MAKE DECISIONS AROUND WHETHER WE SHOULD OR SHOULD
19 NOT PAY FOR CERTAIN TREATMENTS. OUR GOAL TODAY IS TO
20 DISCUSS WHAT'S THE EVIDENCE. THE PANEL'S TASK AND
21 CHALLENGE IS TO FOCUS ON THAT PARTICULAR QUESTION.
22 WE WILL TAKE THAT INFORMATION AND USE THAT
23 IN OUR DELIBERATIVE PROCESS AS WE MAKE DECISIONS
24 AROUND WHETHER WE SHOULD OR SHOULD NOT MAKE ANY
25 NATIONAL COVERAGE DECISION AROUND THE VARIOUS

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1 TREATMENTS FOR ARTERIAL STENOSIS.
2 WE DO HAVE A HISTORY OF HAVING VERY
3 VIGOROUS AND HEALTHY DEBATES IN THESE PARTICULAR
4 MEETINGS. WE WANT THAT TO CONTINUE. WE WANT THE
5 MEETING TO FOCUS ON THOSE DEBATES, SO WE DO ENCOURAGE
6 THE PRESENTERS TO BE SUCCINCT, BRIEF AND TO THE
7 POINT, SO THAT WE CAN GET TO THE QUESTION AND ANSWER
8 TIME OF THE PROGRAM. THERE IS A LIMITED AMOUNT OF
9 TIME SO WE DO WANT TO BE FOCUSED ON SPECIFIC
10 QUESTIONS AND COMMENTS THAT ARE HELPFUL TO THE
11 DISCUSSION.
12 BEFORE I TURN IT OVER TO ALAN GARBER, I
13 WOULD LIKE TO MAKE A SPECIFIC NOTE TODAY THAT ALAN
14 GARBER HAS BEEN OUR CHAIRMAN FOR TWO YEARS. OUR
15 CHARTER ONLY ALLOWS A CHAIRMAN TO FUNCTION FOR TWO
16 YEARS, SO THIS IS ALAN'S LAST MEETING AS CHAIRMAN.
17 HE WILL CONTINUE TO BE A PANEL MEMBER BUT THIS IS HIS
18 LAST MEETING AS CHAIRMAN, AND I THANK HIM FOR THAT
19 SERVICE OVER THE LAST TWO YEARS.
20 THIS IS ALSO ALEX'S LAST MEETING AS VICE
21 CHAIRMAN. HOWEVER, HE HAS BEEN A PANEL MEMBER FOR
22 FOUR YEARS AND THAT'S THE LIMIT OF SERVING ON THE
23 PANEL, YOU HAVE TO TAKE A YEAR SABBATICAL BEFORE YOU
24 CAN BE RENOMINATED TO THE PANEL. SO NOT ONLY IS THIS
25 ALEX'S LAST MEETING AS VICE CHAIR, IT'S ALSO HIS LAST

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1 MEETING AS A PANEL MEMBER, AND WE WANT TO THANK ALEX
2 FOR HIS WORK ON THE PANEL FOR THE LAST YEARS.
3 AND FINALLY, BEFORE TURNING IT OVER TO
4 ALAN, I MUST APOLOGIZE. I'M GOING TO HAVE TO BE OUT
5 MOST OF THE DAY, A COUPLE OF CRITICAL ISSUES HAVE
6 OCCURRED IN OUR ARENA THAT NEED TO BE RESOLVED TODAY
7 AND TOMORROW. DR. SALIVE WILL BE SITTING IN IN MY
8 PLACE WHEN I'M NOT HERE.
9 SO WITH THAT, I'LL TURN IT OVER TO ALAN.
10 DR. GARBER: THANK YOU, STEVE. GOOD
11 MORNING, EVERYONE, AND WELCOME TO THE MEDICAL
12 EVIDENCE DEVELOPMENT AND COVERAGE ADVISORY COMMITTEE
13 MEETING. TODAY WE HAVE A SOMEWHAT PACKED SCHEDULE
14 BUT ALSO I THINK A VERY INTRIGUING ONE, AND ONE THAT
15 I THINK IS GOING TO BE VERY INTERESTING, AND I'M
16 ANTICIPATING DISCUSSIONS AT A HIGH LEVEL. WE HAVE A
17 GREAT SET OF PANELISTS, A GREAT SET OF SCHEDULED
18 SPEAKERS. FROM THE MATERIALS WE HAVE BEEN SENT, I AT
19 LEAST HAVE BEEN VERY GRATIFIED TO SEE HOW DIRECTLY
20 THE COMMENTS ADDRESS THE QUESTIONS THAT WE ARE FACING
21 TODAY.
22 STEVE MENTIONED THAT THIS IS MY LAST
23 MEETING AS CHAIR OF MEDCAC AFTER TWO YEARS OF
24 SERVICE. I WAS ALSO ON THE PREDECESSOR, MCAC, FROM
25 ITS INCEPTION, AND IT HAS BEEN REALLY EXTRAORDINARY

00011

1 TO SEE HOW THIS PROCESS HAS GROWN AND IMPROVED AND
2 BECOME BOTH FORMALIZED BUT ALSO MUCH MORE FOCUSED,
3 AND I BELIEVE IN THE END EFFECTIVE. AND THE QUALITY
4 OF THE DISCUSSION, THE QUALITY OF THE PANEL MEMBERS,
5 THE QUALITY OF THE COMMENTS FROM THE PUBLIC HAS JUST
6 IMPROVED STEADILY OVER TIME, AND I THINK THIS IS
7 TESTIMONY TO THE CMS STAFF IN PARTICULAR, WHO'VE
8 WORKED VERY HARD IN THIS AREA FOR A NUMBER OF YEARS.
9 ANYBODY WHO WAS THERE AT THE BEGINNING
10 KNOWS THAT THERE WAS A CERTAIN AMOUNT OF
11 EXPERIMENTATION AND SORT OF FINDING YOUR WAY. THOSE
12 DAYS ARE FAR BEHIND US NOW AND I THINK WE HAVE A VERY
13 STRONG PROCESS THAT IS ADMIRER AROUND THE WORLD,
14 ALTHOUGH NOT NECESSARILY ALWAYS PRAISED FOR ITS
15 DECISIONS, OF COURSE, BUT THE FACT IS THAT THE
16 DISCUSSION IS ONE THAT GENERALLY REALLY ADVANCES
17 PEOPLE'S THINKING ABOUT THE ISSUES ON THE TABLE.
18 I WANT TO JUST REINFORCE ONE THING THAT
19 MICHELLE MENTIONED. BECAUSE WE'RE ON A TIGHT
20 SCHEDULE, WE WILL BE VERY STRICT IN HAVING SPEAKERS
21 LIMIT THEIR COMMENTS TO THE TIME ALLOTTED AND IN FACT
22 WE HAVE CUT OFF SPEAKERS IN MID-SENTENCE. I
23 APOLOGIZE IN ADVANCE IF I DO THAT TO YOU, IT'S
24 NOTHING PERSONAL, BUT IN THE INTEREST OF FAIRNESS,
25 MAKING SURE THAT EVERYONE WHO IS SCHEDULED TO SPEAK

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1 GETS THEIR OPPORTUNITY, WE DON'T REALLY HAVE AN
2 ALTERNATIVE. AND IN FACT, WE ARE HOPING THAT WE CAN
3 FINISH THE AGENDA A LITTLE BIT EARLIER THAN WHAT'S
4 LISTED, AND WE ARE PLANNING TO LIMIT LUNCH TO A HALF
5 HOUR AS PART OF OUR EFFORTS TO FINISH A LITTLE BIT
6 EARLY.
7 THE MOST IMPORTANT THING, I THINK, FOR
8 EVERYONE ON THE PANEL AND IN THE AUDIENCE IS PLEASE
9 MAKE SURE THAT YOU HAVE A COPY OF THE DISCUSSION
10 QUESTIONS. IT'S THIS THING THAT SAYS JULY 2007
11 MEDCAC QUESTIONS, AND IT'S DATED JULY 17TH. THERE
12 ARE COPIES OUTSIDE THE DOOR AND I THINK ALL THE PANEL
13 MEMBERS SHOULD HAVE A COPY IN FRONT OF THEM, BECAUSE
14 THIS IS GOING TO BE THE FOCAL POINT FOR ALL OF OUR
15 DISCUSSIONS TODAY.
16 AND SO WITHOUT FURTHER ADO, WE WILL LAUNCH
17 INTO THE INTRODUCTIONS OF THE PANEL MEMBERS. AND WHY
18 DON'T WE START FROM THE FAR END THERE. AND I FORGOT
19 TO MENTION THAT PANELISTS SHOULD STATE WHAT CONFLICTS
20 YOU HAVE, IF ANY.
21 DR. TEXTOR: I'M STEPHEN TEXTOR FROM MAYO
22 CLINIC IN ROCHESTER, MINNESOTA, A NEPHROLOGIST, AND I
23 HAVE NO CONFLICTS IN THIS AREA.
24 DR. EDWARDS: MATT EDWARDS, A VASCULAR
25 SURGEON FROM WAKE FOREST UNIVERSITY, AND I HAVE NO

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1 CONFLICTS.
2 DR. BERGTHOLD: LINDA BERGTHOLD, I'M THE
3 CONSUMER REPRESENTATIVE. I'M AN INDEPENDENT
4 HEALTHCARE CONSULTANT ON TECHNOLOGY ASSESSMENT ISSUES
5 AND I HAVE NO CONFLICTS OF INTEREST.
6 MR. LACEY: MICHAEL LACEY. I'M THE
7 DIRECTOR OF REIMBURSEMENT IN HEALTH ECONOMICS AT
8 ACUSPHERE IN BOSTON AND I HAVE NO CONFLICTS.
9 DR. SLAUGHTER: MARK SLAUGHTER, A
10 CARDIOTHORACIC SURGEON AT CHRIST HOSPITAL IN CHICAGO,
11 AND I HAVE NO CONFLICTS.
12 DR. PRESSMAN: BARRY PRESSMAN FROM THE
13 CEDARS SINAI MEDICAL CENTER, LOS ANGELES, A
14 RADIOLOGIST. NO CONFLICTS.
15 DR. MAISEL: BILL MAISEL, A CARDIOLOGIST
16 AT BETH ISRAEL DEACONESS MEDICAL CENTER AT HARVARD
17 MEDICAL SCHOOL IN BOSTON, AND I HAVE NO CONFLICTS.
18 DR. LEWIS: I'M BILL LEWIS, I'M A
19 CARDIOLOGIST IN CLEVELAND, OHIO AT CASE WESTERN
20 RESERVE. I HAVE NO CONFLICTS.
21 DR. FENDRICK: MARK FENDRICK, GENERAL
22 INTERNIST, HEALTH SERVICES RESEARCH, UNIVERSITY OF
23 MICHIGAN. NO CONFLICTS.
24 DR. FLAMM: CAROLE FLAMM, ASSISTANT
25 MEDICAL DIRECTOR FOR THE BLUE CROSS BLUE SHIELD

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1 ASSOCIATION, AND I HAVE NO FINANCIAL CONFLICTS.
2 DR. CHARYTAN: I AM CHAIM CHARYTAN, CHIEF
3 OF RENAL DIVISION AT NEW YORK HOSPITAL IN NEW YORK,
4 QUEENS, AND ALSO WITH A LOT OF EXPERIENCE IN THE
5 REGULATORY ISSUES. I WAS RECENTLY ASKED TO CHAIR A
6 SAFETY MONITORING BOARD FOR A DEVICE FOR RENAL ARTERY
7 STENTING, THAT'S A RECENT ISSUE THAT HAS COME UP. I
8 AM NOT INVOLVED EXCEPT ON THE SAFETY MONITORING
9 BOARD.
10 DR. KRIST: ALEX KRIST, A FAMILY PHYSICIAN
11 AT VIRGINIA COMMONWEALTH UNIVERSITY, NO CONFLICTS.
12 DR. SALIVE: MARCEL SALIVE, MEDICAL
13 OFFICER IN THE COVERAGE AND ANALYSIS GROUP.
14 DR. GARBER: AND AGAIN, I'M ALAN GARBER,
15 WITH THE DEPARTMENT OF VETERANS AFFAIRS AND STANFORD
16 UNIVERSITY, NO CONFLICTS.
17 AND I JUST WANT TO REMIND THE SPEAKERS, I
18 BELIEVE WE'VE BEEN TOLD THIS BEFORE, BUT WHEN YOU
19 SPEAK, PLEASE IDENTIFY YOURSELF, YOUR INSTITUTION AND
20 ANY CONFLICTS YOU MIGHT HAVE, AND THIS IS FOR BOTH
21 SCHEDULED SPEAKERS AND ANY PEOPLE WHO WANT TO SPEAK
22 DURING THE OPEN AND PUBLIC COMMENTARY PERIOD. OKAY.
23 SO, WE WILL NOW HAVE THE PRESENTATION OF
24 THE VOTING QUESTIONS BY SARAH MCCLAIN, FROM CMS.
25 MS. MCCLAIN: GOOD MORNING. WE'LL START

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1 OFF WITH INITIAL DISCUSSION QUESTION NUMBER 1.
2 CONSIDERING THE COMMON INCIDENTAL NATURE
3 OF ATHEROSCLEROTIC RENAL ARTERY STENOSIS, DISCUSS
4 THE:
5 DEGREE OF CORRELATION BETWEEN PERCENT
6 RENAL ARTERY STENOSIS AND KIDNEY FUNCTION.
7 ROLE OF TREATMENT CHOICE BASED UPON
8 PATIENT'S EXISTING MEDICAL CONDITION AND
9 COMORBIDITIES, LIKE RENOVASCULAR HYPERTENSION WITH OR
10 WITHOUT DIABETES, CHRONIC KIDNEY DISEASE,
11 HYPERLIPIDEMIA, PERIPHERAL VASCULAR DISEASE, CORONARY
12 ARTERY DISEASE, OR LEFT VENTRICULAR ABNORMALITIES.
13 INITIAL DISCUSSION QUESTION NUMBER 2.
14 DISCUSS THE ABILITY TO COMPARE STUDIES,
15 PERFORM META-ANALYSES AND DRAW VALID EVIDENCE-BASED
16 CONCLUSIONS BASED UPON EXISTING PUBLISHED
17 DEFINITIONS, MEASUREMENT TECHNIQUES, AND CRITERIA FOR
18 REPORTING PATIENT SELECTION, METHODS AND OUTCOMES.
19 SPECIFIC ISSUES FOR DISCUSSION ARE LISTED
20 ON PAGE THREE OF THE PACKET.
21 INITIAL DISCUSSION QUESTION NUMBER 3.
22 FOR BOTH STATE-OF-THE-ART PERCUTANEOUS
23 TRANSLUMINAL RENAL ANGIOPLASTY WITH STENTING
24 UTILIZING EMBOLIC PROTECTION AND SURGICAL RENAL
25 ARTERY RECONSTRUCTION, DISCUSS: DIAGNOSTIC TESTS OR

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1 BASELINE PATIENT CHARACTERISTICS THAT ACCURATELY
2 PREDICT POST-TREATMENT RENAL FUNCTION OUTCOMES;
3 SUBGROUPS OF MEDICARE PATIENTS WITH ATHEROSCLEROTIC
4 RENAL ARTERY STENOSIS WHO CLEARLY AND CONSISTENTLY
5 BENEFIT FROM RENAL ANGIOPLASTY AND STENTING WITH
6 EMBOLIC PROTECTION OR SURGICAL RENAL ARTERY
7 RECONSTRUCTION; RISKS OF COMPLICATIONS FOR PATIENTS,
8 ESPECIALLY THE OLDER MEDICATION POPULATION, WITH
9 PROGRESSIVE RENAL DYSFUNCTION AND MULTIPLE
10 COMORBIDITIES, ESPECIALLY POST-TREATMENT WORSENING
11 RENAL FUNCTION AND HASTENING OF DIALYSIS.
12 VOTING QUESTION NUMBER 1.
13 FOR THE TREATMENT OF PATIENTS WITH
14 ATHEROSCLEROTIC RENAL ARTERY STENOSIS, HOW CONFIDENT
15 ARE YOU THAT THE EVIDENCE IS ADEQUATE TO DRAW
16 CONCLUSIONS ABOUT SAFETY AND CLINICAL EFFECTIVENESS
17 FOR THE FOLLOWING RENAL ARTERY INTERVENTIONS:
18 SURGICAL RENAL ARTERY RECONSTRUCTION;
19 RENAL ANGIOPLASTY WITHOUT STENT PLACEMENT;
20 RENAL ANGIOPLASTY AND STENTING WITH BARE
21 METAL STENTS;
22 RENAL ANGIOPLASTY AND STENTING WITH
23 DRUG-ELUTING STENTS.
24 ONE, NOT CONFIDENT, TO FIVE, HIGHLY
25 CONFIDENT.

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1 VOTING QUESTION NUMBER 2.
2 BASED ON THE EVIDENCE PRESENTED, HOW
3 CONFIDENT ARE YOU THAT THE PUBLISHED RESULTS APPLY
4 TO:
5 MEDICARE PATIENTS WITH TYPICAL
6 COMORBIDITIES;
7 PROVIDERS, FACILITIES AND PHYSICIANS IN
8 COMMUNITY PRACTICE; AND
9 PATIENT SUBGROUPS NOT REPRESENTED IN THE
10 STUDY POPULATION.
11 ONE, NOT CONFIDENT, THROUGH FIVE, HIGHLY
12 CONFIDENT.
13 VOTING QUESTION NUMBER 3.
14 BASED ON THE EVIDENCE PRESENTED FOR
15 PATIENTS WITH ATHEROSCLEROTIC RENAL ARTERY STENOSIS,
16 HOW CONFIDENT ARE YOU THAT COMPARED TO AGGRESSIVE
17 MEDICAL TREATMENT ALONE, THERE ARE IMPROVED KEY
18 HEALTH OUTCOMES ATTRIBUTABLE TO THE FOLLOWING
19 CO-INTERVENTIONS:
20 SURGICAL RENAL ARTERY RECONSTRUCTION;
21 RENAL ANGIOPLASTY WITHOUT STENT PLACEMENT;
22 RENAL ANGIOPLASTY AND STENTING WITH BARE
23 METAL STENTS;
24 RENAL ANGIOPLASTY AND STENTING WITH
25 DRUG-ELUTING STENTS.

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1 ONE, NOT CONFIDENT, THROUGH FIVE, HIGHLY
2 CONFIDENT.
3 VOTING QUESTION NUMBER 4.
4 BASED ON THE EVIDENCE PRESENTED, SHOULD
5 MEDICARE NATIONAL COVERAGE OF ANY NON-MEDICAL
6 TREATMENTS FOR ATHEROSCLEROTIC RENAL ARTERY STENOSIS
7 BE LIMITED ONLY TO PATIENTS ENROLLED IN QUALIFIED
8 RESEARCH STUDIES?
9 ONE, STRONGLY AGREE, THROUGH FIVE,
10 STRONGLY DISAGREE.
11 FINAL DISCUSSION QUESTION NUMBER 1.
12 DISCUSS STRENGTHS AND WEAKNESSES OF THE
13 FOLLOWING ONGOING INTERNATIONAL TRIALS, ANY PROTOCOL
14 CHANGES, AND IN YOUR OPINION THE ANTICIPATED VALIDITY
15 OF THE DATA AND APPLICABILITY OF KEY HEALTH OUTCOMES
16 TO MEDICARE PATIENTS WITH TYPICAL COMORBIDITIES IN
17 COMMUNITY SETTINGS FOR STAR, RAVE, ASTRAL, NITER AND
18 CORAL.
19 FINAL DISCUSSION QUESTION NUMBER 2.
20 DISCUSS PRACTICAL ISSUES AND
21 MEDICAL/INTERVENTIONAL ENHANCEMENTS FOR FUTURE
22 RANDOMIZED CONTROLLED TRIALS THAT MAY BE PLANNED OR
23 ARE NEARLY READY TO BEGIN. SPECIFIC ISSUES FOR
24 DISCUSSION ARE LISTED ON PAGE SIX OF THE PACKET.
25 DR. GARBER: NEXT WE WILL PROCEED TO THE

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1 PRESENTATION OF THE TECHNOLOGY ASSESSMENT BY ETHAN
2 BALK FROM THE INSTITUTE FOR CLINICAL RESEARCH AND
3 HEALTH POLICY STUDIES.
4 DR. BALK: MY NAME IS ETHAN BALK. I'M AT
5 THE TUFTS NEW ENGLAND MEDICAL CENTER AT THE
6 EVIDENCE-BASED PRACTICE CENTER. WE CONDUCTED A
7 COMPARATIVE EFFECTIVENESS REPORT REVIEW OF MANAGEMENT
8 STRATEGIES FOR RENAL ARTERY STENOSIS AND RECENTLY
9 CONDUCTED AN UPDATE OF THAT REPORT FOR THIS MEETING.
10 JUST TO START WITH A LITTLE BACKGROUND,
11 ATHEROSCLEROTIC RENAL ARTERY STENOSIS CAN RESULT IN
12 REFRACTORY HYPERTENSION, CHRONIC KIDNEY DISEASE,
13 MORBIDITIES ASSOCIATED WITH THESE CONDITIONS, AND
14 THUS INCREASED MORTALITY. RENAL ARTERY STENOSIS
15 OCCURS IN ABOUT 30 PERCENT OF PATIENTS WITH CARDIAC
16 DISEASE AND UP TO 50 PERCENT OF THOSE HAVE DIFFUSE
17 ATHEROSCLEROTIC VASCULAR DISEASES.
18 THE GOALS OF THERAPY GENERALLY ARE
19 IMPROVEMENT IN THE UNCONTROLLED HYPERTENSION,
20 PRESERVATION OR SALVAGE OF THE KIDNEY FUNCTION,
21 IMPROVEMENT IN SYMPTOMS RELATED TO THE HYPERTENSION
22 AND KIDNEY FUNCTION, AND ALSO IMPROVEMENT IN THE
23 QUALITY OF LIFE.
24 AGGRESSIVE MEDICAL THERAPY IS WHAT IS AT
25 LEAST AMONG MANY CIRCLES CONSIDERED TO BE THE

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1 APPROPRIATE MEDICAL APPROACH. IT CONSISTS OF A
2 COMBINATION OF ANTIHYPERTENSIVE MEDICATION;
3 LIPID-LOWERING AGENTS, PRIMARILY STATINS; AND
4 ANTIPLATELET AGENTS, TO DECREASE THE RISK ASSOCIATED
5 WITH ATHEROSCLEROTIC RENAL ARTERY STENOSIS. PATIENTS
6 TREATED WITH MEDICAL THERAPY ALONE, HOWEVER, MAY BE
7 AT RISK FOR DETERIORATION OF KIDNEY DISEASE,
8 WORSENING MORBIDITY AND MORTALITY BECAUSE THE
9 ATHEROSCLEROTIC PROCESS IS CONTINUING.
10 AN ALTERNATIVE IS REVASCULARIZATION. WHAT
11 IS MOST COMMONLY USED CURRENTLY FOR THIS IS
12 ANGIOPLASTY WITH STENT PLACEMENT. THE
13 REVASCULARIZATION AT LEAST IN THEORY CAN HALT OR
14 REVERSE THE PROGRESSION OF THE RENAL ARTERY STENOSIS
15 BUT CARRIES SUBSTANTIAL RISKS OF MORBIDITY,
16 MORTALITY, AND IT'S NOT CLEAR THAT IT AFFECTS THE
17 UNDERLYING KIDNEY DISEASE.
18 SO AGAIN, THE CURRENT MEDICAL THERAPY
19 GENERALLY CONSISTS OF COMBINATIONS OF BLOOD PRESSURE
20 MEDICATIONS, AGAIN CURRENTLY MOSTLY ACE INHIBITORS,
21 ANGIOTENSIN RECEPTOR BLOCKERS, AND ALSO CALCIUM
22 CHANNEL BLOCKERS AND BETA BLOCKERS. STATINS AND
23 ANTIPLATELET AGENTS ARE ALSO USED.
24 AS I MENTIONED, ANGIOPLASTY WITH STENT
25 PLACEMENT IS THE MOST COMMONLY USED REVASCULARIZATION

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1 PROCEDURE NOW. ANGIOPLASTY ALONE IS RELATIVELY
2 INFREQUENT. HOWEVER, IT'S NOTABLE THAT AT LEAST TO
3 THE BEST OF OUR KNOWLEDGE, THERE IS NO MARKETED STENT
4 THAT IS CURRENTLY FDA-APPROVED FOR RENAL ARTERY
5 STENOSIS. THERE ARE FDA-APPROVED STENTS BUT THEY'RE
6 NOT MARKETED. OPEN SURGICAL BYPASS IS GENERALLY
7 RESERVED FOR PATIENTS WITH COMPLICATED DISEASE,
8 PARTICULARLY THOSE WITH CONCURRENT AORTIC DISEASE OR
9 ANEURYSMS OR OTHER MIXED DISEASES.
10 THERE ARE NO PUBLISHED TRIALS THAT
11 DIRECTLY COMPARE THESE TWO APPROACHES, AGGRESSIVE
12 MEDICAL THERAPY AND ANGIOPLASTY WITH STENT. THERE
13 ARE SOME ONGOING PUBLISHED TRIALS, AS WAS NOTED IN
14 THE DISCUSSION QUESTIONS.
15 SO, WE WERE ASKED TO FIND THE EVIDENCE TO
16 ANSWER THREE PRIMARY QUESTIONS. THE FIRST ONE WAS,
17 FOR PATIENTS WITH ATHEROSCLEROTIC RENAL ARTERY
18 STENOSIS, WHAT IS THE EVIDENCE ON THE EFFECTS OF
19 AGGRESSIVE MEDICAL THERAPY VERSUS ANGIOPLASTY WITH
20 STENT PLACEMENT ON LONG-TERM CLINICAL OUTCOMES? AND
21 WE DEFINED THAT WITH A GROUP OF DOMAIN EXPERTS AS
22 BEING AT LEAST SIX MONTHS. WE ALSO LOOKED AT ADVERSE
23 EVENTS.
24 THE SECOND AND THIRD QUESTIONS ARE
25 BRIEFLY, WHAT CLINICAL, IMAGING, LABORATORY AND

00022

1 ANATOMIC CHARACTERISTICS ARE ASSOCIATED WITH IMPROVED
2 OR WORSE OUTCOMES AFTER TREATMENT WITH THE VARIOUS
3 INTERVENTIONS, AND WHAT ADJUNCT INTERVENTIONS ARE
4 ASSOCIATED WITH IMPROVED OR WORSE OUTCOMES AFTER
5 RENAL ARTERY ANGIOPLASTY WITH STENT PLACEMENT?
6 SO WE PERFORMED A SEARCH OF THE
7 LITERATURE, PRIMARILY IN MEDLINE. WE UPDATED THE
8 SEARCH IN APRIL OF 2007 AND LOOKED ONLY AT ENGLISH
9 LANGUAGE ARTICLES. THE POPULATION OF INTEREST WAS
10 ADULTS WITH ATHEROSCLEROTIC RENAL ARTERY STENOSIS.
11 WE EXCLUDED STUDIES OF RENAL ARTERY STENOSIS IN THE
12 SETTING OF KIDNEY TRANSPLANTS, RENAL ARTERY ANEURYSMS
13 REQUIRING REPAIR, AORTIC DISEASE REQUIRING REPAIR,
14 STUDIES WHERE MORE THAN 20 PERCENT OF THE PATIENTS
15 HAD A PREVIOUS REVASCULARIZATION PROCEDURE, AND
16 STUDIES WHERE MORE THAN 20 PERCENT OF THE PATIENTS
17 HAD OTHER CAUSES OR RENAL ARTERY STENOSIS, PRIMARILY
18 FIBROMUSCULAR DYSPLASIA.
19 THE INTERVENTIONS OF INTEREST. AS I
20 NOTED, THE PRIMARY ONES WERE A COMBINATION OF MEDICAL
21 TREATMENTS, ANTIHYPERTENSIVE, ANTIHYPERLIPIDEMIA,
22 ANTIPLATELET DRUGS, COMPARED TO ANGIOPLASTY WITH
23 STENT PLACEMENT.
24 KNOWING THAT THE EVIDENCE ON THIS WAS
25 GOING TO BE SOMEWHAT LIMITED, WE BROUGHT IN THE

00023

1 INTERVENTION OF INTEREST TO ANY MEDICAL TREATMENT
2 USED FOR RENAL ARTERY STENOSIS, ANGIOPLASTY WITHOUT
3 STENT PLACEMENT AND ALSO OPEN SURGICAL
4 REVASCULARIZATION. WE ALSO LOOKED AT NATURAL HISTORY
5 STUDIES, MEANING STUDIES WHERE THEY JUST FOLLOWED
6 PATIENTS WITH THE DISEASE WITHOUT A SPECIFIC
7 PROTOCOL, OR STUDIES WHERE THEY DIDN'T DESCRIBE AT
8 ALL WHAT MEDICATIONS WERE BEING USED. HOWEVER, I'M
9 NOT GOING TO DISCUSS THOSE STUDIES HERE.
10 THE OUTCOMES OF INTEREST WERE PRIMARILY
11 LONG-TERM CLINICAL OUTCOMES, DEFINED AS AT LEAST SIX
12 MONTHS AFTER THE INTERVENTION WAS STARTED OR THE
13 ANGIOPLASTY WAS PERFORMED, AND ADVERSE EVENTS.
14 SPECIFICALLY THESE INCLUDED MORTALITY, KIDNEY
15 FUNCTION, BLOOD PRESSURE CONTROL, CARDIOVASCULAR
16 EVENTS WHICH I'M NOT GOING TO DESCRIBE IN MUCH DETAIL
17 BECAUSE THE EVIDENCE WAS FAIRLY SPOTTY, QUALITY OF
18 LIFE, RESTENOSIS AFTER ANGIOPLASTY WITH STENT
19 PLACEMENT, WHICH AGAIN, I'M NOT GOING TO PRESENT
20 HERE, AND ADVERSE EVENTS.
21 WE USED DIFFERENT ELIGIBILITY CRITERIA FOR
22 DIFFERENT TYPES OF STUDIES BASED ON THE LIKELY IMPACT
23 OF THOSE STUDIES ON OUR CONCLUSIONS, AND ALSO BASED
24 ON THE QUANTITY OF EVIDENCE THAT WE EXPECTED TO FIND.
25 SO FOR COMPARATIVE STUDIES, THOSE THAT COMPARE

00024

1 MEDICAL THERAPY TO REVASCULARIZATION, THOSE WERE OF
2 PRIMARY INTEREST SO WE INCLUDED ANY OF THOSE STUDIES,
3 PROSPECTIVE, RETROSPECTIVE, RANDOMIZED,
4 NONRANDOMIZED, THEY HAD TO HAVE AT LEAST TEN
5 PATIENTS, AND THEY COULD HAVE BEEN DONE AT ANY TIME
6 IN THE PAST. THE REST OF THE STUDIES WERE COHORT
7 STUDIES, PRE-POST STUDIES WHERE IT LOOKED AT ONLY A
8 SINGLE GROUP OF PATIENTS RECEIVING A SINGLE
9 INTERVENTION WITHOUT A DIRECT COMPARISON. FOR
10 MEDICINE, COHORTS OF MEDICINE INTERVENTION, WE
11 INCLUDED PROSPECTIVE STUDIES WITH AT LEAST TEN
12 PATIENTS.
13 FOR ANGIOPLASTY AND STENT COHORTS, WE
14 QUICKLY FOUND THAT THERE WERE A REASONABLE NUMBER OF
15 THESE STUDIES, SO WE LIMITED THESE TO PROSPECTIVE
16 STUDIES WITH AT LEAST 30 PEOPLE. WE ALSO LIMITED
17 THESE AND OTHER SURGICAL STUDIES TO THOSE STUDIES
18 PERFORMED AFTER 1993. THIS DATE WAS CHOSEN BECAUSE
19 THAT WAS ABOUT WHEN JNC-5 CAME OUT, WHICH ADVOCATED A
20 STRICTER CONTROL OF BLOOD PRESSURE. IT WAS ALSO
21 ABOUT THE SAME TIME THAT ACE INHIBITORS STARTED TO BE
22 COMMONLY USED. SO IT'S A TIME FRAME THAT'S MOST
23 RELEVANT TO CURRENT PRACTICE.
24 AND THEN THE SURGICAL COHORTS. WE
25 INCLUDED ANY PROSPECTIVE STUDIES THAT WERE DONE

00025

1 RECENTLY. FOR THE RETROSPECTIVE STUDIES, BECAUSE
2 THERE WERE A LARGE NUMBER OF SMALL STUDIES THAT WERE
3 HARD TO INTERPRET, WE LIMITED THOSE TO THE LARGER
4 RETROSPECTIVE STUDIES.
5 FOR THE PURPOSE OF UNDERSTANDING THE
6 EVIDENCE, WE CREATED THESE TIERS OF EVIDENCE, WHICH
7 WERE USED TO HELP US DESCRIBE THE RELEVANCE OF THE
8 STUDIES TO THE PRIMARY QUESTIONS OF INTEREST. SO THE
9 TIER I STUDIES WOULD BE RANDOMIZED CONTROLLED TRIALS
10 THAT SPECIFICALLY COMPARE STENT TO AGGRESSIVE MEDICAL
11 THERAPY. TIER II STUDIES WERE OTHER RANDOMIZED
12 TRIALS THAT COMPARED ANGIOPLASTY WITH OR WITHOUT
13 STENT TO ANY MEDICAL INTERVENTION THAT HAD AT LEAST A
14 SIX-MONTH FOLLOW-UP SINCE THOSE WERE OUR OUTCOMES OF
15 INTEREST, FOR SIX MONTHS.
16 THE TIER III EVIDENCE FOR OTHER
17 COMPARATIVE STUDIES HAD TO BE A DIRECT COMPARISON,
18 BUT COULD BE ANY INVASIVE INTERVENTION, INCLUDING
19 SURGERY, VERSUS MEDICAL, AND WE DIDN'T HAVE THE TIME
20 RESTRICTION OR FOLLOW-UP RESTRICTION. AND THEN TIER
21 IV EVIDENCE WERE THE COHORT STUDIES, AGAIN, THAT DID
22 NOT MAKE A DIRECT COMPARISON.
23 WE GRADED THESE STUDIES FOR METHODOLOGICAL
24 QUALITY. THIS IS SOMETHING THAT WE COMMONLY DO AND
25 WE HAVE MANY YEARS OF EXPERIENCE DOING. WE FIND THAT

00026

1 IT IS VERY USEFUL TO UNDERSTANDING WHAT THE OVERALL
2 EVIDENCE FINDS AND WE FIND THAT ALSO, WE'RE ABLE TO
3 CONSISTENTLY GRADE STUDIES ACROSS DIFFERENT TOPICS
4 AND DOMAINS. SO WE USED THE THREE-TIER SCALE, GOOD,
5 FAIR AND POOR.
6 GOOD QUALITY STUDIES ARE THOSE THAT ADHERE
7 TO COMMONLY HELD CONCEPTS OF HIGH QUALITY. IN THIS
8 CASE THEY HAD TO BE RANDOMIZED TRIALS THAT WERE WELL
9 DESCRIBED, GOOD REPORTING, NO OBVIOUS ERRORS,
10 APPROPRIATE METHODOLOGY WAS USED, AND A SMALL
11 WITHDRAWAL RATE. FAIR QUALITY STUDIES WERE POSSIBLY
12 SUSCEPTIBLE TO SOME BIAS BUT THE PROBLEMS WERE NOT
13 SUFFICIENT TO INVALIDATE THE RESULTS. THERE WERE
14 SOME DEFICIENCIES IN THESE STUDIES. POOR QUALITY
15 STUDIES, THERE WERE SUBSTANTIAL PROBLEMS THAT MADE US
16 THINK THERE WAS SIGNIFICANT BIAS OR SIGNIFICANT BIAS
17 COULDN'T BE RULED OUT; THESE INCLUDED SERIOUS
18 METHODOLOGICAL ERRORS, LARGE AMOUNTS OF MISSING
19 INFORMATION AND DISCREPANCIES IN REPORTING.
20 SIMILARLY, WE ALSO WEIGHTED THE
21 APPLICABILITY OF THE STUDIES. THIS RELATED PRIMARILY
22 TO THE STUDY POPULATION AND ONLY INDIRECTLY TO THE
23 RELEVANCE OF THE OVERALL TOPIC OF THE OVERALL STUDY
24 TO CURRENT MEDICAL PRACTICE, WHICH WAS CAPTURED IN
25 THE TIERS OF EVIDENCE. SO WE RATED THE STUDIES AS

00027

1 HIGH APPLICABILITY, MODERATE APPLICABILITY, AND LOW
2 APPLICABILITY.
3 BRIEFLY, HIGH APPLICABLE STUDIES ARE THOSE
4 THAT ARE REPRESENTATIVE OF TARGET POPULATION, IN THIS
5 CASE THEY HAD A RANGE OF STENOSIS THAT VARIED AND THE
6 AVERAGE PATIENT WAS BROADLY SIMILAR TO THE TYPICAL
7 PATIENT WHO IS RECEIVING THERAPY FOR RENAL ARTERY
8 STENOSIS, AND THESE HAD TO HAVE AT LEAST 30 PATIENTS.
9 MODERATE APPLICABLE STUDIES INCLUDED A RELEVANT
10 SUBGROUP. LOW APPLICABLE STUDIES HAD A NARROW
11 SUBGROUP WITH LIMITED APPLICABILITY OR THEY WERE
12 FAIRLY OLD STUDIES, BEFORE JNC-5.
13 WE ALSO EVALUATED THE STRENGTH OF THE
14 EVIDENCE TO HELP US DRAW CONCLUSIONS ABOUT THE
15 EVIDENCE. WE GRADED THE EVIDENCE AS EITHER -- ONE
16 THING TO NOTE ABOUT THIS IS THAT ALL OF THESE RATING
17 SYSTEMS ARE SOMEWHAT SUBJECTIVE, BUT THERE'S PROBABLY
18 MORE SUBJECTIVITY TO THIS. WE DID USE OUR OWN BEST
19 UNDERSTANDING OF IT AND ALSO CONSULTED WITH VARIOUS
20 DOMAINS AND OTHER METHODOLOGICAL EXPERTS, GOT A FAIR
21 AMOUNT OF INPUT TO HELP US COME TO THESE CONCLUSIONS.
22 SO ROBUST EVIDENCE WOULD BE WHEN THERE'S A
23 HIGH LEVEL OF ASSURANCE IN THE VALIDITY OF THE
24 RESULTS BASED ON THE QUALITY OF THE STUDIES, THE
25 APPLICABILITY, THE EFFECT SIZE AND THE CONSISTENCY.

00028

1 THERE WOULD HAVE HAD TO HAVE BEEN AT LEAST TWO HIGH
2 QUALITY STUDIES WITH LONG-TERM FOLLOW-UP AND NO
3 IMPORTANT DISAGREEMENT ACROSS THE STUDIES.
4 ACCEPTABLE STUDIES, ACCEPTABLE STRENGTH OF
5 EVIDENCE WAS WHEN THERE WAS GOOD TO MODERATE LEVEL OF
6 ASSURANCE IN THE VALIDITY OF THE RESULTS, LITTLE
7 DISAGREEMENT.
8 WEAK EVIDENCE, THERE WAS LOW LEVEL OF
9 ASSURANCE OF THE VALIDITY OF THE RESULTS. THESE WERE
10 BASED ON STUDIES OF MODERATE TO POOR QUALITY, LIMITED
11 APPLICABILITY.
12 AND THEN THERE WAS A CATEGORY OF
13 INCONSISTENT EVIDENCE, WHEN THERE WAS DISAGREEMENT
14 EITHER WITHIN OR ACROSS STUDIES.
15 SO AS FAR AS HOW WE SYNTHESIZED THE DATA,
16 WE WENT INTO THIS THINKING THAT WE MIGHT BE ABLE TO
17 DO META-ANALYTIC TECHNIQUES, MATHEMATICAL TECHNIQUES
18 TO DEFINE THE DATA, BUT WE QUICKLY FOUND THAT THE
19 RANDOMIZED TRIAL DATA WAS TOO SPARSE TO DO THIS IN A
20 MEANINGFUL WAY. THE COHORT STUDIES TENDED TO BE TOO
21 HETEROGENEOUS IN TERMS OF THE POPULATION, SPECIFIC
22 INTERVENTIONS, THE FOLLOW-UP TIMES, THE OUTCOME
23 DEFINITIONS. SO GIVEN THE STATE OF THE EVIDENCE, WE
24 CONCLUDED THAT A META-ANALYSIS WOULD NOT HAVE
25 IMPROVED MEANINGFUL COMPARISONS ACROSS THE

00029

1 INTERVENTIONS.
2 SO, THESE ARE THE AVAILABLE STUDIES. WE
3 SCREENED THROUGH A BIT MORE THAN 2,300 CITATIONS IN
4 MEDLINE AND FOUND 68 UNIQUE STUDIES. AS I SAID, WE
5 GROUPED THESE BASED ON THE EVIDENCE TIER AND THAT'S
6 HOW THIS TABLE WAS SET UP. MOST IMPORTANTLY, FOR
7 TIER I EVIDENCE DIRECTLY COMPARING STENT TO TRIPLE
8 THERAPY, AGGRESSIVE THERAPY, AS YOU KNOW, THERE ARE
9 NO STUDIES.
10 FOR TIER II EVIDENCE, RANDOMIZED TRIALS OF
11 ANGIOPLASTY VERSUS ANY MEDICAL THERAPY WITH AT LEAST
12 SIX-MONTH FOLLOW-UP, THERE WERE ONLY TWO TRIALS, WITH
13 ONLY A HUNDRED PATIENTS.
14 AND FOR THE TIER III EVIDENCE WE HAD NINE
15 STUDIES, AND THEN FOR THE TIER IV STUDIES OF THE
16 DIFFERENT INTERVENTIONS, THE COHORT STUDIES, WE NOTE
17 THERE WERE VERY FEW STUDIES OF MEDICAL TREATMENTS,
18 SURGERY, AND THERE WERE 28 STENT STUDIES THAT WE
19 LOOKED AT. SO OVERALL THE QUALITY WAS FAIR TO POOR,
20 ABOUT HALF AND HALF, AND MOST OF THE STUDIES WERE OF
21 MODERATE TO LOW APPLICABILITY.
22 SO LET ME START WITH THE TIER II TRIALS.
23 THERE WERE TWO OF THESE, THE SCOTTISH-NEWCASTLE TRIAL
24 WRITTEN UP BY WEBSTER AND COLLEAGUES, AND THE EMMA
25 TRIAL BY PLOUIN AND COLLEAGUES, BOTH PUBLISHED IN

00030

1 1998. THEY BOTH INCLUDED PATIENTS WITH RESISTANT
2 HYPERTENSION. THE EMMA TRIAL USED A SLIGHTLY HIGHER
3 THRESHOLD FOR RENAL ARTERY STENOSIS, SLIGHTLY MORE
4 SEVERE DISEASE. HOWEVER, THEY RESTRICTED THE
5 POPULATIONS TO THOSE WITHOUT SEVERE CHRONIC KIDNEY
6 DISEASE. THE EMMA STUDY RESTRICTED THE POPULATION TO
7 THOSE WITH UNILATERAL DISEASE AND THE WEBSTER TRIAL
8 INCLUDED ABOUT HALF THE PATIENTS, HALF THE PATIENTS
9 WITH BILATERAL DISEASE AND HALF WITH UNILATERAL
10 DISEASE.
11 BOTH OF THE TRIALS WERE SMALL, EACH HAD
12 ABOUT 25 PATIENTS WHO RECEIVED ANGIOPLASTY AND ABOUT
13 25 OR 30 PATIENTS WHO RECEIVED MEDICAL THERAPY.
14 NOTABLY IN THE WEBSTER TRIAL, FIVE OF THE 25 PATIENTS
15 AFTER SIX MONTHS WENT ON TO HAVE EITHER NEPHRECTOMY
16 OR OTHER SURGICAL BYPASS, AND FIVE OF THE PATIENTS
17 WHO WERE ASSIGNED TO MEDICAL THERAPY AFTER SIX MONTHS
18 SUBSEQUENTLY HAD ANGIOPLASTY. IT'S ALSO NOTABLE THAT
19 ALMOST NONE OF THE PATIENTS RECEIVED STENTS.
20 FOR THE MEDICATIONS, THE WEBSTER TRIAL --
21 BOTH STUDIES USED A VARIETY OF MEDICATIONS. THE
22 WEBSTER TRIAL DID NOT USE ANY ACE INHIBITORS AND ONLY
23 SOME OF THE PATIENTS IN THE EMMA TRIAL USED
24 ENALAPRIL.
25 BOTH HAD A PRIMARY ENDPOINT AT SIX MONTHS.

00031

1 THE WEBSTER STUDY ALSO FOLLOWED PATIENTS FOR UP TO 54
2 MONTHS AFTER THE RANDOMIZATION PERIOD WAS OVER AND
3 AGAIN AFTER THERE WAS SOME CROSSOVER.
4 BOTH OF THE STUDIES WERE RATED TO BE FAIR
5 QUALITY AND ONE WAS OF MODERATE APPLICABILITY, ONE
6 LOW APPLICABILITY, PRIMARILY BECAUSE THEY EXCLUDED
7 PATIENTS WITH BILATERAL DISEASE.
8 SO TO REITERATE, THESE STUDIES HAD LIMITED
9 RELEVANCE TO CURRENT PRACTICE BECAUSE VERY FEW OF THE
10 PATIENTS WERE ON ACE INHIBITORS. STATINS AND
11 ANTIPLATELET DRUGS WERE NOT IN THE PROTOCOLS.
12 ESSENTIALLY NONE OF THE PATIENTS WHO HAD ANGIOPLASTY
13 ALSO HAD STENT. THE SAMPLE SIZES WERE VERY SMALL,
14 ONLY ABOUT 50 PATIENTS EACH. THESE WERE NOT POWERED
15 FOR ANY CLINICAL EVENT, AS I WILL POINT OUT LATER
16 AGAIN, AND A SUBSTANTIAL NUMBER CROSSED OVER TO
17 EITHER ANGIOPLASTY OR BYPASS. AND IT WAS, EVEN
18 THOUGH IT MET OUR CRITERIA, THERE WAS NO SHORT-TERM
19 FOLLOW-UP, ONLY A SIX-MONTH FOLLOW-UP FOR THE PRIMARY
20 OUTCOME.
21 THE TIER III STUDIES, THE OTHER
22 COMPARATIVE STUDIES, NONE OF THEM USED STENTS AND
23 NONE OF THEM HAD AGGRESSIVE MEDICAL THERAPY, MEANING
24 TRIPLE THERAPY. THE DRASTIC STUDY, WHICH IS ANOTHER
25 RANDOMIZED TRIAL WHICH IS OFTEN LUMPED, OR IT'S NOT

00032

1 LUMPED, BUT IT'S OFTEN GROUPED WITH THE OTHER TWO
2 TRIALS, AND IF YOU'RE FAMILIAR WITH THE COCHRANE
3 REVIEW ON THIS TOPIC, THEY INCLUDED ALL THREE TRIALS.
4 SO THE DRASTIC STUDY WAS A TRIAL OF ANGIOPLASTY
5 VERSUS AMLODIPINE OR ENALAPRIL, BUT IMPORTANTLY AT
6 THREE MONTHS, HALF OF THE PEOPLE IN THE DRUG ARM
7 RECEIVED ANGIOPLASTY. THERE WERE EIGHT OTHER STUDIES
8 OF VARIOUS TYPES. MOST OF THE STUDIES WERE OF POOR
9 QUALITY, MOST OF THEM WERE CONSIDERED TO BE OF LOW
10 APPLICABILITY.
11 FOR THE TIER IV STUDIES, THE COHORT
12 STUDIES OF MEDICINE, THERE WERE FOUR PROSPECTIVE
13 STUDIES, THESE WERE LIMITED TO PROSPECTIVE STUDIES,
14 WITH ONLY 83 PATIENTS IN TOTAL. THESE WERE A VARIETY
15 OF MEDICAL REGIMENS BUT AT LEAST MOSTLY INCLUDING ACE
16 INHIBITORS. THESE WERE GENERALLY OF POOR QUALITY AND
17 LOW APPLICABILITY. THERE WERE ALSO THREE OTHER
18 STUDIES THAT ONLY PROVIDED DATA ON ADVERSE EVENTS.
19 WITH THE ANGIOPLASTY AND STENT COHORTS, WE
20 FOUND 28 STUDIES. AGAIN, THESE WERE LIMITED TO
21 PROSPECTIVE STUDIES WITH AT LEAST 30 PATIENTS WHO HAD
22 THEIR INTERVENTIONS AFTER STARTING IN 1993. THERE
23 WERE ALMOST 4,000 PATIENTS WITH A WIDE RANGE OF
24 FOLLOW-UP TIMES AND HALF FAIR, HALF POOR QUALITY.
25 AND MOSTLY, OR ABOUT HALF OF THE STUDIES HAD MODERATE

00033

1 APPLICABILITY, SOME WITH HIGH APPLICABILITY.
2 AND THE SURGICAL BYPASS COHORTS, THERE
3 WERE FOUR OF THEM THAT MET CRITERIA. THEY ALL WERE
4 RETROSPECTIVE, AND AGAIN THESE HAD AT LEAST A HUNDRED
5 PATIENTS, WHERE MOST OF THE PATIENTS HAD THE
6 PROCEDURE DONE SINCE 1993. THERE WERE NO ELIGIBLE
7 PROSPECTIVE STUDIES. THERE WERE ALMOST A THOUSAND
8 PATIENTS WITH UP TO 17 YEARS FOLLOW-UP. ALL OF THESE
9 WERE OF POOR QUALITY AND LOW APPLICABILITY.
10 SO MOVING ON TO THE RESULTS OF OUR
11 FINDINGS, THE STUDIES OF MORTALITY, FOR THE TIER II
12 STUDIES, ONLY THE WEBSTER STUDY REPORTED ON
13 MORTALITY. THEY COMBINED THEIR DATA FROM UNILATERAL
14 AND BILATERAL GROUPS, AND LOOKED OVER THE 42 MONTHS.
15 THE SURVIVAL CURVES WERE NEARLY IDENTICAL BETWEEN THE
16 TWO INTERVENTIONS. HOWEVER, IMPORTANTLY, WITH ONLY
17 50 PEOPLE TOTAL, IT WAS CLEARLY UNDERPOWERED TO
18 DETECT ANY DIFFERENCES IN MORTALITY.
19 AMONG THE OTHER COMPARATIVE STUDIES, FOUR
20 OF THE FIVE STUDIES FOUND NO DIFFERENCE IN MORTALITY.
21 AGAIN, THEY WERE ALL SMALL AND UNDERPOWERED. THERE
22 WAS ONE RETROSPECTIVE STUDY THAT DID FIND A
23 DIFFERENCE WITH HIGHER MORTALITY IN THE MEDICAL
24 TREATMENT ARM, BUT IT'S IMPORTANT TO NOTE THAT IT WAS
25 A RETROSPECTIVE STUDY AND THERE WERE MANY PATIENTS IN

00034

1 THE MEDICAL ARM WHO DID NOT RECEIVE SURGERY BECAUSE
2 THEIR COMORBIDITIES WERE SO SEVERE, THEY WERE
3 CONSIDERED HIGH SURGICAL RISK.
4 AND THEN WITH THE INDIRECT COMPARISONS
5 BETWEEN THE COHORT STUDIES, THERE WAS A WIDE ARRAY OF
6 DATA AND WE BASED, SIMPLY OUR SUMMARY WAS THAT, OR
7 OUR CONCLUSION WAS THAT WE COULDN'T FIND ANY
8 DIFFERENCES IN MORTALITY ACROSS THE STUDIES IN THE
9 INTERVENTIONS.
10 SO MOVING ON TO KIDNEY FUNCTION, AGAIN
11 THIS IS GOING BACK TO THE TIER II STUDIES, THE
12 RANDOMIZED TRIALS, BOTH OF THEM FOUND NO SIGNIFICANT
13 DIFFERENCE IN KIDNEY FUNCTION. THE CHANGES IN KIDNEY
14 FUNCTION WERE RELATIVELY SMALL, BUT WITHIN THIS
15 DEGREE OF NONSIGNIFICANCE WERE INSIGNIFICANT, OR
16 INCONSISTENT.
17 SO ON THE LEFT HERE IS THE WEBSTER STUDY
18 THAT REPORTED CHANGE IN SERUM CREATININE. ON THE
19 RIGHT IS THE PLOUIN, THE EMMA STUDY THAT REPORTED
20 CHANGE IN CREATININE CLEARLY. WE ATTEMPTED TO PUT
21 THIS ON ABOUT THE SAME SCALE, BUT IT'S DIFFICULT TO
22 DO. SO THE BLUE AND THE GREEN ARE ANGIOPLASTY, THE
23 RED AND THE PINK -- I'M SORRY. THE BLUE AND THE
24 GREEN ARE MEDICATION, THE RED AND THE PINK ARE
25 ANGIOPLASTY. SIX-MONTH DATA AND FINAL DATA UP TO 54

00035

1 MONTHS FOR WEBSTER. AND SO AGAIN, NONSIGNIFICANT,
2 BUT WITHIN THAT, SOMETIMES MEDICATION PATIENTS GOT
3 WORSE, HAD THEIR KIDNEY FUNCTION WORSEN MORE ON
4 MEDICATION THAN WITH ANGIOPLASTY, BUT SOMETIMES THE
5 CREATININE GOT WORSE ON ANGIOPLASTY. THE WEBSTER
6 STUDY DID REPORT ON END-STAGE RENAL DISEASE
7 DEVELOPMENT AND FOUND SIMILAR RATES OF EVENTS, ABOUT
8 EIGHT AND SEVEN PERCENT, COMBINING BILATERAL AND
9 UNILATERAL ARMS.
10 AMONG THE TIER III, THE OTHER COMPARATIVE
11 STUDIES, THERE WERE INCONSISTENT FINDINGS ABOUT
12 KIDNEY FUNCTION, OR THE STUDIES FOUND THAT
13 ANGIOPLASTY WAS BETTER THAN MEDICAL THERAPY. ONE OF
14 THE STUDIES FOUND THAT THE MEDICAL THERAPY WAS BETTER
15 THAN ANGIOPLASTY OR SURGERY, AND THREE OF THE STUDIES
16 FOUND NO DIFFERENCE IN KIDNEY FUNCTION. ONLY ONE OF
17 THE EIGHT COMPARATIVE STUDIES FOUND THAT KIDNEY
18 FUNCTION ON AVERAGE IMPROVED FROM BASELINE AFTER
19 ANGIOPLASTY OR SURGERY, IN CONTRAST TO THE MEDICAL
20 ARM.
21 AMONG THE TIER IV STUDIES FOR KIDNEY
22 FUNCTION, TWO OF THE MEDICATION STUDIES, EITHER
23 MULTIDRUG OR ENALAPRIL, FOUND THAT SERUM CREATININE
24 ON AVERAGE ROSE .1 TO .3 MILLIGRAMS PER DECILITER,
25 AND GFR DECREASED BY A SMALL AMOUNT, FOUR MILLIMETERS

00036

1 PER MINUTE, ABOUT SIX PERCENT.
2 22 OF THE STENT COHORTS FOUND ON AVERAGE
3 THAT SERUM CREATININE DROPPED A SMALL AMOUNT, .1, BUT
4 THERE WAS A WIDE RANGE IN CHANGE IN SERUM CREATININE
5 FROM A DECREASE OF 1.1 TO AN INCREASE OF .2
6 MILLIGRAMS PER DECILITER ON AVERAGE. GFR ON AVERAGE
7 WENT UP BY A SMALL AMOUNT, WITH A FAIRLY NARROW RANGE
8 OF CHANGE. HOWEVER, THEY FOUND THAT WITHIN STUDIES,
9 EIGHT TO 51 PERCENT OF THE PATIENTS IMPROVED THEIR
10 KIDNEY FUNCTION.
11 THERE WERE THREE OF THE SURGICAL STUDIES
12 REPORTING ON KIDNEY FUNCTION. ONE FOUND THAT 74
13 PERCENT OF THE PATIENTS WERE FREE OF CHRONIC KIDNEY
14 DISEASE AT FIVE YEARS. ONE FOUND THAT GFR ON AVERAGE
15 ROSE BY SEVEN MILLILITERS PER MINUTE, BUT THAT 17
16 PERCENT OF THE PATIENTS DEVELOPED END-STAGE RENAL
17 DISEASE. AND A THIRD STUDY FOUND THAT 72 PERCENT OF
18 THE PATIENTS EITHER HAD IMPROVED OR UNCHANGED KIDNEY
19 FUNCTION, BUT AGAIN, 17 PERCENT DEVELOPED KIDNEY
20 FAILURE.
21 MOVING ON TO BLOOD PRESSURE, GOING BACK TO
22 THE TIER II RANDOMIZED TRIALS, AGAIN, FEW OF THESE
23 STUDIES LOOKED AT ACE INHIBITORS. THE FINDINGS WERE
24 INCONSISTENT. WEBSTER FOUND THAT -- SO I'VE GOT
25 SYSTOLIC PRESSURE HERE, DIASTOLIC PRESSURE HERE,

00037

1 UNILATERAL DISEASE TO THE LEFT, BILATERAL DISEASE ON
2 THE RIGHT, AND WEBSTER IS HERE. SO WEBSTER IS HERE,
3 EMMA IS HERE, THIS IS THE LONG-TERM FOLLOW-UP FOR
4 WEBSTER AND FOR BILATERAL, BOTH OF THESE ARE WEBSTER
5 AT SIX MONTHS AND FINAL.
6 SO AT SIX MONTHS FOR BOTH STUDIES, THERE
7 WERE NO SIGNIFICANT CHANGES. AGAIN THESE ARE PRIMARY
8 ENDPOINTS, WHETHER UNILATERAL OR BILATERAL DISEASE.
9 BUT, THERE WAS A FINDING THAT ANGIOPLASTY WAS
10 SIGNIFICANTLY BETTER FOR BILATERAL DISEASE AT THE
11 FINAL TIME BETWEEN THREE AND FOUR TO 54 MONTHS, BUT
12 AGAIN, THERE WAS SOME CROSSOVER AT SIX MONTHS.
13 THE PLOUIN STUDY ALSO DID FIND A BENEFIT
14 IN DIASTOLIC BLOOD PRESSURE BUT NOT SYSTOLIC BLOOD
15 PRESSURE AFTER AN ANGIOPLASTY, AND THIS WAS IN THE
16 UNILATERAL GROUP OF PATIENTS.
17 AMONG THE TIER III STUDIES, THE OTHER
18 COMPARATIVE STUDIES, THERE WERE EIGHT STUDIES. MOST
19 FOUND NO DIFFERENCE IN BLOOD PRESSURE BETWEEN THE
20 DIFFERENT INTERVENTIONS. SIX OF THE STUDIES FOUND NO
21 SIGNIFICANT DIFFERENCE. THERE WAS A MIX OF WHETHER
22 THE INVASIVE OR THE DRUG THERAPIES WERE BETTER WITHIN
23 THAT CONSTRAINT. TWO OF THE STUDIES DID FIND THAT
24 ANGIOPLASTY RESULTED IN SIGNIFICANTLY BETTER BLOOD
25 PRESSURE RESULTS THAN MEDICAL THERAPY.

00038

1 AMONG THE COHORT STUDIES, THE FOUR
2 MEDICATION STUDIES, ALL FOUND THAT ON AVERAGE
3 PATIENTS DID DO WELL, MEDICATION WAS EFFECTIVE AT
4 LOWERING BLOOD PRESSURE.
5 AMONG THE STENT STUDIES, THERE WERE 27.
6 IN GENERAL, AGAIN, THEY FOUND THE DECREASE IN BLOOD
7 PRESSURE. WITHIN STUDIES, 18 PERCENT OF PATIENTS HAD
8 CURE OF HYPERTENSION, MEANING THAT THEY NO LONGER
9 REQUIRED MEDICATION TO CONTROL THEIR BLOOD PRESSURE,
10 AND WITHIN STUDIES, 35 TO 79 PERCENT OF PATIENTS HAD
11 IMPROVEMENT IN THEIR BLOOD PRESSURE.
12 AMONG TWO SURGICAL STUDIES, ONE OF THE
13 STUDIES FOUND A LARGE DECREASE IN BLOOD PRESSURE, 53
14 OVER 23 MILLIMETERS OF MERCURY, 68 PERCENT OF THE
15 PATIENTS AT THREE YEARS AND 59 PERCENT OF THE
16 PATIENTS AT FIVE YEARS HAD EITHER CURE OR IMPROVEMENT
17 IN THEIR HYPERTENSION. AND IN THE OTHER STUDY, 12
18 PERCENT OF THE PATIENTS HAD CURE IN THE HYPERTENSION,
19 AND AT EIGHT WEEKS, 73 PERCENT HAD SOME IMPROVEMENT
20 IN THEIR HYPERTENSION.
21 ONE STUDY, THE DRASTIC STUDY RECENTLY
22 REPORTED ON QUALITY OF LIFE. THEY LOOKED AT ONLY THE
23 COMPARISON OF ANGIOPLASTY ALONE AND MEDICATION ALONE,
24 SO THE PATIENTS WHO SWITCHED OVER AT THREE MONTHS
25 WERE DROPPED FROM THIS EVALUATION. SO THEY FOUND

00039

1 THAT FOR PHYSICAL SYMPTOMS ASSOCIATED WITH
2 HYPERTENSION, THERE WAS A DECREASED NUMBER OF
3 COMPLAINTS, A LARGER DECREASE IN THE NUMBER OF
4 COMPLAINTS AFTER ANGIOPLASTY, BUT THIS WAS NOT A
5 SIGNIFICANT FINDING.
6 THE OVERALL SF-36 AND EUROQOL WAS NO
7 DIFFERENT AFTER THE TWO INTERVENTIONS, BUT FOR THE
8 SOCIAL FUNCTIONING PORTION OF SF-36, THEY FOUND
9 INCONSISTENT RESULTS AT THREE VERSUS 12 MONTHS.
10 BASICALLY THERE WAS A FLIP IN WHICH WAS -- BOTH AT
11 THREE AND 12 MONTHS THERE WAS STATISTICALLY
12 SIGNIFICANT FINDINGS, BUT THERE WAS A SWITCH AS FAR
13 AS WHICH INTERVENTION WAS BETTER.
14 FOR ADVERSE EVENTS, LOOKING AT ALL THE
15 STUDIES TOGETHER, NONE OF THE COMPARATIVE STUDIES
16 DIRECTLY COMPARED ADVERSE EVENTS. IN GENERAL THEY AT
17 BEST BASICALLY LISTED SOME ADVERSE EVENTS THAT
18 OCCURRED BUT MADE NO ATTEMPT TO COMPARE THE SEVERITY
19 OR OTHER ASPECTS OF THE ADVERSE EVENTS. THE ADVERSE
20 EVENTS THAT WERE FOUND WERE GENERALLY THOSE THAT ONE
21 WOULD EXPECT TO FIND WITH THESE INTERVENTIONS WHICH
22 ARE GENERALLY KNOWN. FOR THE ACE INHIBITORS AND
23 OTHER HYPERTENSIVE AGENTS, THE ADVERSE EVENTS RELATED
24 PRIMARILY TO VASCULAR ADVERSE EVENTS LIKE ORTHOSTATIC
25 HYPOTENSION OR OTHER HYPOTENSION, A KNOWN PHENOMENON,

00040

1 AND THEN A SERIES OF OTHER ADVERSE EVENTS,
2 GASTROINTESTINAL, HEADACHES, NAUSEA, THINGS LIKE
3 THAT.
4 FOR ANGIOPLASTY, THE 30-DAY MORTALITY
5 BETWEEN STUDIES RANGED FROM LESS THAN ONE PERCENT UP
6 TO THREE PERCENT. THERE WAS TRANSIENT ACUTE KIDNEY
7 INJURY THAT OCCURRED BETWEEN ONE AND 13 PERCENT OF
8 PATIENTS WITHIN THE STUDIES. RENAL ARTERY OR
9 PARENCHYMAL INJURY ALSO OCCURRED IN LESS THAN ONE
10 PERCENT OR UP TO 10 PERCENT OF PATIENTS WITHIN
11 STUDIES. THERE WERE ALSO REPORTS OF MAJOR
12 HEMORRHAGE, RENAL ARTERY OCCLUSION AND SPASM, AND
13 FALSE ANEURYSM.
14 AMONG THE SURGICAL STUDIES, THE 30-DAY
15 MORTALITY WAS HIGHER THAN FOR ANGIOPLASTY, 3.7 TO 9.4
16 PERCENT. THE PERIOPERATIVE MORBIDITY, IN ONE STUDY
17 IT WAS 16 PERCENT. AND PROCEDURAL COMPLICATIONS,
18 ANOTHER STUDY WAS 22 PERCENT.
19 SO MOVING ON TO THE SECOND QUESTION,
20 PREDICTORS OF OUTCOMES, 31 STUDIES PROVIDED DATA
21 RELEVANT TO THIS QUESTION. THERE WAS A CONSENSUS
22 THAT SEVERITY OF STENOSIS, POOR KIDNEY FUNCTION,
23 SEVERITY OF COMORBIDITIES, PARTICULARLY SEVERITY OF
24 CARDIOVASCULAR DISEASE, WERE PREDICTORS OF POORER
25 CLINICAL OUTCOMES. THE EXCEPTION TO THIS WAS THE

00041

1 DRASTIC STUDY, WHICH DID NOT FIND AN ASSOCIATION
2 BETWEEN BASELINE SEVERITY OF STENOSIS AND POORER
3 CLINICAL OUTCOMES. NONE OF THE STUDIES, THOUGH,
4 FOUND THAT ANY OF THESE PREDICTORS ACTUALLY PREDICTED
5 WHICH INTERVENTION WOULD BE BETTER FOR INDIVIDUAL
6 PATIENTS; THIS WAS JUST OVERALL CLINICAL OUTCOMES.
7 THERE WAS LACK OF CONSENSUS WHETHER
8 BILATERAL DISEASE OR AGE OR SEX WERE PREDICTORS OF
9 CLINICAL OUTCOMES. HOWEVER, NOTABLY, AS I DISCUSSED
10 BEFORE, IN THE WEBSTER STUDY, ANGIOPLASTY IN THE
11 SETTING OF BILATERAL DISEASE WAS MORE EFFECTIVE FOR
12 BLOOD PRESSURE CONTROL THAN MEDICAL THERAPY. THIS
13 WAS IN CONTRAST TO THOSE PATIENTS WITH UNILATERAL
14 DISEASE. AND THERE WAS CONSENSUS THAT THERE WAS NO
15 ASSOCIATION BETWEEN BASELINE BLOOD PRESSURE AND
16 PRESENT HYPERTENSION WITH CLINICAL OUTCOMES.
17 REGARDING DIAGNOSTIC TESTS, THERE WERE
18 FOUR DIAGNOSTIC TESTS THAT, WHERE THEY FOUND NO
19 ASSOCIATION BETWEEN THE READING OF THE TESTS AND
20 OUTCOMES. THESE INCLUDED THE CAPTOPRIL TEST,
21 RENOGRAM, ARTERIAL NOREPINEPHRINE, AND UNILATERAL
22 RENIN SECRETION. ONE STUDY DID FIND THAT NONSPIRAL
23 FLOW IN RENAL ARTERIES ON MRA WAS ASSOCIATED WITH
24 PROGRESSION OF KIDNEY DISEASE. THIS WAS A COHORT
25 STUDY SO THERE WAS NO COMPARISON ABOUT HOW THEY WOULD

00042

1 HAVE DONE WITHOUT THE ANGIOPLASTY.
2 AND THERE WAS INCONSISTENT RESULTS
3 REGARDING RESISTIVE INDEX OF OVER 80 PERCENT ON
4 DOPPLER ULTRASOUND. TWO STUDIES LOOKED AT THIS. ONE
5 FOUND THAT AN RI OF OVER 80 PERCENT WAS PREDICTIVE OF
6 WORSENING KIDNEY FUNCTION AND BLOOD PRESSURE CONTROL
7 AFTER ANGIOPLASTY, COMPARED TO IMPROVEMENT IN THOSE
8 WITH LOWER RI, BUT THE OTHER STUDY FOUND THAT THERE
9 WAS POSSIBLY LARGER IMPROVEMENT IN SERUM CREATININE
10 IN THOSE PATIENTS WITH AN RI OF OVER 80 PERCENT. NO
11 DIFFERENCE IN THE PERCENTAGE OF PATIENTS WHOSE KIDNEY
12 FUNCTION DETERIORATED OR IMPROVED BASED ON THEIR RI
13 READING PRIOR TO THE INTERVENTION.
14 FOR THE THIRD QUESTION, THERE WERE NO
15 STUDIES THAT EVALUATED ADJUNCT TREATMENTS OR RELATED
16 FACTORS AT THE TIME OF ANGIOPLASTY OR SURGERY,
17 BASICALLY WHAT CO-INTERVENTIONS AT THE TIME OF
18 SURGERY MIGHT IMPROVE OUTCOMES. HOWEVER, NOTABLY WE
19 DID NOT DO A COMPARISON, WE DID NOT LOOK AT A
20 COMPARISON OF ANGIOPLASTY WITH STENT VERSUS
21 ANGIOPLASTY WITHOUT STENT.
22 SO THERE ARE A NUMBER OF LIMITATIONS TO
23 THE EVIDENCE. AS I POINTED OUT, THERE WERE VERY FEW
24 RANDOMIZED TRIALS. THESE WERE ALSO FELT TO BE OF
25 LIMITED RELEVANCE TO CURRENT PRACTICE. THERE WERE A

00043

1 SMALL NUMBER OF PATIENTS, ONLY A HUNDRED PATIENTS
2 TOTAL, FOR THE TIER II EVIDENCE, AND AGAIN, NO
3 RANDOMIZED TRIAL EVALUATING CURRENT TREATMENTS, THERE
4 WAS NO TIER I EVIDENCE. OFTEN THE STUDIES WERE OF
5 POOR QUALITY, HARD TO GET THE OTHER STUDY TYPES. FOR
6 THE MEDICATION COHORT STUDIES, THESE WERE FEW IN
7 NUMBER AND THEY DIDN'T USE THE TRIPLE THERAPY, THE
8 AGGRESSIVE THERAPY OF INTEREST.
9 THE SMALL NUMBERS AND ITS LIMITATION
10 LIMITS INDIRECT COMPARISON WITH THE STENT COHORTS.
11 AND ALSO NOTABLY, THE STRICT TYPE OF CRITERIA THAT WE
12 USED FOR THE COHORT STUDIES MAY HAVE ELIMINATED SOME
13 STUDIES THAT MIGHT BE DEEMED IMPORTANT BY SOME
14 EXPERTS IN THE FIELD.
15 SO THESE ARE OUR CONCLUSIONS. I'M GOING
16 TO READ OUR CONCLUSIONS FROM THE REPORT, BUT
17 GENERALLY THE, OUR FINDINGS WERE THAT THE STUDIES ARE
18 INCONCLUSIVE BECAUSE OF THE SMALL NUMBER OF
19 RANDOMIZED TRIALS WITH FEW PATIENTS AND QUESTIONABLE
20 RELEVANCE TO CURRENT PRACTICE. SORRY. OKAY.
21 WEAK EVIDENCE SUGGESTS NO DIFFERENCE IN
22 MORTALITY RATES WITH MEDICAL TREATMENT ALONE OR WITH
23 ANGIOPLASTY, THOUGH COMPARATIVE STUDIES WERE TOO
24 SMALL TO ACCURATELY ESTIMATE RELATIVE EFFECT. THERE
25 IS WEAK EVIDENCE SUGGESTING SIMILAR RATES OF

00044

1 CARDIOVASCULAR EVENTS BETWEEN INTERVENTIONS, ALTHOUGH
2 I DID NOT PRESENT THIS INFORMATION HERE. THERE IS
3 WEAK EVIDENCE SUGGESTING NO DIFFERENCE IN QUALITY OF
4 LIFE WITH MEDICAL TREATMENT ALONE OR WITH
5 ANGIOPLASTY.
6 THERE IS ACCEPTABLE EVIDENCE THAT OVERALL
7 THERE IS NO DIFFERENCE IN KIDNEY OUTCOMES BETWEEN
8 PATIENTS TREATED MEDICALLY ALONE OR THOSE RECEIVING
9 ANGIOPLASTY WITHOUT STENT, BUT THE RELEVANCE OF THIS
10 FINDING TO CURRENT PRACTICE IS QUESTIONABLE DUE TO
11 CHANGES IN TREATMENT OPTIONS. HOWEVER, IMPROVEMENTS
12 TO KIDNEY FUNCTION WERE ONLY REPORTED AMONG PATIENTS
13 RECEIVING ANGIOPLASTY.
14 THE EVIDENCE REGARDING THE RELATIVE EFFECT
15 OF ANGIOPLASTY AND MEDICATION ON BLOOD PRESSURE
16 CONTROL IS INCONSISTENT. THE RANDOMIZED TRIALS DID
17 NOT FIND A CONSISTENT EFFECT. OTHER COMPARATIVE
18 STUDIES MOSTLY FOUND NO DIFFERENCE. COHORTS IN
19 MEDICAL TREATMENT GENERALLY FOUND LARGER DECREASES IN
20 BLOOD PRESSURE THAN IN COHORTS OF ANGIOPLASTY WITH
21 STENT. HOWEVER, COHORT STUDIES OF ANGIOPLASTY WITH
22 STENT DID REPORT THAT UP TO 18 PERCENT OF PATIENTS
23 WERE CURED OF HYPERTENSION.
24 THE EVIDENCE DOES NOT ADEQUATELY ASSESS
25 THE RELEVANT HARMS DUE TO ADVERSE EVENTS AND

00045

1 COMPLICATIONS OF MEDICAL TREATMENT AND ANGIOPLASTY.
2 AND THERE IS WEAK EVIDENCE THAT PATIENTS WITH
3 BILATERAL DISEASE MAY HAVE MORE FAVORABLE OUTCOMES
4 WITH ANGIOPLASTY THAN WITH MEDICAL THERAPY, COMPARED
5 TO PATIENTS WITH UNILATERAL DISEASE.
6 THERE WAS RECURRING CONSISTENT EVIDENCE
7 THAT DOES NOT SUPPORT WHETHER ANY OTHER CLINICAL
8 FEATURES OR DIAGNOSTIC TESTS PREDICT OUTCOMES AFTER
9 ANGIOPLASTY OR WITH MEDICAL THERAPY, AND THERE IS NO
10 EVIDENCE REGARDING THE VALUE OF PERIPROCEDURAL
11 INTERVENTIONS WITH ANGIOPLASTY.
12 SO TO SUMMARIZE, THE EVIDENCE IS LIMITED
13 TO DIRECT COMPARISONS OF INTERVENTIONS NOT CURRENTLY
14 IN USE AND SOME INDIRECT COMPARISONS ACROSS COHORT
15 STUDIES. OVERALL, THE CURRENT EVIDENCE DOES NOT
16 SUPPORT ONE TREATMENT APPROACH OVER THE OTHER FOR
17 PATIENTS WITH ATHEROSCLEROTIC RENAL ARTERY STENOSIS.
18 TWO-THIRDS OF THE STUDIES WERE OF POOR METHODOLOGICAL
19 QUALITY AND HALF WERE OF LIMITED APPLICABILITY TO THE
20 POPULATION OF INTEREST. THE ONLY TRIALS WERE SMALL
21 AND OF POSSIBLY LIMITED RELEVANCE, AND THERE WAS NO
22 CONSISTENTLY BETTER EFFECT WITH ONE INTERVENTION OVER
23 ANOTHER.
24 AMONG THE STUDIES REVIEWED, THE PREDICTIVE
25 VALUE OF DIAGNOSTIC TESTS EITHER FOR LONG-TERM

00046

1 OUTCOMES OR TO HELP DETERMINE THE BEST TREATMENT IS
2 UNCERTAIN.
3 I DON'T KNOW IF I MENTIONED THIS AT THE
4 BEGINNING, BUT I ALSO WANTED TO STATE THAT I HAVE NO
5 CONFLICTS OF INTEREST. THANK YOU.
6 DR. GARBER: THANK YOU, DR. BALK. OUR
7 NEXT PRESENTER WILL BE DR. CHRISTOPHER COOPER, FROM
8 THE UNIVERSITY OF TOLEDO.
9 DR. COOPER: I HAVE BEEN ASKED TO PRESENT
10 THE CASE FOR RENAL ARTERY STENTING FOR TREATMENT OF
11 RENAL ARTERY STENOSIS, AND THIS PRESENTATION IS
12 LARGELY ABSTRACTED FROM A PUBLICATION IN CIRCULATION
13 EARLIER THIS YEAR.
14 IN TERMS OF DISCLOSURES, I'D LIKE TO
15 DISCLOSE THREE LAYERS OF FINANCIAL INTEREST. ONE IS,
16 I SERVE AS THE PRINCIPAL INVESTIGATOR FOR THE CORAL
17 STUDY FUNDED BY THE NIH. SECONDLY, I HAVE RESEARCH
18 SUPPORT FROM BOTH COMPANIES WHICH SUPPORT RENAL
19 STENTING OR STENT-RELATED PRODUCTS AND FROM COMPANIES
20 WHICH PROVIDE ANTIHYPERTENSIVE MEDICAL THERAPY
21 DIRECTLY RELATED TO PATIENTS WITH ISCHEMIC RENAL
22 DISEASES. AND FINALLY, I WOULD LIKE TO DISCLOSE THAT
23 I DO HAVE PATIENT CARE-RELATED CONFLICTS OF INTEREST
24 SINCE I DO RENAL INTERVENTIONAL PROCEDURES, AND I AM
25 ALSO INVOLVED IN THE MEDICAL MANAGEMENT OF PATIENTS

00047

1 WITH ISCHEMIC RENAL SYNDROMES. FINALLY, I HAVE BEEN
2 INCLUDED IN DISCUSSIONS WITH SCA&I ABOUT THEIR
3 RESPONSE TO CMS'S POLICY REVIEW AND EXPRESSED MY
4 OPINIONS ON THE MATTER TO SCA&I.
5 RENAL ARTERY STENOSIS IS A COMMON PROBLEM
6 IN REGARD TO THE ELDERLY CMS POPULATION. KEN HANSEN
7 FROM WAKE HAS DEMONSTRATED NICELY THAT IN AN
8 UNSELECTED GROUP, ABOUT SEVEN PERCENT OF FOLKS IN THE
9 UNITED STATES HAVE SIGNIFICANT ISCHEMIC RENAL
10 DISEASE, SO THIS IS A QUITE RELEVANT POPULATION. THE
11 MAJORITY OF ATHEROSCLEROTIC STENOSES ARE OSTIAL
12 NARROWINGS WHICH ARE ATTRIBUTED OFTENTIMES TO
13 EXTENSION OF AORTIC PLAQUE INTO THE OSTIA OF THE
14 RENAL ARTERY. AS A CONSEQUENCE, THEY OFTEN OCCUR IN
15 THE SETTING OF A HIGHLY DISEASED AORTA AND THEY MAY
16 BE UNILATERAL, THEY MAY BE BILATERAL, OR THEY MAY BE
17 INVOLVING A SOLITARY FUNCTIONING KIDNEY.
18 IN TERMS OF THE EFFECT OF RENAL ARTERY
19 STENOSIS ON HYPERTENSION, THERE HAS BEEN SOME
20 DISCUSSION IN THE PAST AS TO WHETHER IT DOES CAUSE
21 HYPERTENSION. I THINK THERE IS NO DOUBT THAT A
22 STENOSIS CAN CAUSE HYPERTENSION. HOWEVER, IT MAY BE
23 DIFFICULT IN AN INDIVIDUAL PATIENT TO ASCERTAIN
24 WHETHER THEIR HYPERTENSION PER SE IS ATTRIBUTABLE TO
25 THE STENOSIS OR TO SOME CONFOUNDING EFFECT SUCH AS

00048

1 ESSENTIAL HYPERTENSION.
2 WHAT IS KNOWN BIOLOGICALLY IS THAT DECLINE
3 IN PRESSURE WITHIN THE RENAL ARTERY IS SENSED AT THE
4 JUXTAGLOMERULAR APPARATUS WHICH STIMULATES RELEASE OF
5 RENIN. RENIN CATALYZES CONVERSION OF ANGIOTENSINOGEN
6 TO A I. AND A II NOT ONLY IS A HYPERTENSIVE AGENT,
7 BUT IT ALSO PROMOTES ALDOSTERONE RELEASE FROM THE
8 ADRENAL CORTEX, FURTHER INCREASING THE HYPERTENSIVE
9 RESPONSE.
10 HOWEVER, THERE HAVE BEEN A NUMBER OF OTHER
11 MEDIATORS IDENTIFIED OVER THE PAST 10 OR 15 YEARS
12 WHICH HELP PERPETUATE THAT HYPERTENSION IS RELATED TO
13 RENAL ARTERY STENOSIS, INCLUDING SYMPATHETIC
14 ACTIVATION, RELEASE OF REACTIVE OXYGEN SPECIES,
15 CONTRALATERAL NEPHROSCLEROSIS, ENDOTHELIAL
16 DYSFUNCTION WHICH MAY BE IMPORTANT, BUT THEN
17 INTERESTINGLY SECONDARY HYPERALDOSTERONISM, WHICH
18 SOME THINK MAY BE DUE TO THIS CHRONIC STIMULATION OF
19 ALDOSTERONE RELEASE.
20 A FEW WORDS ABOUT RENAL ARTERY STENOSIS
21 AND KIDNEY FUNCTION. RENAL ARTERY STENOSIS IS AN
22 UNCOMMON CAUSE OF KIDNEY FAILURE PER SE. THERE WAS
23 SOME INTEREST 15 OR 20 YEARS AGO THAT RENAL ARTERY
24 STENOSIS IS A CAUSE OF END-STAGE RENAL DISEASE. I
25 THINK PEOPLE HAD TROUBLE REPLICATING IT AS A COMMON

00049

1 CAUSE OF END-STAGE RENAL DISEASE. HOWEVER, RENAL
2 INSUFFICIENCY IS COMMON IN PATIENTS WITH RENAL ARTERY
3 STENOSIS, AND THE POTENTIAL MEDIATORS MAY BE
4 HEMODYNAMIC OR RELATED TO HYPOPERFUSION OF THE
5 KIDNEYS. THEY MAY BE RELATED TO THE TOXIC EFFECTS OF
6 RENIN, ANGIOTENSIN II, ENDOTHELIUM OR TGF BETA
7 DIRECTLY ON THE KIDNEY. AT THE LEVEL OF THE RENAL
8 TUBULE THERE IS GOOD BASIC EVIDENCE THAT TUBULAR
9 NECROSIS OCCURS AND PROGRAMMED CELL DEATH OCCURS IN
10 HYPOPERFUSED KIDNEYS. BUT IMPORTANTLY, THERE ARE
11 OTHER CONFOUNDING CAUSES IN INDIVIDUAL PATIENTS WHICH
12 MAKE IT DIFFICULT TO ASCERTAIN WHETHER THE STENOSIS
13 PER SE OR SOMETHING ELSE IS LEADING TO DYSFUNCTION,
14 AND THESE INCLUDE ESSENTIAL HYPERTENSION, DIABETES,
15 ATHEROEMBOLISM, AND ADVANCING AGE IN MANY OF OUR
16 PATIENTS.
17 ONE OF THE HALLMARKS OF THIS DISORDER IS
18 THAT IT'S ASSOCIATED WITH POOR SURVIVAL. THERE HAVE
19 BEEN A NUMBER OF STUDIES WHICH HAVE LOOKED AT
20 SURVIVAL IN PATIENTS WITH ISCHEMIC KIDNEY DISEASE,
21 THIS IS PROBABLY THE BEST, BY CONLON, USING THE DUKE
22 DATABASE. THIS IS FOUR-YEAR SURVIVAL. IF YOU DON'T
23 HAVE RENAL ARTERY STENOSIS, YOU HAD ABOUT A 90
24 PERCENT FOUR-YEAR SURVIVAL; IF YOU DID HAVE RENAL
25 ARTERY STENOSIS, YOUR SURVIVAL WAS LESS, AT ABOUT 57

00050

1 PERCENT.
2 IMPORTANTLY, THOUGH, THERE WAS A GREAT
3 EFFECT OF STENOSIS BEARING ON SURVIVAL, WHICH IS TO
4 SAY THE MORE SEVERE YOUR LESION, THE MORE LIKELY YOU
5 ARE TO HAVE A FATAL EVENT. THE CHALLENGE WITH THIS
6 TYPE OF OBSERVATION, THOUGH, IS WHETHER THIS IS A
7 CAUSAL RELATIONSHIP, I.E., ARE THESE STENOSES CAUSING
8 PEOPLE TO HAVE FATAL EVENTS, OR IS THIS SIMPLY A GOOD
9 MARKER OF RISK FOR ADVANCED ATHEROSCLEROSIS AND THE
10 RISK FACTORS WHICH LEAD TO ATHEROSCLEROSIS, INCLUDING
11 DIABETES, ESSENTIAL HYPERTENSION, ET CETERA.
12 ONE OF THE IMPORTANT RELATIONSHIPS THAT
13 HAS BEEN IDENTIFIED RECENTLY IS THAT BETWEEN ISCHEMIC
14 RENAL DISEASE AND CLINICAL EVENTS. A FEW YEARS AGO
15 WE LOOKED AT TWO DATA SETS, ONE WAS A LARGE SINGLE
16 SENTRY COHORT, THE SECOND WAS A LARGE MULTICENTER
17 FDA-APPROVAL TRIAL, TO TRY TO UNDERSTAND WHAT HAPPENS
18 TO PATIENTS WITH ISCHEMIC RENAL DISEASE. AND
19 INTERESTINGLY, AT A MEDIAN TWO-YEAR FOLLOW-UP, ABOUT
20 ONE-THIRD OF THE PATIENTS DIDN'T EXPERIENCE AN
21 ADVERSE EVENT. DESPITE A STRONG ASSOCIATION WITH
22 RENAL FUNCTION, 90 PERCENT OF THE ADVERSE EVENTS ARE
23 NOT RENAL EVENTS, THEY'RE CARDIOVASCULAR EVENTS.
24 AND HERE'S A DEPICTION OF THE RELATIONSHIP
25 BETWEEN RENAL DISEASE AND THE PROBABILITY OF AN

00051

1 EVENT. AGAIN, THIS IS RELATIVELY SHORT-TERM
2 FOLLOW-UP, BUT AS YOU CAN SEE, IF YOU HAVE AN
3 ESTIMATED GFR WHICH IS QUITE LOW, YOUR RISK OF FATAL
4 EVENT MAY BE AS HIGH AS 60 PERCENT, THE MAJORITY OF
5 WHICH ARE CARDIOVASCULAR AND RENAL. HOWEVER, IF WE
6 LOOK AT THE ACTUAL EVENTS WHICH ARE OCCURRING IN THIS
7 POPULATION AND LOOK AT THE TIME TO FIRST EVENT, THE
8 FIRST EVENT IS THE FATAL EVENT IN ABOUT A THIRD OF
9 THE PATIENTS, CONGESTIVE HEART FAILURE IN ABOUT A
10 THIRD OF THE PATIENTS, MYOCARDIAL INFARCTION ABOUT 13
11 PERCENT, STROKE IN EIGHT PERCENT, DOUBLING OF
12 CREATININE IN ABOUT SEVEN PERCENT, RENAL REPLACEMENT
13 THERAPY IN THREE PERCENT. SO AGAIN, DESPITE THE
14 STRONG RELATIONSHIP BETWEEN ADVANCED RENAL DISEASE
15 AND ADVERSE EVENTS, THE MAJORITY OF THEM ARE NOT
16 RENAL EVENTS PER SE, THEY ARE CARDIOVASCULAR EVENTS.
17 WELL, THE REAL QUESTION, OR ONE OF THE
18 IMPORTANT QUESTIONS TO CONSIDER IS, IS THIS AN ISSUE
19 OF ASSOCIATION OR CAUSATION? I'D LIKE TO SUGGEST
20 THAT IN A VERY ATTRACTIVE HYPOTHESIS, THAT IN FACT
21 THESE STENOSES ARE LEADING TO HIGH RATES OF ADVERSE
22 EVENTS. WE START WITH A MILIEU OF ATHEROSCLEROSIS WE
23 TALKED ABOUT IN THE ABDOMINAL AORTA. WE ADD THE
24 EFFECT OF NEUROENDOCRINE ACTIVATION. THE STENOSIS
25 LEADS TO HYPOPERFUSION OF THE KIDNEYS. AS WE'VE

00052

1 ALREADY DISCUSSED, THERE'S ACTIVATION OF THE
2 NEUROENDOCRINE SYSTEM INCLUDING RENIN, ANGIOTENSIN,
3 SYMPATHETIC ACTIVATION, WHICH LEADS TO CONTRALATERAL
4 NEPHROSCLEROSIS, VENTRICULAR HYPERTROPHY,
5 ACCELERATION OF ATHEROSCLEROSIS AND CHANGES IN THE
6 BRAIN.
7 AND THEN WE FINALLY ADD ON TOP OF THAT THE
8 UNIQUE RISK FACTOR OF CHRONIC KIDNEY DISEASE.
9 THERE'S BEEN A LOT OF INTEREST IN THE PAST FIVE YEARS
10 OR SO ABOUT HOW CHRONIC KIDNEY DISEASE LEADS TO
11 CARDIAC VASCULAR EVENTS. ENDOTHELIAL DYSFUNCTION IS
12 RELATED TO ASYMMETRIC LARGENING, MEDIAL
13 CALCIFICATION. A NUMBER OF FACTORS HAVE BEEN
14 PROPOSED AS MECHANISMS WHEREBY CKD LEADS TO EVENTS,
15 BUT CERTAINLY THIS MAY BE A VERY UNFAVORABLE NEW VIEW
16 OF ATHEROSCLEROSIS, NEUROENDOCRINE ACTIVATION AND
17 CKD.
18 DOES MEDICAL THERAPY HAVE LIMITATIONS?
19 PROBABLY SO. THERE MAY BE LAPSES IN MEDICAL THERAPY
20 RELATED TO COMPLIANCE AND COSTS. WE KNOW FROM
21 ENHANE'S DATA THAT ONLY HALF THE PATIENTS WHO ARE
22 HYPERTENSIVE TAKE THEIR MEDICINE, MOST AREN'T
23 CONTROLLED. WE KNOW THAT ANTIHYPERTENSIVE THERAPIES
24 HAVE SIDE EFFECTS WHICH MAY BE SIGNIFICANT IN THE
25 ELDERLY POPULATION. IT'S AT LEAST THEORETICALLY

00053

1 POSSIBLE THAT THERE COULD BE CONTINUED PROGRESSION OF
2 CKD DUE TO CHRONIC RENAL ISCHEMIA. AND FINALLY, IT'S
3 NOT CLEAR WHAT THE LONG-TERM EFFECTS OF ACTIVATION OF
4 THE RENIN-ANGIOTENSIN SYSTEM OR THE SYMPATHETIC
5 ACTIVATION ARE ON CARDIOVASCULAR OUTCOMES INDEPENDENT
6 OF BLOOD PRESSURE CONTROL.
7 ALL RIGHT. SO WHAT'S THE EVIDENCE BASE
8 FOR RENAL INTERVENTION? WELL, I THINK THIS HAS BEEN
9 COVERED AND I'M JUST GOING TO TRY TO GIVE AN OVERVIEW
10 OF WHAT I THINK ARE THE IMPORTANT DEVELOPMENTS IN THE
11 FIELD. BUT SIMPLY PUT, EARLY HISTORICALLY-CONTROLLED
12 WORK SUGGESTED IMPROVED SURVIVAL IN SURGICALLY
13 REVASCULARIZED PATIENTS. HOWEVER, THIS OBSERVATION
14 WAS LIMITED BY PATIENT SELECTION AND WOLLENWEBER AND
15 HUNT BOTH SAID THAT A CONTROLLED RANDOMIZED TRIAL
16 NEEDED TO BE PERFORMED IN ORDER TO ASSERT WHETHER
17 THIS EFFECT WAS REAL OR NOT.
18 IMPORTANTLY, ANGIOPLASTY WITHOUT STENTING
19 AND SURGERY APPEAR EQUIVALENT FOR BLOOD PRESSURE
20 CONTROL AND RENAL FUNCTION. THIS WAS A RANDOMIZED
21 TRIAL PUBLISHED IN 1993. HOWEVER, SURGICAL
22 REVASCULARIZATION HAD SIGNIFICANTLY MORE MAJOR
23 COMPLICATIONS, 34 VERSUS 17 PERCENT, DESPITE THE
24 ABILITY OF SURGERY TO ACHIEVE A HIGHER PRIMARY
25 PATENCY RATE. AND THESE AUTHORS RECOMMENDED

00054

1 ANGIOPLASTY AS A PRIMARY TREATMENT STRATEGY BECAUSE
2 IT AVOIDED THE HIGH MORTALITY AND MORBIDITY EARLY ON
3 ASSOCIATED WITH SURGERY, AND LARGELY THAT WAS A
4 TRANSITION POINT.
5 AS HAS BEEN ALLUDED TO, THERE HAVE BEEN
6 THREE RANDOMIZED TRIALS OF ANGIOPLASTY CONTRASTED TO
7 MEDICAL THERAPY, WHICH WERE NEGATIVE FOR THEIR
8 PRIMARY ENDPOINTS OF BLOOD PRESSURE CONTROL. AGAIN,
9 WE'VE HEARD THAT THESE DID NOT INCLUDE STENT, THERE
10 WERE HIGHER RATES OF CROSSOVER, AND THE FOLLOW-UP
11 TENDED TO BE RELATIVELY SHORT TERM. AND FINALLY, THE
12 SAMPLE SIZES WERE FRANKLY INADEQUATE TO DETECT A
13 MEANINGFUL DIFFERENCE IN BLOOD PRESSURE CONTROL.
14 SUBSEQUENTLY IT'S BEEN DEMONSTRATED THAT
15 STENTING IS SUPERIOR TO ANGIOPLASTY FOR THE MAJORITY
16 OF ATHEROSCLEROTIC STENOSES FOR THE PREVENTION OF
17 RESTENOSIS. THIS WAS PUBLISHED BY VAN DER VEN IN
18 LANCET IN 1999. AND THUS, STENTING HAS BECOME THE
19 DOMINANT MODE OF REVASCULARIZATION. IMPORTANTLY,
20 THOUGH, OUR CURRENT GENERATION OF FDA APPROVAL TRIALS
21 FOCUS ON DEVICE PERFORMANCE SPECIFIC TO THIS RATE OF
22 RESTENOSIS RATED AGAINST ANGIOPLASTY, WHICH I WOULD
23 SUGGEST TO YOU IS NOW A TREATMENT OF HISTORICAL
24 RELEVANCE. SO THE STRATEGY IS TO TREAT FAILED
25 BALLOON ANGIOPLASTY, CONTRAST RESTENOSIS RATES

00055

1 AGAINST SOME OBJECTIVE PERFORMANCE CRITERIA. THE
2 CHALLENGE IS THAT FOR CLINICIANS, THESE TYPES OF
3 STUDIES PROVIDE LITTLE INFORMATION ABOUT
4 DECISION-MAKING FOR PATIENT CARE, ALTHOUGH THEY MAY
5 PROVIDE FDA WITH VALUABLE INFORMATION ABOUT
6 RESTENOSIS RATES PER SE RELATED TO A DEVICE.
7 FINALLY, AS HAS BEEN ALLUDED TO, THERE ARE
8 A NUMBER OF SINGLE CENTER CASE REPORTS AND COHORT
9 STUDIES OF STENTING. BROADLY THEY CAN BE LUMPED AS
10 DEMONSTRATING BENEFIT FOR RENAL FUNCTION. HARDEN IN
11 LANCET, WATSON IN CIRCULATION, DEMONSTRATED THAT
12 INFLECTION IN THE SLOPE OF RECIPROCAL CREATININE
13 OCCURS. OTHER PEOPLE HAVE DEMONSTRATED SIMILAR
14 FINDINGS, THOUGH, IN MEDICALLY TREATED PATIENTS. AS
15 HAS BEEN ALLUDED TO, BLOOD PRESSURE CONTROL APPEARS
16 TO BE IMPROVED AFTER STENTING, BUT THIS HAS ALSO BEEN
17 DEMONSTRATED IN PATIENTS WITH MEDICAL THERAPY, WHICH
18 REMAINS CONSISTENT, WHICH IS TERMED A CLINICAL
19 OBSERVATIONAL EFFECT.
20 I WOULD LIKE TO DIGRESS A MOMENT ON WHAT I
21 THINK IS SOME OF THE CONFUSION ABOUT THE EFFECT OF
22 REVASCULARIZATION ON RENAL FUNCTION, AND I'LL
23 EMBARRASS STEVE TEXTOR FOR THIS IMPORTANT PANEL TAKEN
24 FROM A PUBLICATION HE HAD DONE IN AMERICAN SOCIETY OF
25 NEPHROLOGY A FEW YEARS BACK, WHICH IS LOOKING AT

00056

1 SURGICAL REVASCULARIZATION, BUT I REALLY THINK THAT
2 THERE'S IMPORTANT INFORMATION HERE.
3 IF YOU LOOK AT PATIENTS UNDERGOING
4 REVASCULARIZATION, WHAT YOU SEE IS THE FOLLOWING:
5 ABOUT A QUARTER OF THE PATIENTS HAVE A SIGNIFICANT
6 IMPROVEMENT IN RENAL FUNCTION. ABOUT HALF THE
7 PATIENTS HAVE STABLE RENAL FUNCTION AND ABOUT ONE IN
8 FIVE HAVE A SIGNIFICANT INCREASE IN THEIR SERUM
9 CREATININE. THIS HAS MEANING IN TWO -- THIS FINDING
10 OBVIOUSLY, I WOULD SUGGEST TO YOU, IS ALSO CONSISTENT
11 WITH WHAT IS OBSERVED WITH STENT REVASCULARIZATION.
12 IF WE LOOK AT THE PUBLISHED DATA FROM ASPIRE II,
13 WHICH WAS AN FDA APPROVAL REGISTRY, IF WE LOOK AT THE
14 CHANGE IN SERUM CREATININE OVER TIME, 1.4, 1.4, 1.5,
15 A NEGLIGIBLE CHANGE, BUT IMPORTANTLY WHAT ONE
16 OBSERVES IS THAT THE STANDARD DEVIATION TERM
17 CONTINUES TO BROADEN, WHICH SUGGESTS THAT THERE ARE
18 PATIENTS THAT ARE GETTING BETTER, PATIENTS THAT ARE
19 GETTING WORSE, AND PATIENTS THAT AREN'T CHANGED.
20 AND AS A CONSEQUENCE WHEN YOU SPEAK TO
21 PROVIDERS OF THIS THERAPY, OFTENTIMES PEOPLE WILL
22 RECOUNT THE ONE OR TWO PATIENTS THAT GOT
23 SIGNIFICANTLY BETTER AND MAY MAKE THE CLAIM THAT I
24 THINK STENTING IS AN EXCELLENT THERAPY AND EVERYBODY
25 SHOULD GET IT. ALTERNATIVELY, IF YOU'RE A

00057

1 NEPHROLOGIST IN PRACTICE, THE PATIENTS YOU'RE LIKELY
2 TO BE REFERRED TO ARE THOSE WHOSE RENAL FUNCTION
3 DECLINES AND REQUIRE DIALYSIS. AND SO AS A
4 CONSEQUENCE, WHAT I WOULD SUGGEST TO YOU IS THAT THE
5 ONE THING THAT WE HAVE LEARNED ABOUT THE THERAPIES OF
6 REVASCULARIZATION IS THAT THERE IS DIVERGENCE OF
7 OUTCOME OVER TIME AND BLUNTLY, IT'S HARD TO PREDICT
8 WHO'S GOING TO DO BETTER AND WHO IS NOT GOING TO DO
9 BETTER.
10 WELL, IF RENAL ARTERY STENOSIS IS
11 ASSOCIATED WITH NEUROHUMORAL ACTIVATION AND POOR
12 OUTCOMES, AND CAN CAUSE HYPERTENSION AND CHRONIC
13 KIDNEY DISEASE, WHY DO WE NEED MORE STUDIES? I'LL
14 SAY WITH SOME DEGREE OF CERTAINTY THAT ALL PATIENTS
15 WITH RENAL ARTERY STENOSIS NEED EFFECTIVE MEDICAL
16 THERAPY, THEY NEED TO BE ON ANTIHYPERTENSIVES, THEY
17 NEED TO BE ON STATINS, THEY NEED TO BE ON
18 ANTIPLATELET THERAPY, THEY NEED TO HAVE THEIR GLUCOSE
19 CONTROLLED IF THEY'RE DIABETIC. ALL THESE
20 INTERVENTIONS HAVE BEEN PROVEN IN RANDOMIZED TRIALS.
21 THE ISSUE IS, ARE THE OUTCOMES
22 ATTRIBUTABLE TO RENAL ARTERY STENOSIS, AND DOES
23 STENTING CHANGE THE OUTCOME WHEN ADDED TO THE EFFECT
24 OF MEDICAL THERAPY. AS A CONSEQUENCE, IF YOU TRAVEL
25 AROUND THE UNITED STATES, WHICH I HAVE HAD THE

00058

1 PLEASURE TO DO AS PART OF THE CORAL STUDY LEADERSHIP
2 TEAM, WE'VE NOW VISITED APPROXIMATELY 80 MEDICAL
3 CENTERS INSIDE THE UNITED STATES WHO ACTIVELY CARE
4 FOR THESE PATIENTS, WHAT YOU SEE IS BROAD DIVERGENCE
5 IN THE OPINIONS OF MEDICAL EXPERTS. AND THIS MAY
6 SEEM SILLY, BUT WITHIN THE INTERNAL MEDICINE
7 COMMUNITY AND NEPHROLOGY COMMUNITY, THE GENERAL
8 VICTIM IS SCREENED RARELY AND STENTED EVEN LESS
9 BECAUSE OF CONCERNS ABOUT PATIENTS WITH DECLINING
10 RENAL FUNCTION AFTER THE PROCEDURE AND WHETHER THESE
11 THERAPIES ACTUALLY DO IMPROVE BLOOD PRESSURE CONTROL
12 OR RENAL FUNCTION.
13 IN CONTRAST, IF YOU SPEAK TO INVESTIGATORS
14 WHO ARE SURGEONS OR INTERVENTIONAL CARDIOLOGISTS OR
15 INTERVENTIONAL RADIOLOGISTS, QUITE OFTEN THERE'S A
16 COMPULSION TO TREAT EVERYBODY, BECAUSE IF WE DON'T,
17 THE PATIENT'S KIDNEY FUNCTION MAY GET WORSE. AND THE
18 CONSEQUENCE WHICH I THINK IS SOMEWHAT TROUBLING IS
19 THAT THE TYPE OF CARE YOU RECEIVE MAY BE MORE
20 DICTATED BY THE SPECIALTY AFFILIATION OF THE GUY YOU
21 SHOW UP TO SEE RATHER THAN THE MEDICAL CONDITION THAT
22 YOU ACTUALLY HAVE.
23 FINALLY, I'VE BEEN ASKED BY --
24 DR. GARBER: EXCUSE ME. DR. COOPER, I'M
25 GOING TO HAVE TO ASK YOU TO WRAP UP.

00059

1 DR. COOPER: OKAY, VERY GOOD. I'VE BEEN
2 ASKED BY CMS TO BRIEFLY GIVE AN OVERVIEW OF CORAL.
3 THERE IS A RANDOMIZED TRIAL OF PATIENTS WITH RENAL
4 ARTERY STENOSIS WHO ARE RANDOMIZED TO STENT OR NO
5 STENT. THEY ARE GIVEN OPTIMAL MEDICAL THERAPY
6 INCLUDING A STATIN, ANGIOTENSIN RECEPTOR BLOCKER,
7 ET CETERA. THE PRIME ENDPOINT IS CLINICAL EVENT. IT
8 SHOULD BE POWERED ADEQUATELY TO DETECT CLINICAL
9 EVENTS.
10 CMS HAS ASKED ME TO TALK ABOUT ENROLLMENT
11 IN CORAL. RIGHT NOW WE'RE ON OUR REVISED TARGET.
12 ENROLLMENT WAS SLOW AT THE BEGINNING, ALTHOUGH IT HAS
13 IMPROVED.
14 IN ADDITION, THEY HAVE ASKED FOR AN
15 OPINION ABOUT OR EVIDENCE ABOUT THE IMPACT OF U.S.
16 AND NON-U.S. ENROLLMENT. AS ONE CAN SEE, U.S.
17 ENROLLMENT HAS IMPROVED OVER TIME AND ENROLLMENT
18 OUTSIDE THE U.S. HAS RECENTLY INCREASED. THE ISSUE
19 OF OUS ENROLLMENT IS AN INTERESTING ONE. IT HELPS US
20 ACHIEVE OUR OVERALL ENROLLMENT OBJECTIVE BUT DOES
21 LIMIT THE REPRESENTATION OF THE U.S. POPULATION AND
22 LESSENS APPLICABILITY TO THE U.S. HEALTHCARE SYSTEM.
23 SO THE CASE FOR RENAL ARTERY STENTING IS,
24 ISCHEMIC RENAL DISEASE IS ASSOCIATED WITH POOR
25 OUTCOMES. STENTING IS THE APPROPRIATE DOMINANT MODE

00060

1 OF REVASCULARIZATION. IT HAS A LOT OF PROMISE BUT
2 THE ROLE IN ADDITION TO MEDICAL THERAPY REMAINS
3 UNCLEAR, AS HAS BEEN DISCUSSED PREVIOUSLY, AND CORAL
4 IS DESIGNED TO ADDRESS THIS QUESTION. HOWEVER,
5 YOU'RE NOT GOING TO HAVE AN ANSWER FOR SEVERAL YEARS
6 AND A DEFINITIVE RESULT WILL DEPEND ON ACHIEVING
7 ADEQUATE ENROLLMENT.
8 DR. GARBER: THANK YOU, DR. COOPER. NEXT,
9 DR. DWORKIN.
10 DR. DWORKIN: I'M LANCE DWORKIN, THE STUDY
11 CHAIR FOR THE CORAL TRIAL. I WORK CLOSELY WITH CHRIS
12 COOPER ON THAT. I'M ALSO A NEPHROLOGIST AT BROWN
13 MEDICAL SCHOOL AND I WAS ASKED TO PRIMARILY PRESENT
14 THE ARGUMENTS FROM AN ARTICLE THAT APPEARED AS A
15 COMPANION TO THE ONE CHRIS WROTE IN CIRCULATION,
16 MAKING A CASE AGAINST ANGIOPLASTY AND STENTING.
17 BY WAY OF DISCLOSURES UNDER THE CORAL
18 TRIAL, I DON'T FEEL I HAVE ANY SIGNIFICANT CONFLICTS
19 OF INTEREST.
20 A LOT OF THE DATA THAT YOU'RE GOING TO SEE
21 FROM ALL OF US, I THINK, IS A LITTLE BIT REPETITIVE
22 BECAUSE WE'RE ALL OPERATING FROM THE SAME MEAGER
23 DATABASE, WHICH HOPEFULLY WILL JUST ALLOW ME TO MOVE
24 QUICKLY. I THINK THE POINT OF THIS SLIDE IS THAT
25 THIS IS A COMMON PROBLEM IN THE ELDERLY POPULATION,

00061

1 AND IT'S PARTICULARLY COMMON IN PEOPLE THAT HAVE
2 VASCULAR DISEASE IN OTHER BEDS, SO PERIPHERAL
3 VASCULAR DISEASE, CORONARY ARTERY DISEASE AND
4 CEREBRAL VASCULAR DISEASE.
5 CHRIS ALREADY SHOWED YOU SOME OF THIS
6 DATA ON OUTCOMES. THESE PATIENTS ARE ILL. THESE ARE
7 SOME OF THE COMMON COMORBIDITIES SEEN IN PATIENTS
8 WITH RENOVASCULAR DISEASE. UNCONTROLLED OR SEVERE
9 HYPERTENSION IS THE MOST COMMON COMPLAINT.
10 PREVALENCE OF DIABETES IS ABOUT 20 PERCENT. MOST
11 HAVE A SMOKING HISTORY, EITHER CURRENT OR REMOTE.
12 THERE'S THE CONCORDANCE WITH OTHER VASCULAR DISEASE.
13 AND IN OUR OWN SERIES OF PATIENTS AT BROWN, ABOUT 50
14 PERCENT OF THE PATIENTS PRESENT ALREADY WITH SOME
15 DEGREE OF RENAL INSUFFICIENCY.
16 I THINK THE IMPORTANT THING FOR ME AS A
17 NEPHROLOGIST IS THAT ALTHOUGH PROGRESSION TO
18 END-STAGE RENAL DISEASE OR PRESERVING KIDNEY FUNCTION
19 IS OFTEN GIVEN AS AN ARGUMENT FOR PERFORMING RENAL
20 INTERVENTION, ACTUALLY OVER AT LEAST A COUPLE YEARS
21 OF FOLLOW-UP, THE NUMBER OF PATIENTS THAT PRESENT AND
22 PROGRESS TO END-STAGE RENAL DISEASE ASSOCIATED WITH
23 RENOVASCULAR DISEASE IS ACTUALLY VERY SMALL.
24 CHRIS ALREADY MENTIONED THE SURVIVAL DATA,
25 THAT RENAL ARTERY STENOSIS ADVERSELY AFFECTS SURVIVAL

00062

1 IN CASES OF CORONARY ARTERY DISEASE, AND HE SHOWED
2 YOU THIS SLIDE BUT NOT THIS ONE, WHICH REALLY SHOWS
3 THE IMPACT OF INCREASING SEVERITY OF STENOSIS ON
4 OUTCOMES AND AS THE DEGREE OF STENOSIS INCREASES,
5 SURVIVAL OVER FIVE YEARS HERE DECREASES.
6 SO WHAT IS THE EXPLANATION FOR THE HIGH
7 ADVERSE EVENT RATE IN PATIENTS WITH RENAL ARTERY
8 STENOSIS? AND THIS WAS ALREADY MENTIONED, THIS
9 NOTION THAT THERE IS NEUROHUMORAL ACTIVATION,
10 ACTIVATION OF THE RENIN/ANGIOTENSIN/ALDOSTERONE
11 SYSTEM, SYMPATHETIC NERVOUS SYSTEM MAY BE DRIVING
12 THESE OUTCOMES. I THINK IT'S HARD TO KNOW, HOWEVER,
13 HOW THIS PLAYS OUT IN TERMS OF WHICH THERAPEUTIC
14 INTERVENTION WILL BE BETTER, BECAUSE WHILE YOU MAY BE
15 ABLE TO REVERSE SOME OF THESE CHANGES BY OPENING THE
16 RENAL ARTERY, WE ALSO HAVE EFFECTIVE MEDICAL
17 INTERVENTIONS, DRUGS THAT CAN BLOCK THESE SYSTEMS.
18 THE ASSOCIATION BETWEEN REN VASCULAR
19 DISEASE AND RENAL FUNCTION, AND THE FACT THERE IS
20 INCREASING EVIDENCE AT LEAST THAT IN PATIENTS WITH
21 CHRONIC KIDNEY DISEASE, THEY HAVE AN INCREASED RISK
22 FOR CARDIOVASCULAR DISEASE. AND THEN THERE IS THIS
23 POSSIBILITY, AND THAT IS THAT THE ADVERSE OUTCOME IS
24 JUST A CONSEQUENCE OF THE FACT THAT BY THE TIME THESE
25 PATIENTS ARE IDENTIFIED, THEY ALREADY HAVE DIFFUSE

00063

1 SEVERE ATHEROSCLEROTIC DISEASE, AND YOU MIGHT SUSPECT
2 THAT IN THIS CONTEXT, FIXING A LESION IN A SINGLE
3 BLOOD VESSEL MIGHT NOT HAVE THAT DRAMATIC OF IMPACT.
4 SO THESE ARE THE MOST COMMON
5 JUSTIFICATIONS GIVEN FOR INTERVENING IN RENAL ARTERY
6 STENOSIS, AND I USE THE WORD JUSTIFICATIONS RATHER
7 THAN INDICATIONS BECAUSE AS YOU'VE ALREADY HEARD,
8 THERE REALLY ISN'T GOOD EVIDENCE THAT THESE OUTCOMES
9 ARE IMPROVED BY INTERVENTIONS. SO RESISTANT
10 HYPERTENSION IS PROBABLY THE MOST COMMON
11 JUSTIFICATION. TO STABILIZE OR PREVENT PROGRESSION
12 TO END-STAGE RENAL DISEASE IN PATIENTS WITH EITHER
13 DECLINING OR IMPAIRED KIDNEY FUNCTION, WHICH IS
14 COMMON. AND THEN ANOTHER COMMON JUSTIFICATION ARE TO
15 REDUCE THE SEVERITY OR ADMISSIONS FOR CONGESTIVE
16 HEART FAILURE.
17 SO WHAT'S THE EVIDENCE FOR THIS? AGAIN,
18 YOU'VE ALREADY SEEN THESE TRIALS SUMMARIZED AND I
19 WON'T BELABOR THIS. THESE ARE THE THREE RANDOMIZED
20 CONTROLLED TRIALS. THEY HAD VARIOUS PROBLEMS.
21 SUFFICE IT TO SAY THAT THERE REALLY HASN'T BEEN,
22 EXCEPT IN THIS ONE STUDY OF BILATERAL DISEASE WITH A
23 RELATIVELY SMALL NUMBER OF PATIENTS HERE, A
24 SIGNIFICANT DIFFERENCE IN BLOOD PRESSURE IN THE
25 RANDOMIZED CONTROLLED TRIALS OF PATIENTS TREATED

00064

1 MEDICALLY VERSUS THOSE TREATED WITH
2 REVASCULARIZATION.
3 IN ALL OF THESE STUDIES THERE IS A
4 TENDENCY FOR THE NUMBER OF DRUGS REQUIRED TO CONTROL
5 BLOOD PRESSURE TO DECLINE. THESE PATIENTS ALWAYS
6 REQUIRE MULTIPLE DRUGS TO CONTROL THEIR BLOOD
7 PRESSURE, TYPICALLY THREE, FOUR, FIVE MEDICATIONS,
8 AND ON AVERAGE THE NUMBER OF MEDICATIONS NEEDED
9 DECLINES BY ABOUT ONE MEDICATION. WHETHER OR NOT
10 THAT'S A CHANGE THAT WOULD BE ASSOCIATED WITH
11 SIGNIFICANTLY BETTER OUTCOMES FOR PATIENTS, I DON'T
12 THINK IS KNOWN.
13 WHAT ABOUT THE EFFECTS OR WHY ISN'T
14 REVASCULARIZATION BETTER AS A TREATMENT FOR
15 HYPERTENSION? WELL, ONE OF THE PROBLEMS I THINK IS
16 ILLUSTRATED BY THIS. THIS IS ACTUALLY AN ANIMAL
17 MODEL, THE GOLDBLATT HYPERTENSIVE MODEL OF ONE
18 KIDNEY, OR TWO KIDNEYS, WITH HYPERTENSION. AND THIS
19 IS A STUDY IN RATS WHICH LOOKS AT THE EFFECTS OF
20 UNCLIPPING THE RENAL ARTERY, SO ESSENTIALLY DOING
21 ANGIOPLASTY IN RATS THAT HAVE HYPERTENSION AS A
22 RESULT OF CONSTRICTING THE RENAL ARTERY EITHER AT
23 THREE MONTHS OF HYPERTENSION OR AT SIX MONTHS OF
24 HYPERTENSION.
25 AND WHAT YOU CAN SEE IS THAT IF YOU

00065

1 REVASCULARIZE EARLY, THAT HYPERTENSION IN FACT
2 IMPROVES AND IS CURED. HOWEVER, IF YOU REVASCULARIZE
3 LATE, THE HYPERTENSION IS SUSTAINED, EVEN THOUGH THE
4 RENAL ARTERY LESION IS NO LONGER HERE. AND WHAT IS
5 THE EXPLANATION FOR THAT? WELL, THERE ARE PROBABLY A
6 NUMBER OF FACTORS; SOME OF THESE FACTORS ARE
7 VASCULAR, CHANGES IN ARTERIAL THICKENING AND
8 ENDOTHELIAL DYSFUNCTION THAT TENDS TO SUSTAIN
9 HYPERTENSION. AND THEN A MAJOR PROBLEM IS PROBABLY
10 UNDERLYING KIDNEY DISEASE IN THESE PATIENTS, AND THIS
11 IS KIDNEY DISEASE THAT IS NOT DIRECTLY RELATED TO THE
12 RENAL ARTERY STENOSIS.
13 HYPERTENSIVE NEPHROSCLEROSIS IN PATIENTS
14 WITH UNILATERAL DISEASE, THE KIDNEY THAT'S NOT DISTAL
15 TO A STENOSIS IS EXPOSED TO HIGH PERFUSION PRESSURES
16 AND IS INJURED, AND THEN WHAT WE CALL ISCHEMIC
17 NEPHROPATHY IN THE KIDNEY THAT'S DISTAL TO THE
18 STENOSIS, WHERE THERE'S ACTIVATION OF CYTOKINES AND
19 INFLAMMATION AND FIBROSIS AS WELL. AND ONCE YOU HAVE
20 SEVERE RENAL FUNCTIONAL IMPAIRMENT, EVEN IF YOU OPEN
21 UP THE ARTERY, THAT'S UNLIKELY TO IMPROVE
22 HYPERTENSION SIGNIFICANTLY. AND THIS IS ALSO
23 RELEVANT TO THE CHANGES IN KIDNEY FUNCTION.
24 AND AGAIN, YOU'VE ALREADY SEEN THIS SLIDE
25 AND AS A NEPHROLOGIST, MY INTERPRETATION OF THIS DATA

00066

1 IS THAT IF YOU REVASCULARIZE PATIENTS THAT HAVE RENAL
2 ARTERY STENOSIS AND IMPAIRED KIDNEY FUNCTION AT THE
3 TIME OF THE PROCEDURE, ABOUT A QUARTER IMPROVE, ABOUT
4 A HALF ARE UNCHANGED, AND ABOUT 20 PERCENT GET WORSE,
5 SO ON BALANCE IT'S A WASH. KIDNEY FUNCTION DOESN'T
6 CHANGE FOR THE GROUP AS A WHOLE. SOME PATIENTS
7 DEFINITELY IMPROVE, BUT THE NUMBER THAT IMPROVE ARE
8 NOT REALLY MUCH GREATER THAN THE NUMBER THAT ARE
9 SERIOUSLY HARMED BY THE INTERVENTION. AND IN THE
10 RANDOMIZED CONTROLLED TRIALS, MOST HAVE SHOWN NO
11 SIGNIFICANT DIFFERENCE IN KIDNEY FUNCTION OVER
12 RELATIVELY SHORT PERIODS OF FOLLOW-UP, IN THIS CASE
13 ONLY ABOUT 12 MONTHS IN THE DRASTIC TRIAL, WHICH
14 YOU'VE HEARD ABOUT.
15 SO THERE'S NOT MUCH EVIDENCE THAT THIS IS
16 GOING TO IMPROVE KIDNEY FUNCTION. AND WHY IS THAT?
17 WELL, IT'S NOT SURPRISING FOR A COUPLE OF REASONS.
18 FIRST OF ALL, PROSPECTIVE DATA LOOKING AT THE NATURAL
19 HISTORY OF THESE RENAL ARTERY LESIONS SHOW THAT
20 ACTUALLY IT'S A MINORITY OF THEM THAT PROGRESS TO
21 COMPLETE OCCLUSION OVER A REASONABLY LONG PERIOD OF
22 FOLLOW-UP OF SEVERAL YEARS. AND IN THIS LARGE SERIES
23 FROM THE GROUP IN SEATTLE, ONLY ABOUT THREE PERCENT
24 OF THE RENOVASCULAR LESIONS WENT ON TO COMPLETE
25 OCCLUSION AND, THEREFORE, WOULD BE POSSIBLY A CAUSE

00067

1 OF END-STAGE RENAL DISEASE.
2 AND THEN LOOKED AT ANOTHER WAY, THERE'S A
3 VERY POOR CORRELATION BETWEEN THE DEGREE OF ANATOMIC
4 STENOSIS AND KIDNEY FUNCTION, AGAIN SUGGESTING THAT
5 IT'S NOT THE MAIN RENAL ARTERY DISEASE PER SE THAT'S
6 CAUSING RENAL DYSFUNCTION, AND HERE'S A COUPLE OF
7 DIFFERENT DATA SETS THAT LOOK AT THIS. SO THIS IS
8 THE CREATININE CLEARANCE RATE MEASURED IN A GROUP OF
9 PATIENTS WITH DIFFERENT DEGREES OF RENOVASCULAR
10 DISEASE RANGING FROM LESS THAN A 50 PERCENT STENOSIS
11 OF A SINGLE ARTERY UP TO HIGH GRADE BILATERAL
12 STENOSIS, AND YOU CAN SEE ALL OF THESE PATIENTS HAVE
13 IMPAIRED KIDNEY FUNCTION WITH AN AVERAGE CREATININE
14 CLEARANCE BETWEEN 30 AND 40, BUT THERE IS NO
15 DIFFERENCE AT ALL BETWEEN THE DIFFERENT GROUPS.
16 AND THIS IS A STUDY LOOKING ISOTOPICALLY
17 AT GFR IN PATIENTS WITH UNILATERAL STENOSIS IN THE
18 KIDNEY DISTAL TO THE STENOSIS VERSUS GFR IN THE
19 KIDNEY WITH THE NORMAL RENAL ARTERY, AND WHAT YOU CAN
20 SEE IS THAT OFTEN THE GFR IN THE KIDNEY WITH THE
21 NORMAL RENAL ARTERY IS AS LOW OR EVEN LOWER THAN THE
22 GFR IN THE KIDNEY THAT'S DISTAL TO THE STENOSIS,
23 AGAIN SUGGESTING THAT THE MAJOR CAUSE OF RENAL
24 DYSFUNCTION IN THESE PATIENTS IS NOT THE RENAL ARTERY
25 LESION BUT INTRINSIC KIDNEY DISEASE, AND THEREFORE

00068

1 UNLIKELY TO BE BENEFITED BY REVASCULARIZATION.
2 THERE'S REALLY NOTHING TO SAY ABOUT HEART
3 FAILURE. THERE ARE NO RANDOMIZED CONTROLLED TRIALS.
4 OBSERVATIONAL STUDIES SUGGEST THAT SOME PATIENTS DO
5 BETTER AFTER STENTING, BUT OBVIOUSLY PATIENTS DO
6 BETTER WITH INTENSIVE MEDICAL THERAPY ALSO.
7 SO IT'S FAIR TO SAY THAT MOST OF THESE
8 TRIALS ARE SERIOUSLY FLAWED. THEY TEND TO LOOK AT
9 SURROGATE ENDPOINTS LIKE BLOOD PRESSURE AND
10 CREATININE RATHER THAN HARD CLINICAL OUTCOMES LIKE
11 SURVIVAL OR CARDIOVASCULAR EVENTS. MANY EMPLOYED A
12 VERY IMPRECISE DEFINITION OF RENAL ARTERY STENOSIS,
13 ENROLLING PATIENTS WITH ONLY A 50 PERCENT STENOSIS OR
14 GREATER. WHEN WE DO THIS IN CORAL, WE FIND THAT
15 THESE ARE OFTEN OVER-READ, SO IF YOU SHOOT FOR A 50
16 PERCENT STENOSIS, ABOUT A QUARTER OF THE PATIENTS END
17 UP HAVING LESS THAN THAT.
18 MANY OF THE STUDIES WERE SEVERELY HAMPERED
19 BY LARGE NUMBERS OF CROSSOVERS, AND THEN I THINK
20 ALMOST NONE OF THEM PAID ADEQUATE ATTENTION TO THE
21 MEDICAL THERAPY THAT PATIENTS ARE RECEIVING, AND
22 OBVIOUSLY COMPARING AN INTERVENTION TO AN INADEQUATE
23 MEDICAL INTERVENTION IS A BIASED APPROACH.
24 SO WHAT IS OPTIMAL MEDICAL THERAPY IN
25 RENAL ARTERY STENOSIS? THIS HAS ALREADY BEEN

00069

1 DISCUSSED A LITTLE BIT. IT INCLUDES TIGHT CONTROL OF
2 BLOOD PRESSURE DOWN TO, THESE ARE JUST JNC-7 TARGETS.
3 THIS REQUIRES MULTIPLE DRUGS, AND IN THE CORAL STUDY
4 AT LEAST, WE FELT THAT BLOCKADE OF THE
5 RENIN/ANGIOTENSIN/ALDOSTERONE SYSTEM MAY BE CRITICAL.
6 WE FEEL THAT THIS MAY BE ONE OF THE BAD ACTORS IN
7 PATIENTS WITH RENAL ARTERY STENOSIS. IT'S IMPORTANT
8 TO NOTE THAT IN MANY OF THE STUDIES THAT HAVE BEEN
9 TALKED ABOUT, THESE DRUGS WERE SPECIFICALLY AVOIDED
10 BECAUSE OF CONCERN THAT THEY COULD PRODUCE ACUTE
11 RENAL FAILURE. THAT IS A REAL RISK, BUT IN FACT THE
12 INCIDENCE OF SEVERE ACUTE RENAL FAILURE IN PATIENTS
13 WITH RENOVASCULAR DISEASE TREATED WITH THESE DRUGS IS
14 RELATIVELY LOW, AND IT IS POSSIBLE TO USE THESE
15 AGENTS IN THE MAJORITY OF PATIENTS WITH RENOVASCULAR
16 DISEASE. THAT MAY BE CRITICALLY IMPORTANT TO
17 IMPROVING LONG-TERM OUTCOMES AND THERE IS SOME
18 OBSERVATIONAL DATA THAT SUGGESTS THAT THAT IS TRUE.
19 THESE ARE THE OTHER CONCOMITANT THERAPIES
20 THAT SHOULD BE APPLIED. TREATING DYSLIPIDEMIA,
21 SMOKING CESSATION, SOME KIND OF ANTIPLATELET THERAPY.
22 BECAUSE MANY OF THESE PATIENTS ARE DIABETIC, GLYCEMIC
23 CONTROL. AND THEN ALSO BECAUSE OF THE CHRONIC KIDNEY
24 DISEASE, MANAGEMENT OF THE CONSEQUENCES OF THAT.
25 AND IT'S DIFFICULT TO PREDICT WHAT THE

00070

1 EXACT OUTCOME OF THAT TYPE OF APPROACH WILL BE. AS
2 YOU'VE ALREADY HEARD, THERE REALLY AREN'T GOOD
3 PROSPECTIVE TRIALS LOOKING AT THE IMPACT OF AN
4 INTENSIVE MEDICAL REGIMEN LIKE THAT ON CLINICAL
5 OUTCOMES IN PATIENTS WITH RENOVASCULAR DISEASE, BUT
6 BY EXTRAPOLATION FROM OTHER POPULATIONS YOU CAN MAKE
7 SOME PREDICTIONS.
8 AND SO, THIS IS A STUDY OR REALLY A REVIEW
9 THAT WAS PUBLISHED A FEW YEARS AGO IN LANCET WHICH
10 PREDICTED THE CUMULATIVE RISK REDUCTION OF USING FOUR
11 RELATIVELY SIMPLE MEDICAL INTERVENTIONS. SO ASPIRIN,
12 BETA BLOCKERS, LIPID LOWERING AND ACE INHIBITORS,
13 THERE'S RELATIVE RISK REDUCTIONS FROM EACH OF THESE.
14 AND AGAIN, THIS IS NOT FROM A RENAL ARTERY STENOSIS
15 POPULATION, BUT IT'S FROM OTHER POPULATIONS WITH
16 HYPERTENSION AND OTHER TYPES OF COMORBIDITIES. AND
17 WHAT THIS PREDICTS IS ABOUT A 75 PERCENT CUMULATIVE
18 RISK REDUCTION IN A HYPERTENSIVE POPULATION IF THESE
19 THERAPIES ARE PROVIDED, AND IF YOU ADD SMOKING
20 CESSATION, IT EVEN GETS A LITTLE BETTER.
21 AND I THINK THIS IS ANOTHER ONE OF THE
22 PROBLEMS FOR INTERVENTIONS. SO EVEN IF IT'S A GOOD
23 THERAPY AND EVEN IF IT REDUCES CLINICAL EVENT RATES
24 IN THE PATIENTS WITH RENAL ARTERY STENOSIS, AS
25 MEDICAL THERAPY HAS GOTTEN BETTER AND AS WE HAVE NOW

00071

1 EFFECTIVE WAYS OF CONTROLLING BLOOD PRESSURE,
2 CONTROLLING LIPIDS AND TREATING THIS VERY
3 AGGRESSIVELY, THAT WE'RE GOING TO BE REDUCING EVENT
4 RATES IN THESE PATIENTS WHEN WE TREAT THEM WITH THIS
5 TYPE OF REGIMEN, AND IT JUST BECOMES HARDER AND
6 HARDER FOR THE INTERVENTIONS TO DO BETTER.
7 JUST TO MAKE THIS POINT, THIS IS AGAIN,
8 ACTUALLY WE'RE RELYING ON STEVE TEXTOR HERE, WHO'S
9 PUBLISHED A LOT, AND THIS IS JUST SOME LONG-TERM
10 OUTCOMES DATA THAT HIS GROUP HAS PUBLISHED FROM THE
11 MAYO CLINIC LOOKING AT PATIENTS TREATED WITHOUT
12 REVASCULARIZATION. SO THESE ARE PATIENTS WITH RENAL
13 ARTERY STENOSIS FOLLOWED FOR A NUMBER OF YEARS
14 WITHOUT REVASCULARIZATION, AND WHAT YOU CAN SEE IS
15 THAT IN FACT YOU CAN ACHIEVE GOOD BLOOD PRESSURE
16 CONTROL. ALMOST HALF OF THE PATIENTS HAD BLOOD
17 PRESSURE TREATED TO THE JNC TARGET OF LESS THAN 140
18 OVER 90, THE CREATININE REMAINS RELATIVELY STABLE
19 OVER TIME, RELATIVELY FEW OF THESE PATIENTS NEED TO
20 BE REVASCULARIZED, END-STAGE RENAL DISEASE IS VERY
21 UNCOMMON.
22 AND MORTALITY IS SIGNIFICANT, BUT
23 REMEMBER, WE'RE DEALING WITH AN ELDERLY POPULATION
24 WITH A LOT OF COMORBIDITIES AND THIS MAY NOT REALLY
25 BE THAT DIFFERENT IN AN ANGIOPLASTY OR STENT-TREATED

00072

1 GROUP.
2 SO JUST TO WRAP UP, RENAL ARTERY STENOSIS
3 IS A COMMON PROBLEM THAT IS RELATIVELY EASY TO FIND.
4 THE BEST TREATMENT, I FEEL, IS STILL UNKNOWN. THE
5 PATIENTS ARE ILL. ALL PATIENTS REQUIRE AN INTENSIVE
6 MULTIFACETED MEDICAL INTERVENTION. THE OUTCOMES FROM
7 REVASCULARIZATION ARE UNPREDICTABLE. WE DON'T REALLY
8 HAVE A WAY OF DECIDING UP FRONT WHICH PATIENTS WILL
9 BENEFIT VERSUS WHICH WILL NOT, AND THE INTERVENTION
10 DOES HAVE SOME RISKS.
11 A CLINICAL TRIAL IS NEEDED. THE CORAL
12 TRIAL YOU'VE HEARD ABOUT A LITTLE BIT, HOPEFULLY WILL
13 ADDRESS SOME OF THESE QUESTIONS AND, YOU KNOW, OUR
14 ONLY CONCERN IS THAT ENROLLMENT IN THESE CLINICAL
15 TRIALS BE ENCOURAGED. SO THAT IS ALL I HAVE TO SAY.
16 THANK YOU.
17 DR. GARBER: THANK YOU, DR. DWORKIN. NEXT
18 SPEAKING WILL BE DR. THOMAS SOS.
19 DR. SOS: GOOD MORNING. A LOT OF THIS IS
20 BASED ON 34 YEARS OF EXPERIENCE IN BEING INVOLVED IN
21 RENAL ARTERY, AND PARTLY UNDER THE TUTELAGE, EARLY
22 TUTELAGE OF JOHN LOWER AND HIS GROUP. A LOT OF THIS
23 WAS SUMMARIZED IN A PAPER IN ENDOVASCULAR TODAY
24 ENTITLED RENAL STENTING TO DATE, IS THIS PROCEDURE
25 UNDERUSED OR OVERUSED? YES. SO WHAT I WOULD LIKE TO

00073

1 DO IS SPEND THE REST OF THE HALF HOUR EXPLAINING TO
2 YOU WHAT I MEANT BY THAT.
3 FIRST OF ALL, THE REAL QUESTION IS WHETHER
4 STENTING IN RENAL ARTERY DISEASE IS JUSTIFIED TO
5 PREVENT ISCHEMIC NEPHROPATHY AND RENOVASCULAR
6 HYPERTENSION AND TO INCREASE LIFE EXPECTANCY AND
7 PERHAPS REDUCE COMPLICATIONS. AND THE ANSWER IS YES
8 AND NO, SO IF I COULD GO THROUGH THAT, WHEN SHOULD WE
9 INTERVENE AND WHEN SHOULDN'T WE, WHAT DO WE KNOW OR
10 AT LEAST WHAT DO WE THINK WE KNOW?
11 WE ALL KNOW THAT RENAL ARTERY STENOSIS,
12 HYPERTENSION AND RENAL INSUFFICIENCY ARE RELATED AND
13 THAT RENOVASCULAR HYPERTENSION, HYPERTENSIVE
14 NEPHROPATHY AND ISCHEMIC NEPHROPATHY ARE THE
15 CONSEQUENCES AND WHEN THEY ALL OCCUR TOGETHER, WE CAN
16 HAVE RENOVASCULAR HYPERTENSION AND ISCHEMIC
17 NEPHROPATHY.
18 SO, HOW DO WE DECIDE WHO WE SHOULD TREAT?
19 WELL, YOU CAN OBVIOUSLY LOOK AT THE BENEFIT, THE
20 RISK, AND COMPARE IT TO THE NATURAL HISTORY. AND
21 WHAT I WOULD LIKE TO IS SORT OF SORT OUT ALL THESE
22 THINGS AND SEE WHICH FACTORS AFFECT THEM.
23 FIRST OF ALL, ONE OF THE ACCEPTED CRITERIA
24 FOR INTERVENTION, AND I'M GOING TO TRY TO GO THROUGH
25 THE CLINICAL, ANATOMIC AND PHYSIOLOGIC CRITERIA AND

00074

1 TRY TO PUT THEM INTO THIS BALANCE OF RISK, BENEFIT
2 AND NATURAL HISTORY, AT LEAST WHAT WE THINK WE KNOW
3 ABOUT IT.
4 WE KNOW THE CLINICAL CHARACTERISTICS OF
5 RENOVASCULAR HYPERTENSION AND WE KNOW THAT BASICALLY
6 THE END RESULT, END ORGAN DAMAGE IS GREATER WITH
7 RENOVASCULAR HYPERTENSION THAN WITH CORRESPONDING
8 LEVELS OF ESSENTIAL HYPERTENSION, AND WE ALL KNOW THE
9 RISK FACTORS. FOR ISCHEMIC NEPHROPATHY, WE THINK WE
10 KNOW THE CLINICAL CHARACTERISTICS, AND THAT IS NO
11 INTRINSIC FRANK RENAL DISEASE, RECENT ONSET AND
12 PROGRESSIVE AZOTEMIA, HYPERTENSION, OTHER VASCULAR
13 DISEASE, SMOKING, AND USUALLY UNEQUAL KIDNEY SIZE,
14 REPRESENTING THE UNEQUAL INVOLVEMENT OF THE TWO RENAL
15 ARTERIES.
16 SO WHEN SHOULD WE INTERVENE? WELL,
17 GENERALLY SPEAKING, IN RENAL DYSFUNCTION WHICH IS
18 RECENT IN ONSET OR PROGRESSIVE, AND IS MODERATE OR
19 SEVERE. IN HYPERTENSION WHICH IS SEVERE OR DIFFICULT
20 TO CONTROL. IN PULMONARY EDEMA WHICH IS RECURRENT
21 FLASH EDEMA. AND PERHAPS IN JEOPARDIZED RENAL
22 PARENCHYMA, AND I'LL EXPLAIN THAT IN A FEW MOMENTS.
23 WHAT ARE THE CONTRAINDICATIONS CLINICALLY?
24 WHILE ALL THESE WERE LISTED AT ONE TIME, I THINK THAT
25 MOST OF THEM ARE NOT.

00075

1 NOW WHAT IS THE BEST ANATOMIC SCREENING?
2 WELL, YOU CAN GO THROUGH MRA, DUPLEX ULTRASOUND, CTA,
3 INTRA-ARTERY DIGITAL, AND THESE ARE THE ANATOMIC
4 CRITERIA THAT MOST OF US ACCEPT. CERTAINLY A SEVERE
5 STENOSIS RESULTING IN AN 85 PERCENT CROSS-SECTIONAL
6 AREA STENOSIS, ANGIOGRAPHIC POST-STENOTIC DILATATION,
7 COLLATERALS, AND REDUCTION OF RENAL SIZE BEYOND THE
8 EXPECTED VARIATIONS, THAT IS A LENGTH DISCREPANCY AT
9 LEAST 1.5 CENTIMETERS AND A DOCUMENTED DIMINUTION IN
10 LENGTH OF AT LEAST ONE CENTIMETER.
11 ARE THESE ANATOMIC CONTRAINDICATIONS TO
12 THE INTERVENTION? WELL, AT ONE TIME THEY WERE
13 THOUGHT TO BE. MOST OF US AGREE THAT THEY ARE NOT.
14 I THINK THE MOST IMPORTANT IS PHYSIOLOGIC
15 SCREENING AND THE CRITERIA WE APPLY TO THEM.
16 RADIONUCLIDE SCANNING IS CURRENTLY EASY BUT
17 UNFORTUNATELY UNRELIABLE IN BILATERAL DISEASE AND IN
18 THE PRESENCE OF SERUM CREATININE. RENAL RENIN ASSAY
19 IS ALSO AN ATTRACTIVE PHYSIOLOGICAL TEST, BUT AGAIN,
20 IT'S UNRELIABLE IN BILATERAL DISEASE AND THE PRESENCE
21 OF INCREASED SERUM CREATININE, AND IT IS INVASIVE.
22 DUPLEX ULTRASOUND IS UNFORTUNATELY
23 TECHNICALLY DIFFICULT AND OPERATOR-DEPENDENT, BUT
24 EVERY SINGLE PATIENT WHO UNDERGOES RENAL ANGIOPLASTY
25 OR STENT COULD POTENTIALLY, AND I BELIEVE MORE THAN

00076

1 POTENTIALLY, SHOULD HAVE A MEASUREMENT OF THE AORTA
2 RENAL PRESSURE GRADIENT AND SHOULD HAVE A MINIMUM OF
3 A 10 PERCENT PEAK SYSTOLIC PRESSURE GRADIENT TO
4 JUSTIFY INTERVENTION. NOW, I USED TO TALK ABOUT THE
5 10 PERCENT GRADIENT WITHOUT ANY GOOD DATA WHEN PEOPLE
6 WERE TALKING ABOUT ABSOLUTE GRADIENTS OF 10 AND 15,
7 AND SOMETIMES 20-MILLIMETER GRADIENT. INTERESTINGLY,
8 DEBRUYNE DID A VERY NICE STUDY THAT DEMONSTRATED IN
9 HUMANS AFTER STENTING AND PRODUCING GRADIENT
10 STENOSIS, THAT GRADIENT READINGS DID NOT BEGIN UNTIL
11 YOU REACHED A 10 PERCENT DROPOFF, A 10 PERCENT
12 CHANGE, AND THEN YOU COULD SEE THAT GRADIENT READINGS
13 BEGAN FROM THE STENOTIC KIDNEY AND ELEVATED, WERE
14 SLIGHTLY ELEVATED SYSTEMICALLY.
15 SO I THINK THAT THIS STUDY SHOWS, AT LEAST
16 IN TERMS OF RENIN PRODUCTION, WHICH MOST OF US AGREE
17 IS A MARKER FOR THE MEASURE, THE BEST WAY TO EVALUATE
18 AT LEAST EXPERIMENTALLY IS IN THE PRESENCE OF A
19 SIGNIFICANT RENAL ARTERY STENOSIS. SO THAT I THINK
20 ILLUSTRATES THAT A 10 PERCENT GRADIENT IS CERTAINLY
21 THE MINIMUM JUSTIFIABLE.
22 PRACTICALLY, HOW DO WE MEASURE THIS? WE
23 SHOULD HAVE A CATHETER WHICH IS SMALLER THAN FOUR
24 FRENCH IN THE RENAL ARTERY AND MINIMALLY TO THE
25 STENOSIS, A SHEATH LARGE ENOUGH IN THE AORTA OR THE

00077

1 FEMORAL ARTERY TO MEASURE THE AORTIC PRESSURE, AND IF
2 THERE'S NO GRADIENT, IT MEANS EITHER THAT THE
3 STENOSIS IS NOT PHYSIOLOGICALLY SIGNIFICANT OR THAT
4 THERE'S AN INCREASED RENAL PERIPHERAL VASCULAR
5 RESISTANCE, THE EQUIVALENT OF THE RESISTIVE INDEX
6 BEING INCREASED, AND IN THESE CASES THERE SHOULD BE
7 NO INTERVENTION BECAUSE THE KIDNEY IS NONSALVAGEABLE,
8 OR SHOULDN'T BE.
9 SO WHAT IS OUR ALGORITHM? WE BELIEVE THAT
10 CLINICAL SUSPICION AND PLASMA RENIN ACTIVITY WITH ACE
11 INHIBITION, THE SO-CALLED CAPITAL CHALLENGE TEST, IS
12 CERTAINLY A PRETTY GOOD OFFICE TEST TO SCREEN
13 PATIENTS, AND THEN WE HAVE AVAILABLE ALL THESE TESTS.
14 THE IMPORTANT THING IS TO TAKE ONE, THE ONE YOU
15 REALLY DO BEST. I BELIEVE MRA WITH GADOLINIUM IS
16 STILL, IN SPITE OF ALL THE SCARE WITH THE FIBROTIC,
17 WHATEVER IT'S CALLED, LESIONS, IT'S PROBABLY ONLY IN
18 150 PATIENTS REPORTED WORLDWIDE AND IT SHOULDN'T
19 SCARE PEOPLE AWAY FROM GADOLINIUM IN APPROPRIATE
20 PATIENTS. AND IF YOU HAVE A STENOSIS WHICH LOOKS
21 SIGNIFICANT, YOU SHOULD DO A DIGITAL THAT MEASURES
22 THE PRESSURE AND, IF APPROPRIATE, INTUBATE OR TAKE
23 THE PATIENT TO MEDICAL THERAPY.
24 AN ISCHEMIC NEPHROPATHY IS EVEN EASIER.
25 IF THE PATIENT DOES NOT HAVE KNOWN MEDICAL

00078

1 PARENCHYMAL DISEASE, YOU DO AN ULTRASOUND OR AN MRA
2 LOOKING FOR RENAL SIZE ASYMMETRY, RENAL ARTERY
3 STENOSIS, PERHAPS INCREASED RESISTIVE INDEX, BUT I
4 DON'T BELIEVE THAT SHOULD DEPRIVE ANYONE OF
5 INTERVENTION. MEASURE THE GRADIENT AND DO A DIGITAL.
6 IF APPROPRIATE, INTERVENE, OR SEND THE PATIENT TO
7 MEDICAL THERAPY. AND QUITE HONESTLY, TWO-THIRDS OF
8 OUR PATIENTS AT CORNELL NOW FALL INTO THE ISCHEMIC
9 NEPHROPATHY GROUP, NOT IN THE HYPERTENSION GROUP,
10 BECAUSE THE HYPERTENSION GROUP IS SO HETEROGENEOUS
11 AND THE ENDPOINT OF HYPERTENSION WITH CHANGING DRUG
12 REGIMENS IN BETWEEN IS VIRTUALLY USELESS IN MY
13 OPINION.
14 SO WHEN SHOULD YOU NOT INTERVENE? WELL,
15 WHEN THERE IS NO SIGNIFICANT GRADIENT, WHEN THE BLOOD
16 PRESSURE IS EASILY CONTROLLED, WHEN THERE'S MILD
17 STABLE RENAL DYSFUNCTION. AND CERTAINLY IN
18 INCIDENTALY DISCOVERED STENOSIS WITHOUT PRIOR
19 CLINICAL EVALUATION, YOU SHOULD NOT INTERVENE.
20 SO OBVIOUSLY WHAT I'D LIKE TO DO IS TO
21 SORT OF GO THROUGH NOW WHAT I BELIEVE IS SOME OF THE
22 JUSTIFICATION OR LACK OF JUSTIFICATION IN THE
23 LITERATURE. CERTAINLY YOU WANT TO INTERVENE WHEN THE
24 BENEFIT IS GREATER THAN THE RISK, AND THEY EXCEED
25 THAT OF THE NATURAL HISTORY OF THE DISEASE.

00079

1 SO LET'S TALK A LITTLE BIT ABOUT THE
2 NATURAL HISTORY. I THINK THE BEST STUDY, THE
3 PROSPECTIVE STUDY BY CAPS THAT I ALREADY ALLUDED TO,
4 AND THEY BASICALLY SHOWED THAT ALTHOUGH RENAL ARTERY
5 STENOSIS IS PROGRESSIVE, PROGRESSION TO OCCLUSION IS
6 VERY RARE. AND THESE ARE SOME OF THE DATA AND IT
7 SHOWS THAT THE HIGHER THE STENOSIS AT THE BEGINNING,
8 THE GREATER THE PROGRESSION. IT ALSO SHOWED THAT 60
9 PERCENT STENOSIS PROGRESSED GREATER THAN NORMAL. AND
10 IT SHOWED THAT PROGRESSION OF OCCLUSION IS VERY
11 INFREQUENT AND RARE, AS YOU ALREADY HEARD.
12 NOW ONE DAY I JUST LOOKED AT THE U.S.
13 CENSUS DATA AND I MUST SAY THAT WAS QUITE A WHILE
14 AGO, SO THIS DATA IS NOT PROPORTIONATELY ACCURATE,
15 BUT THIS IS WHEN THERE WERE 78 MILLION PEOPLE IN THE
16 U.S. POPULATION OLDER THAN 50, AND WHAT I DID WAS I
17 LOOKED AT THE DATA IN THE LITERATURE FOR THE
18 PREVALENCE OF THE DISEASE AND THE PROGRESSION OF THE
19 DISEASE, AND I APPLIED THAT TO THE U.S. POPULATION,
20 AND THESE ARE THE DATA. AND IT CAME OUT THAT ABOUT
21 8.5 MILLION PATIENTS SHOULD BE PROGRESSING TOWARD
22 RENAL DYSFUNCTION, BUT WE KNOW FROM MY OWN DATA THAT
23 IT'S AROUND 11,000. NOW YOU CAN ALTER EACH OF THESE
24 BY A FACTOR OF SEVERAL, BUT IT'S STILL VALID.
25 THIS IS THE SAME FOR PATIENTS OLDER THAN

00080

1 74 AND IT'S SIMILAR DATA.
2 SO, I BELIEVE THAT THE PREVALENCE AND
3 PROGRESSION OF RENAL ARTERY STENOSIS AND RENAL
4 DYSFUNCTION ARE EXAGGERATED. ALMOST ALL PROGRESSION
5 DATA PREDATE CURRENT SMOKING CESSATION, DIET,
6 EFFECTIVE BLOOD PRESSURE AND GLUCOSE CONTROL, AND
7 STATINS. AND NO LARGE RETROSPECTIVE -- OR NO LARGE
8 PROSPECTIVE RANDOMIZED STUDY HAS EVER BEEN DONE TO
9 COMPARE MEDICAL THERAPY, SURGERY OR STENTING, CORAL
10 HOPEFULLY BEING THE EXCEPTION.
11 ALL RIGHT. SO LET ME LOOK AT A WHOLE
12 BUNCH OF DIFFERENT POTENTIAL TREATMENTS. ONE OF THE
13 REAL MAJOR ISSUES, I BELIEVE, THAT CONFRONTS ALL OF
14 US, IS WHAT DO WE DO WITH CLINICALLY AND
15 PHYSIOLOGICALLY NONSIGNIFICANT RENAL ARTERY STENOSIS?
16 IN OTHER WORDS, DOES PROPHYLACTIC RENAL ARTERY
17 STENTING WORK, WHAT'S THE EVIDENCE FOR IT?
18 WELL, A LOT OF THE EVIDENCE IS BASED ON
19 THE FACT THAT RENAL ARTERY STENOSIS MAY BE AN
20 INDEPENDENT VARIABLE IN LIFE EXPECTANCY. AND SOME OF
21 THE DATA CITED TO SUPPORT THIS IS THIS STUDY FROM
22 SCOTLAND WITH 121 CONSECUTIVE PATIENTS WHO HAD RENAL
23 ARTERY STENOSIS AND HYPERTENSION. THE QUESTION IS,
24 AND I SUSPECT RENAL ARTERIAL HYPERTENSION, WHICH IS
25 DIFFERENT THAN RENAL ARTERY STENOSIS. AND THEY

00081

1 SHOWED THAT THE FIVE TO 12-YEAR SURVIVAL WAS LOWER
2 THAN IN AGE AND SEX-MATCHED HYPERTENSIVE CONTROLS WHO
3 DID NOT HAVE RENAL ARTERY STENOSIS.
4 THE PROBLEM WITH THIS IS THAT RENAL ARTERY
5 STENOSIS IS NOT RENAL ARTERY HYPERTENSION, AND RENAL
6 ARTERY STENOSIS IS ALSO A MARKER FOR GENERALIZED
7 VASCULAR DISEASE INCLUDING CORONARY AND
8 CEREBROVASCULAR, WHICH DO AFFECT LIFE EXPECTANCY. IN
9 FACT, THESE AUTHORS THEMSELVES SAID THAT MULTIVARIATE
10 ANALYSIS SHOWED THAT AGE, CIGARETTE SMOKING AND
11 PRESENCE OF ATHEROMATOUS DISEASE WERE SIGNIFICANTLY
12 AND INDEPENDENTLY RELATED TO OUTCOMES AMONG THE
13 PATIENTS WITH RENOVASCULAR DISEASE.
14 THE SECOND PAPER THAT'S CITED BY ADVOCATES
15 OF SO-CALLED PROPHYLACTIC STENTING IS A PAPER BY
16 ZELLER, WHO SHOWED THAT EVENT-FREE SURVIVAL AFTER
17 RENAL ARTERY STENTING WAS SIGNIFICANT. BUT AN
18 ANALYSIS OF THE SUBSET SHOWED THAT WHEN YOU HAD
19 RELATIVELY LOW SERUM CREATININE TO START, PERHAPS
20 THAT IS NORMAL, VERSUS IN BETWEEN AND VERY SEVERE
21 ELEVATION OF SERUM CREATININE, SHOWED PROGRESSIVELY
22 DIMINISHED SURVIVAL. THIS IS KIND OF INTUITIVE AND
23 WE ALL KNOW THAT. HOWEVER, HE WENT ON TO CONCLUDE
24 THAT SURVIVAL AFTER SUCCESSFUL STENTING FOR SEVERE
25 RENAL ARTERY STENOSIS DEPENDS ON BASELINE SERUM

00082

1 CREATININE AND LEFT VENTRICULAR FUNCTION, AND EFFORTS
2 MUST BE MADE TO AVOID THE DEVELOPMENT OF ADVANCED
3 ISCHEMIC NEPHROPATHY AND CONGESTIVE HEART FAILURE,
4 AND APPLE PIE SHOULD BE HANDED OUT FREELY. WE ALL
5 AGREE.
6 HE WENT ON, HOWEVER, TO SAY THESE DATA
7 EMPHASIZE THE NEED FOR CORRECT AND EARLY DIAGNOSIS OF
8 RENAL ARTERY STENOSIS AND THE NEED TO TREAT THESE
9 PATIENTS AS EARLY AS POSSIBLE TO PREVENT THE
10 DEVELOPMENT OF RENAL FAILURE, WITH A REDUCED LIFE
11 EXPECTANCY. THE TROUBLE IS THAT BY TREATMENT, HE
12 MEANT STENT THESE PATIENTS AS EARLY AS POSSIBLE.
13 NOW, THESE DATA DO PROVE THE NEED FOR CORRECT AND
14 EARLY DIAGNOSIS OF THE RENAL ARTERY STENOSIS, BUT
15 THEY DO NOT PROVE THE NEED TO STENT CLINICALLY AND
16 PHYSIOLOGICALLY NONSIGNIFICANT STENOSES AS EARLY AS
17 POSSIBLE. THEY PROBABLY DO PROVE THE NEED TO
18 MEDICALLY TREAT THESE PATIENTS WITH STATINS,
19 ET CETERA, TO PREVENT THE DEVELOPMENT OF RENAL
20 INSUFFICIENCY, ET CETERA.
21 NOW THE ADVOCATES OF PROPHYLACTIC AND
22 EARLY STENTING SAY THAT IF YOU INTERVENE EARLY, YOU
23 WILL BE WORKING IN A CLEANER AORTA, IT WILL BE A
24 TECHNICALLY EASIER PROCEDURE WITH HIGHER SUCCESS,
25 FEWER COMPLICATIONS, AND YOU MAY BE ABLE TO ALTER THE

00083

1 CLINICAL COURSE OF THE PATIENT. AGAINST THIS IS THE
2 FACT THAT THERE IS NO LONG-TERM BENEFIT PROVEN, AND
3 THERE CAN BE NO IMMEDIATE BENEFIT IN SOMEBODY WHO IS
4 NOT AS SYMPTOMATIC NOR HAS SIGNIFICANT DISEASE.
5 CURRENT MODERN MEDICAL THERAPY MAY BE EQUALLY
6 EFFECTIVE AND THE COMPLICATIONS MAY LEAD TO DIALYSIS,
7 EITHER EARLY OR LATE WHEN THEY BECOME MORE
8 SIGNIFICANT.
9 NOW MEDICAL THERAPY, THE GOALS ARE
10 PREVENTION, SLOWING PROGRESSION, ALTERING THE
11 CLINICAL COURSE, JUST AS IN INTERVENTIONS, AND THE
12 METHODS ARE OBVIOUSLY GLYCEMIC CONTROL, LIPID
13 CONTROL, ANTIHYPERTENSIVES, ALTERED LIFESTYLE, AND I
14 GUESS PLATELET INHIBITION AS YOU ALREADY HEARD, AND
15 WE DON'T KNOW HOW EFFECTIVE THAT IS EITHER.
16 SO IF YOU DECIDE, HOWEVER, NOT TO
17 INTERVENE FOR A PHYSIOLOGICALLY NONSIGNIFICANT
18 STENOSIS, BUT YOU KNOW THAT THE STENOSIS EXISTS, YOU
19 ARE OBLIGATED TO HAVE AGGRESSIVE LIPID, GLUCOSE AND
20 LIFESTYLE MODIFICATIONS, FOLLOW THE PATIENT'S BLOOD
21 PRESSURE, SERUM CREATININE, RENAL SIZE, PERCENT
22 STENOSIS EVERY THREE TO SIX MONTHS. AND IF SERUM
23 CREATININE GOES UP OR THE BLOOD PRESSURE BECOMES
24 UNCONTROLLED OR THE KIDNEY SIZE DIMINISHES, THEN I
25 THINK YOU ARE JUSTIFIED IN INTERVENING. BY THE WAY,

00084

1 THESE ARE PROBABLY VERY MUCH THE SAME THAT YOU WOULD
2 DO IN A PATIENT WHO DID HAVE INTERVENTIONS.
3 NOW LET'S LOOK AT THE JUSTIFICATION FOR
4 MEDICAL THERAPY FOR CLINICALLY AND PHYSIOLOGICALLY
5 NONSIGNIFICANT RENAL ARTERY STENOSIS. WELL, WE KNOW
6 FROM THIS META-ANALYSIS OF TEN STUDIES IN THE CAROTID
7 ARTERIES THAT FOR ATHEROSCLEROSIS, WE KNOW THAT
8 STATINS ARE EFFICIENT AND SAFE TO DECREASE THE RATE
9 OF CAROTID ATHEROSCLEROSIS IN THE LONG TERM, AND
10 AGGRESSIVE STATINS MAY EVEN PROVIDE SUPERIOR EFFICACY
11 FOR CAROTID ATHEROSCLEROSIS REGRESSION.
12 WE ALSO KNOW THE CORONARY BENEFIT, THE
13 INFLUENCE OF ALTERING THE LDL AND HDL LEVELS, AND
14 THIS STUDY SHOWS VERY NICELY THAT AS THERE IS
15 REDUCTION OF LDL OR HDL, CORONARY PLAQUE REGRESSES,
16 AND THIS IS THE PLAQUE VOLUME REGRESSING, AND HERE IS
17 THE LEVEL, THE HDL, AND THE CHANGES IN PLAQUE LEVEL
18 AGAIN GOING BEYOND INTO REGRESSION, AND YOU CAN SEE
19 THAT IN BOTH OF THESE PLAQUE REGRESSIONS.
20 YOU CAN ALSO LOOK AT ANOTHER STUDY ON
21 INTENSIVE VERSUS MODERATE LIPID LOWERING, WHICH IS A
22 FAIRLY CLASSIC STUDY NOW ON ACUTE CORONARY SYNDROMES,
23 AND YOU CAN SEE THAT GIVING A MORE AGGRESSIVE LEVEL
24 OF PRAVASTATIN RESULTS IN DIMINUTION OF THE MACE THAT
25 DEFINITELY LEADS TO A MAJOR CARDIOVASCULAR EVENT.

00085

1 AND HERE YOU CAN SEE THAT EVEN IN A RELATIVELY SHORT
2 PERIOD OF TIME, OUT TO A YEAR AND A HALF, WE CAN
3 BEGIN TO SEE, AND TO TWO YEARS, WE CAN BEGIN TO SEE A
4 SIGNIFICANT REDUCTION OF MACE IN THESE PATIENTS.
5 HERE'S ANOTHER PEER STUDY LOOKING AT THE
6 LEVEL OF STATIN THERAPY AND AGAIN, YOU CAN SEE THAT
7 WITH CONTROLS OF LDL LEVELS, THE PROGRESSION OF
8 ATHERORENAL DISEASE BECOMES SIGNIFICANTLY BELOW, OR
9 AT LEAST EVEN BELOW BASELINE, AND IN CRP IT'S EVEN
10 MORE SIGNIFICANT.
11 SO, A VERY RECENT PAPER ON FACTORS
12 AFFECTING LONG-TERM SURVIVAL FOLLOWING RENAL ARTERY
13 STENTING CONCLUDED THAT PATIENTS RECEIVING
14 LIPID-LOWERING TREATMENT HAD A REDUCTION IN MORTALITY
15 COMPARED TO THESE NOT BEING TREATED. THESE RESULTS
16 MAY REPRESENT PLAQUE STABILIZATION OR DELAYED
17 PROGRESSION OF ATHEROSCLEROTIC CORONARY ARTERY
18 DISEASE. IT MAY ALSO REPRESENT AN EFFECT ON RENAL
19 ARTERY STENOSIS PROGRESSION AND POSSIBLY PRESERVATION
20 OF RENAL FUNCTION LEADING TO AN OVERALL LOWER
21 MORTALITY.
22 NOW, THIS IS THE FIRST STUDY THAT EVEN
23 HINTED SPECIFICALLY ABOUT THE BENEFIT FOR RENAL
24 ARTERY DISEASE WITH LIPID REDUCTION. AND
25 INTERESTINGLY, ZELLER COMMENTED ON THIS, AND HE SAID

00086

1 THE BENEFICIAL OUTCOME OF THIS STATIN DRUG THERAPY
2 FOR PATIENTS WITH RENAL ARTERY STENOSIS CONFIRMS THE
3 STUDY RESULTS OF SECONDARY PREVENTION WITH STATINS IN
4 PATIENTS WITH CAD AND CAROTID ARTERY DISEASE.
5 OKAY. SO LET'S LOOK AT THE RISKS OF
6 INTERVENTION. WHILE WE ALL KNOW THAT CHOLESTEROL
7 EMBOLIZATION IS PROBABLY THE FIRST AND FOREMOST,
8 THERE ARE ALL KINDS OF MECHANICAL PROBLEMS IN
9 CONTRAST NEPHROPATHY, AND WITH STENT EMPLOYMENT ALL
10 KINDS OF TECHNICAL ISSUES. BUT CHOLESTEROL
11 EMBOLIZATION IS PROBABLY THE CRITICAL ISSUE WHICH HAS
12 BEEN REPORTED IN TWO OR THREE PERCENT, BUT VERY FEW
13 STENT SERIES HAVE MANY PATIENTS WITH AZOTEMIA, THAT
14 IS PATIENTS WHO WILL SHOW THAT CHOLESTEROL
15 EMBOLIZATION HAS GLOBALLY CLINICALLY OCCURRED. AND
16 IN SPITE OF THAT, MOST STENT SERIES REPORT A 25
17 PERCENT DETERIORATION OF RENAL FUNCTION, WHICH IS
18 OFTEN ASCRIBED TO NATURAL HISTORY, CONTRAST
19 NEPHROTOXICITY, BUT CHOLESTEROL EMBOLIZATION AT LEAST
20 USED TO BE VERY RARELY LOOKED FOR, EVEN THOUGH MANY
21 OF US SCREAMED ABOUT IT FOR MANY YEARS.
22 NOW, I THINK THIS IS PROBABLY THE BEST WAY
23 TO BEGIN TO UNDERSTAND THIS. THIS IS THE GFR CURVE,
24 AND YOU CAN SEE THAT I COULD TAKE OUT ONE OF YOUR
25 KIDNEYS OR CHOLESTEROL EMBOLIZING TOTALLY, AND IN

00087

1 TERMS OF GLOBAL RENAL FUNCTION MEASURED BY SERUM
2 CREATININE, YOU WOULD NEVER KNOW THE DIFFERENCE, YOUR
3 SERUM RENAL FUNCTION WOULD BE NORMAL. AND IT REALLY
4 ISN'T UNTIL YOU REACH THE KNEE OF THIS EXPONENTIAL
5 CURVE WHERE EVEN 10 PERCENT ADDITIONAL LOSS OF RENAL
6 PARENCHYMA WILL PUT YOU FROM MARGINAL RENAL FUNCTION
7 ON TO DIALYSIS.
8 SO IF YOU ARE MUCKING AROUND WITH PATIENTS
9 IN THE GREEN ZONE, YOU CAN STILL CHOLESTEROL-EMBOLIZE
10 THEM AND NO ONE, INCLUDING YOU AND THE PATIENT, WILL
11 BE WISER. IF YOU ARE TREATING PATIENTS WHERE THE
12 PATIENT POPULATION IS MORE SENSITIVE, THEN YOU WILL
13 FIND MORE CHOLESTEROL EMBOLI.
14 SO, THAT SORT OF LEADS ME TO AN ANALYSIS
15 OF EMBOLIC PROTECTION AND, LET'S SEE, HOW DO WE
16 DECIDE WHETHER IT WORKS. WELL, WHAT'S THE PROBLEM,
17 WHAT ARE THE SOLUTIONS, THE QUALITY AND QUANTITY OF
18 EVIDENCE, ARE THERE CONFOUNDING VARIABLES, AND
19 PERHAPS OTHER SOLUTIONS. SO WE KNOW THAT CHOLESTEROL
20 EMBOLIZATION MANIFESTS WITH DETERIORATION OF RENAL
21 FUNCTION, LIVEDO RETICULARIS, ABDOMINAL PAIN THAT CAN
22 BUILD IN THE GI TRACT, AND PERIPHERAL EOSINOPHILIA.
23 AND I'VE ALREADY SHOWN THAT IT IS RELATIVELY RARELY
24 REPORTED, AND PERHAPS WE WILL FIND OUT FROM CORAL
25 WHAT THE ANSWER IS.

00088

1 LET ME JUST SHOW YOU A TYPICAL PATIENT
2 WITH A LOVELY AORTA AS YOU SEE HERE, SEVERE RENAL
3 ARTERY STENOSIS BILATERALLY, AND YOU CAN SEE WHAT THE
4 PROBLEM IS. HERE IS THE RENAL ARTERY OSTIUM
5 SURROUNDED BY ALL THIS HORRENDOUS ATHEROSCLEROMA, AND
6 YOU KNOW THAT JUST SCRAPING A DIAGNOSTIC CATHETER BY
7 THIS, NEVER MIND TRYING TO PUT A PROTECTION DEVICE OR
8 A GUIDE WIRE ACROSS IT, IS GOING TO SCRAPE OFF
9 CHOLESTEROL PARTICLES AND EMBOLIZE THEM. IN THIS
10 PARTICULAR PATIENT, BECAUSE THE OTHER KIDNEY WAS NOT
11 AS SEVERELY INVOLVED, WE DID INTERVENE AND
12 SUCCESSFULLY PLACED A STENT, AND THIS PATIENT
13 ACTUALLY GOT A SLIGHT BIT BETTER.
14 HERE IS AN EXAMPLE OF WHAT HAPPENS. THIS
15 IS CERTAINLY NOT AMENABLE TO A PROTECTION DEVICE.
16 THIS CHOLESTEROL EMBOLIZATION OCCURRED ONE WEEK AFTER
17 A SUCCESSFUL INTERVENTION WHEN THE CREATININE
18 INITIALLY RESPONDED, AND A WEEK LATER BUMPED, AND WE
19 KNOW THAT ONCE YOU STIR UP CHOLESTEROL IN THE AORTIC
20 WALL, IT MAY CONTINUE TO EMBOLIZE EVEN WITHOUT
21 FURTHER INTERVENTION.
22 NOW, THERE WAS A VERY INTERESTING EX VIVO
23 STUDY WHERE THEY TOOK A CHUNK OF THE AORTAL ARTERY
24 AND DID TYPICAL MANIPULATIONS INVOLVED, AND THEY
25 MEASURED THE SIZE AND NUMBER OF PARTICLES. THE

00089

1 MANIPULATIONS INVOLVED PUTTING GUIDE WIRES ACROSS,
2 BALLOONS AND STENTS, ET CETERA. BUT SIGNIFICANTLY,
3 IF YOU LOOK AT THE PATIENTS WHO HAVE PARTICLES OF
4 SMALLER THAN 10 MICRONS AND PARTICLES THAT ARE HALF A
5 MILLIMETER TO A MILLIMETER, YOU WILL NOTICE THAT
6 SMALLER THAN 10 MICRON WERE THREE MILLION, AND LARGER
7 THAN HALF A MILLIMETER WERE FOUR. SO THE REAL
8 PROBLEM IS THE VERY TINY CHOLESTEROL EMBOLI, AND THE
9 FILTERS HAVE A FILTER PORE SIZE OF 100 MICRONS.
10 CLEARLY THEY ARE NOT GOING TO FILTER THESE PARTICLES.
11 THE QUALITY OF EVIDENCE IS EVEN WORSE.
12 THIS IS A PAPER BY HENRY, 2005, WHO SAID THAT DESPITE
13 GOOD IMMEDIATE AND LONG-TERM RESULTS, POST-PROCEDURAL
14 DETERIORATION OF RENAL FUNCTION IS A CONCERN. IN 20
15 TO 40 PERCENT OF PATIENTS, ATHEROEMBOLISM IS A BIG
16 DEAL.
17 THE SAME DR. HENRY IN 2003 SHOWED THAT IN
18 56 PATIENTS, 18 HAD RENAL INSUFFICIENCY. HE USED A
19 PROTECTION DEVICE AND SHOWED THAT MOST OF THE
20 PATIENTS WERE STABLE, A FEW IMPROVED, AND NONE GOT
21 WORSE. THAT SOUNDS TERRIFIC.
22 IN 2001 THE SAME DR. HENRY SHOWED THAT IN
23 28 PATIENTS, 12 WITH RENAL INSUFFICIENCY, HE GOT
24 SIMILARLY GREAT RESULTS WITH PROTECTION. TERRIFIC.
25 THERE'S ONLY ONE PROBLEM. IN 1999 WITHOUT

00090

1 PROTECTION DEVICES, THE SAME DR. HENRY SHOWED 210
2 PATIENTS, OF WHOM 48 HAD RENAL INSUFFICIENCY. AND 29
3 PERCENT IMPROVED, 67 PERCENT WERE STABLE, AND ONLY
4 TWO PATIENTS OR FOUR PERCENT GOT WORSE. SO THIS IS
5 STATISTICALLY TOTALLY INVALID. THIS MUCH LARGER
6 SHOWS THE SAME RESULTS AS PROTECTION WHEN HE USED IT.
7 HERE'S ANOTHER -- HOW MUCH TIME DO I HAVE
8 LEFT?
9 DR. GARBER: YOU HAVE ABOUT THREE MINUTES.
10 DR. SOS: OKAY. I'VE GOT TO SPEED UP.
11 THIS IS ANOTHER STUDY ABOUT PROTECTION BY HOLDEN IN
12 2003, WHERE HE BASICALLY COMPARED HIS RESULTS WITHOUT
13 PROTECTION AND WITH PROTECTION, AND IT SHOWED
14 MARKEDLY IMPROVED RESULTS WITH PROTECTION, VERY FEW
15 ADVERSE EVENTS AS COMPARED TO WITHOUT, BUT THE
16 NUMBERS WERE SMALL. THE ONLY PROBLEM WAS THAT HIS
17 TECHNIQUE INVOLVED GETTING ACROSS WITH A SMALL
18 CATHETER, USING THE APPROPRIATE DRUGS, USING A VERY
19 SMALL GUIDE WIRE, AND THEN JAMMING AN EIGHT FRENCH OR
20 ALMOST THREE-MILLIMETER DIAMETER DEVICE THROUGH
21 BEFORE HE DEPLOYED THE FILTER. SO I THINK THAT THIS
22 WAS A SHAM PROTECTION DEVICE AND IT'S SORT OF LIKE
23 GOING OUT IN THE RAIN AND WALKING AROUND LIKE THIS,
24 AND THEN WHEN YOU GET HOME YOU PUT UP YOUR UMBRELLA.
25 IN 2006 HE ACTUALLY DID HAVE BETTER RESULTS WITH A

00091

1 BETTER TECHNIQUE AND THESE ARE PROBABLY, DEPENDING ON
2 WHETHER YOU TRUST HIM AFTER ALL THAT, SHOWED
3 IMPROVEMENT.
4 THERE'S ANOTHER STUDY BY EDWARDS, 26
5 PATIENTS, AGAIN A VERY SMALL STUDY, WHICH SHOWED THAT
6 VERY FEW PATIENTS GOT WORSE AFTER USING PROTECTION.
7 SO THERE ARE MANY, MANY PROBLEMS WITH THE
8 PROTECTION DEVICE. THERE ARE TECHNICAL ISSUES, THERE
9 ARE ISSUES OF THE SIZE OF THE PORES, THERE ARE ISSUES
10 THAT CHOLESTEROL EMBOLIZATION MAY OCCUR BEFORE YOU
11 DEPLOY YOUR PROTECTION DEVICE, AND THEY MAY NOT WORK
12 BECAUSE THE PORE SIZE IS TOO BIG, OR THERE MAY BE
13 ISCHEMIA, OR JUST EMPLOYING THE DEVICE MAY BE A REAL
14 ISSUE. SO MICROCHOLESTEROL EMBOLIZATION IS A
15 PROBLEM, THERE MAY BE OTHER WAYS TO DEAL WITH IT, BUT
16 CERTAINLY WE SHOULD DEAL WITH IT, AND CORAL MAY GIVE
17 US THE ANSWER.
18 SO IN SUMMARY, IS STENTING IN CLINICALLY
19 AND PHYSIOLOGICALLY SIGNIFICANT RENAL ARTERY STENOSIS
20 JUSTIFIED TO PREVENT OR REVERSE ISCHEMIC NEPHROPATHY
21 AND RENOVASCULAR HYPERTENSION, AND THE ANSWER TO THAT
22 IS YES.
23 PALMAZ ONCE SAID ONCE THE DIAGNOSIS OF
24 RENAL ARTERY STENOSIS IS ESTABLISHED, PARTICULARLY IN
25 PATIENTS WITH DECREASED RENAL FUNCTIONAL RESERVE,

00092

1 RENAL ARTERY STENOSIS SHOULD BE TREATED WITHOUT
2 DELAY. TO THAT I ADDED HEMODYNAMICALLY SIGNIFICANT
3 RENAL ARTERY STENOSIS.
4 SO THE BENEFITS: THE DRASTIC STUDY
5 REPORTEDLY SHOWED THAT THERE WAS NO BENEFIT. IN
6 FACT, YOU'LL SEE THE RANDOMIZATION. 22 WENT TO
7 ANGIOPLASTY OR THE MEDICAL GROUP, AND I THINK
8 ACTUALLY INSTEAD OF BEING THE CASE AGAINST, THE
9 RESULTS SHOWED FEWER DRUGS, MEDICAL GROUP WAS WORSE,
10 SO ACTUALLY IT PROVES THE CASE FOR INTERVENTION.
11 I'M JUST GOING TO RUSH PAST ALL THIS IF I
12 COULD. WHAT I WANT TO SHOW YOU, IF I CAN GET THIS
13 THING TO MOVE, THE PROBLEM WITH ALL THESE STUDIES IS
14 THAT THE OUTCOME CRITERIA, THE PATIENT SELECTION AND
15 QUANTITATIVE, QUALITATIVE, THEY DON'T ALL REPORT THE
16 SAME DATA AND THEY'RE SORT OF COMPARING PEARS AND
17 APPLES.
18 AND THIS IS FOR RECURRENT PULMONARY EDEMA.
19 NOW, THIS IS THE RENAL FUNCTIONAL RESULT WITHOUT
20 PROTECTION, AND YOU CAN SEE PRETTY MUCH OVERALL THE
21 SAME DATA THAT WE'VE BEEN HEARING, 28 PERCENT
22 IMPROVED, 44 PERCENT STABLE, 28 PERCENT WORSE. AND
23 AGAIN THE QUESTION IS -- OOPS, CAN I GO BACK? HOW DO
24 I GO BACK ONE SLIDE? OKAY, GREAT.
25 SO, IS CORAL THE ANSWER? WELL, THE

00093

1 INITIAL PROTOCOL RANDOMIZED AFTER THE AORTOGRAM IN
2 MANY PATIENTS WITH MODERATE LESIONS, GRADIENTS OR
3 PAIN, AND IN THE OTHERS A VISUAL ESTIMATE WHICH WE
4 ALL KNOW IS PRETTY INACCURATE WHEN USED, AND THE
5 PROTECTION DEVICE INITIALLY WAS PRETTY CRUDE. THE
6 PROTOCOL WAS REVISED AND NOW RANDOMIZES
7 NONINVASIVELY, WHICH I BELIEVE IS A BIG ADVANTAGE,
8 AND THE USE AND PROTECTION DEVICE IS ALSO OPTIONAL,
9 WHICH I ALSO THINK IS BIG ADVANTAGE.
10 SO THERE IS NO EVIDENCE-BASED CLINICAL
11 DATA TO SUPPORT PROPHYLACTIC ANGIOPLASTY AND
12 STENTING. THE LONG-TERM DURABILITY OF STENTS IS NOT
13 KNOWN. EFFECTIVE LIPID CONTROL MAY BE JUST AS GOOD.
14 THEREFORE, PROPHYLACTIC STENTING IS NOT JUSTIFIED.
15 AND THAT'S WHAT THIS SLIDE SAYS, NO PROPHYLACTIC
16 STENTING OF NONSIGNIFICANT LESIONS. ON THE OTHER
17 HAND, SMELL THE STATINS. IT'S THE STATINS, STUPID,
18 THE NEW PARADIGM.
19 IS STENTING IN RENAL ARTERY STENOSIS
20 JUSTIFIED TO PREVENT ISCHEMIC NEPHROPATHY AND MACE?
21 YES.
22 SO PROPHYLACTIC STENTING IS NOT JUSTIFIED.
23 IN CLINICAL AND PHYSIOLOGICAL RENAL ARTERY STENOSIS,
24 INTERVENTION WITH STENTS IS JUSTIFIED. THANK YOU
25 VERY MUCH.

00094

1 DR. GARBER: THANK YOU, DR. SOS. NEXT,
2 DR. LINAS, AND I'M GOING TO ASK YOU TO BE VERY STRICT
3 IN STICKING WITH YOUR TIME HERE.
4 DR. LINAS: THANK YOU VERY MUCH FOR
5 INVITING ME TO SPEAK. MY NAME IS STU LINAS, I'M FROM
6 THE UNIVERSITY OF COLORADO HEALTH SCIENCES CENTER.
7 THE ONLY DISCLOSURE I HAVE, I'M ON THE DSSB OF THE
8 CORAL STUDY.
9 I WAS ASKED TO SPEAK REGARDING A PAPER
10 PUBLISHED IN THE AMERICAN JOURNAL OF NEPHROLOGY
11 EARLIER THIS YEAR AUTHORED BY A NUMBER OF
12 INDIVIDUALS, ONE OF WHICH YOU'VE HEARD MENTIONED
13 SEVERAL TIMES ALREADY TODAY, AND OUR TITLE WAS
14 CONTROVERSIES IN RENAL ARTERY STENOSIS: A REVIEW BY
15 THE AMERICAN SOCIETY OF NEPHROLOGY ADVISORY GROUP ON
16 HYPERTENSION.
17 THIS IS WHAT I WOULD LIKE TO ACCOMPLISH
18 TODAY. AFTER A BRIEF OVERVIEW I'M GOING TO TRY TO
19 DEAL WITH THE FOLLOWING QUESTIONS: DO WE KNOW THE
20 PREVALENCE OF RENAL ARTERY STENOSIS, AND MOST
21 IMPORTANTLY, ISCHEMIC NEPHROPATHY? WHAT ARE THE
22 RISKS ASSOCIATED WITH RENAL ARTERY STENOSIS? WHAT IS
23 THE NATURAL HISTORY OF RENAL ARTERY STENOSIS? WHAT
24 IS THE BEST TEST TO DIAGNOSE RENAL ARTERY STENOSIS
25 AND ISCHEMIC NEPHROPATHY. AND FINALLY, WHAT ARE THE

00095

1 RESULTS WITH BLOOD PRESSURE AND CKD OF CURRENT
2 THERAPIES?
3 RENAL ARTERY STENOSIS CAN BE OF TWO
4 VARIETIES, IT CAN CAUSE RENOVASCULAR HYPERTENSION OR
5 ISCHEMIC NEPHROPATHY. AT LEAST FOR -- THE DATA I
6 WANT TO SHOW YOU TODAY, WE'RE TALKING ABOUT
7 INDIVIDUALS OVER THE AGE OF 40, AND ALL THESE
8 PATIENTS HAVE ATHEROSCLEROSIS.
9 NOW THE DEFINITION OF ISCHEMIC NEPHROPATHY
10 THAT WE USE WAS PROPOSED BY DR. TEXTOR A COUPLE YEARS
11 AGO, DEFINED AS IMPAIRMENT OF RENAL FUNCTION BEYOND
12 OCCLUSIVE DISEASE OF THE MAIN RENAL ARTERY. YOU'LL
13 SEE WHY THAT'S IMPORTANT IN JUST A LITTLE BIT.
14 SO WHAT IS THE PREVALENCE OF RENAL ARTERY
15 STENOSIS VERSUS ISCHEMIC NEPHROPATHY? WELL, IF YOU
16 DO A BROAD BRUSH STROKE OF ATHEROSCLEROTIC RENAL
17 ARTERY STENOSIS, THE PREVALENCE OF A 50 PERCENT OR
18 GREATER NARROWING OF THE RENAL ARTERY IS ALL OVER THE
19 PLACE, OVERALL SOMEWHERE BETWEEN 11 AND 40 PERCENT.
20 THIS IS THE VARIATION DURING AUTOPSY, UNDER AGE 60,
21 OVER AGE 60, IN THE PRESENCE OF CORONARY STENOSIS, IN
22 THE ABSENCE, TRIPLE VASCULAR DISEASE, ET CETERA,
23 ET CETERA. IT REALLY IS ALL OVER THE PLACE. AND IN
24 TRYING TO GET A HANDLE ON THAT, IT LOOKS LIKE IT
25 DEPENDS ON THE POPULATIONS YOU LOOK AT.

00096

1 SO THIS IS A STUDY THAT DR. LEVIN DID A
2 COUPLE YEARS AGO LOOKING AT THE PREVALENCE OF RENAL
3 ARTERY STENOSIS IN PATIENTS UNDERGOING CARDIAC
4 CATHETERIZATION WHO WERE CONSIDERED AT RISK FOR THE
5 DISEASE. THE RISK FACTORS ARE THE USUAL PLAYERS,
6 SEVERE HYPERTENSION, UNEXPLAINED CKD, PULMONARY EDEMA,
7 WITH HYPERTENSION, SEVERE ATHEROSCLEROSIS, EITHER
8 CAROTID OR PERIPHERAL VASCULAR. AND SO WHAT THESE
9 INVESTIGATORS FOUND IN A GROUP OF ABOUT 840 PATIENTS,
10 40 PERCENT OF THE TOTAL GROUP HAD 50 PERCENT RENAL
11 ARTERY STENOSIS. ABOUT 14 PERCENT HAD 50 PERCENT
12 LESION OR MORE, SEVEN PERCENT A 70 PERCENT LESION OR
13 MORE. IT OCCURRED IN PATIENTS WITH SEVERE
14 ATHEROSCLEROSIS; THIS WAS A MUCH SMALLER NUMBER THAN
15 I WOULD HAVE EXPECTED. 16 PERCENT WITH RENAL
16 DYSFUNCTION, NINE PERCENT OF HYPERTENSIVES,
17 ET CETERA, ET CETERA.
18 WHEN ONE DID MULTIVARIATE ASSOCIATIONS,
19 THE BIGGEST ASSOCIATION IN THIS STUDY WAS THE
20 PRESENCE OF CAROTID DISEASE, PERIPHERAL VASCULAR
21 DISEASE. INTERESTING, AND THOUGH NOT REPORTED IN
22 OTHER STUDIES, MORE IN WOMEN, AGE, ET CETERA,
23 ET CETERA. AND SO AT LEAST IN THIS POPULATION, A 40
24 PERCENT PREVALENCE WITH PERIPHERAL VASCULAR DISEASE.
25 NOW LOOK AT THIS POPULATION. VERY

00097

1 DIFFERENT THAN ALLUDED TO BEFORE. THIS IS THE
2 PREVALENCE OF RENOVASCULAR DISEASE IN THE ELDERLY, A
3 POPULATION-BASED STUDY. THIS WAS A CARDIOVASCULAR
4 HEALTH STUDY, MULTICENTER, LONGITUDINAL COHORT STUDY
5 IN FORSYTH COUNTY, NORTH CAROLINA, AND DUPLEX WAS
6 USED TO DETERMINE THE INCIDENCE, AND HERE IT IS. THE
7 OVERALL INCIDENCE IN THIS FREE LIVING POPULATION WAS
8 ABOUT SEVEN PERCENT, VERSUS THE 40 PERCENT IN THE
9 HIGH RISK POPULATION. THIS IS THE AGE INFORMATION,
10 THIS ONE MORE MALE THAN FEMALE.
11 KIND OF THE SAME ACROSS RACE. WE DON'T
12 HAVE TIME TO DISCUSS IT TODAY, THIS HAS BEEN
13 CONTROVERSIAL, BUT IT'S SAID TO OCCUR FEWER TIMES IN
14 AFRICAN-AMERICANS. PROBABLY NOT SO BASED ON THIS AND
15 OTHER DATA. SO THAT'S RENAL ARTERY STENOSIS, MUCH
16 MORE IMPORTANT FOR US TODAY.
17 WHAT ABOUT RENAL ARTERY STENOSIS AS A
18 CAUSE OF END-STAGE RENAL DISEASE? AND IT REALLY
19 DEPENDS ON THE CRITERIA USED TO MAKE THE DIAGNOSIS OF
20 RENAL ARTERY STENOSIS. IS IT DOPPLER DUPLEX DATA, IS
21 IT AORTOGRAM, PATHOLOGY, OR MOST IMPORTANTLY, IS IT
22 THE DEFAULT DIAGNOSIS IN THE CORRECT CLINICAL
23 SETTING? AND WHEN YOU LOOK AT THIS DATA, YOU COME TO
24 THE CONCLUSION THAT IT'S SOMEWHERE BETWEEN FIVE AND
25 EIGHT PERCENT OF THOSE WITH END-STAGE RENAL DISEASE.

00098

1 THIS IS A RECENT STUDY THAT SHOWS THE
2 PROPORTION OF PATIENTS WITH RENOVASCULAR DISEASE
3 LISTED AS THE PRIMARY CAUSE OF END-STAGE RENAL
4 DISEASE FROM THE USRDS DATA SYSTEM. YOU'VE GOT A
5 HANDOUT, UNFORTUNATELY I MISLABELED IT. THE UPPER
6 LINE IS CORRECT HERE, THIS IS THE DIAGNOSTIC CLAIMS
7 DATA, AND YOU CAN SEE OVER THE LAST TEN YEARS THIS
8 HAS INCREASED FROM ABOUT SEVEN PERCENT UP TO MAYBE 11
9 OR 12 PERCENT, BUT IF YOU LOOK AT THE MEDICAL
10 EVIDENCE REPORTS OF THOSE COMING ON TO END-STAGE
11 RENAL THERAPY, IT'S BEEN PRETTY ROCK STABLE AT
12 SOMEWHERE BETWEEN FIVE AND SIX PERCENT. AND SO AT
13 LEAST AS A CAUSE OF END-STAGE RENAL DISEASE, MAYBE
14 IT'S BEEN PRETTY STABLE OVER THE LAST COUPLE OF
15 DECADES.
16 SO WHAT ARE THE RISKS ASSOCIATED WITH
17 RENAL ARTERY STENOSIS? YOU'VE HEARD A LOT OF THIS
18 ALREADY. THIS DATA I'M GOING TO SHOW YOU IS ALSO
19 MEDICARE CLAIMS DATA, A FIVE PERCENT SAMPLE THAT
20 KALRA PUT TOGETHER. THESE ARE COMPARISONS TO THE
21 GENERAL POPULATION FROM A COUPLE YEARS AGO AND THIS
22 IS THE ADVERSE EVENT RATE PER THOUSAND PATIENT YEARS
23 OF THOSE WITH RENAL ARTERY STENOSIS COMPARED TO A
24 CONTROLLED POPULATION. ABOUT A THREEFOLD INCREASE IN
25 ATHEROSCLEROTIC HEART DISEASE, ABOUT A THREEFOLD

00099

1 INCREASE IN STROKE OR TIA, THREEFOLD INCREASE IN
2 PERIPHERAL VASCULAR DISEASE, HEART DISEASE, MOST
3 IMPORTANT IN DEATH PER SE, AND IN THIS PARTICULAR
4 STUDY A 29-FOLD INCREASE IN THE PRESENCE OF RENAL
5 REPLACEMENT THERAPY.
6 YOU'VE HEARD THE DATA ABOUT RENAL ARTERY
7 STENOSIS OVERALL SURVIVAL, YOU'VE SEEN THE DATA FROM
8 CHRIS COOPER OF PLUS-MINUS RENAL ARTERY STENOSIS.
9 THIS IS THE DATA ON SURVIVAL OF THOSE WITH LESIONS
10 THAT ARE LESS THAN 75 PERCENT OF THE RENAL ARTERY AND
11 LESIONS THAT ARE GREATER THAN 75 PERCENT OF THE RENAL
12 ARTERY, AND THERE'S A NICE CORRELATION OF SURVIVAL
13 HERE, IN THAT IF YOU HAVE THE DISEASE, OVER THE SEVEN
14 OR EIGHT YEARS OF FOLLOW-UP, THIS IS A BAD ACTOR AS
15 FAR AS SURVIVAL IS CONCERNED.
16 HOW ABOUT SURVIVAL AFTER DEVELOPING
17 END-STAGE RENAL DISEASE, AND IT TURNS OUT THAT
18 COMPARED TO OTHER TYPES OF CKD, THIS IS A BAD ACTOR.
19 SO, THESE ARE INDIVIDUALS DYING IN THE FIRST YEAR,
20 THIS IS USRDS DATA FROM 2006. ALL END-STAGE RENAL
21 DISEASE IN THIS COUNTRY, ABOUT A BALLPARK, 22 PERCENT
22 ONE-YEAR DEATH RATE. TYPE 2 DIABETES, ABOUT THE
23 SAME. HYPERTENSION, YOU KNOW, A HAIR MORE. BUT
24 THESE ARE INDIVIDUALS WITH RENAL ARTERY STENOSIS,
25 ABOUT A 40 PERCENT DECREASE IN SURVIVAL, INCREASE IN

00100

1 DEATH RATE THE FIRST YEAR OF THOSE WHO HAVE RENAL
2 ARTERY STENOSIS.
3 SO WHAT'S THE NATURAL HISTORY OF RENAL
4 ARTERY STENOSIS? IF YOU HAVE IT, WHAT'S IT MEAN AS
5 FAR AS THE PATIENT IS CONCERNED? WELL, IT REALLY
6 DEPENDS ON WHAT YOU'RE LOOKING AT IT FOR, THE NATURAL
7 HISTORY. ARE WE TALKING ABOUT RENAL ARTERY DIAMETER,
8 ARE WE TALKING ABOUT GFR, OR, MOST IMPORTANTLY, ARE
9 WE TALKING ABOUT RENAL ATROPHY?
10 AND SO THIS IS THE RENAL ARTERY DIAMETER
11 DATA THAT WE PUT TOGETHER. WE FELT THAT IF ONE LOOKS
12 AT PROGRESSION, SOMEWHERE BETWEEN 25 AND 75 PERCENT,
13 AND I'LL COME BACK TO THAT. OCCLUSION, SOMEWHERE
14 BETWEEN EIGHT AND 16 PERCENT. AND THE RESULTS REALLY
15 DEPEND ON THE INITIAL EXTENT OF THE LESION; A TIGHT
16 LESION IS WORSE FOR YOU THAN NOT SO TIGHT LESION.
17 THE TIME OF FOLLOW-UP. MOST IMPORTANTLY, YOU'LL SEE,
18 THE METHODS USED TO DETERMINE RENAL ARTERY STENOSIS
19 AND THE INDICATIONS FOR THE ADDITIONAL STUDIES. WAS
20 IT A CORONARY ARTERY DISEASE DRIVE-BY ARTERIOGRAM,
21 WAS IT FOR PERIPHERAL VASCULAR DISEASE, OR WAS IT
22 SPECIFICALLY FOR RENAL ARTERY STENOSIS.
23 AND SO HERE IS SOME OF THE CORONARY ARTERY
24 ANGIOGRAM STUDY. THIS IS A SEVEN OR EIGHT-YEAR
25 FOLLOW-UP OF INDIVIDUALS THAT HAD ANGIOGRAMS AND WERE

00101

1 FOLLOWED UP. YOU CAN SEE THAT WHETHER ONE HAD A 25
2 PERCENT LESION DURING THE FIRST ANGIOGRAM, THIS
3 INCREASED FROM ABOUT FIVE TO 10 PERCENT; A 50 PERCENT
4 LESION A BIT MORE; A 75 PERCENT LESION. BOTTOM LINE
5 IS THAT OVER SEVEN OR EIGHT YEARS OF FOLLOW-UP, THE
6 CORONARY DATA SAYS THAT IF YOU HAD IT INITIALLY, IT'S
7 GOING TO PROGRESS OVER THE NEXT SEVEN OR EIGHT YEARS.
8 THIS IS THE DATA FROM SEATTLE ON RENAL
9 ARTERY DIAMETER BY DUPLEX SCAN IN PATIENTS WITH
10 PERIPHERAL VASCULAR DISEASE. IT'S INTERESTING DATA.
11 FIVE YEARS OF FOLLOW-UP. THESE ARE INDIVIDUALS WHO
12 HAD NORMAL RENAL ARTERIES TO START WITH, LESS THAN 60
13 PERCENT LESIONS, GREATER THAN 60 PERCENT LESIONS.
14 AND WHAT I WANT YOU TO SEE HERE IS THAT AT THE END OF
15 FIVE YEARS, IF YOU HAD PERIPHERAL VASCULAR DISEASE TO
16 START WITH, EVEN THOUGH YOU HAD A NORMAL VESSEL TO
17 START WITH, AFTER FIVE YEARS, 20 PERCENT NOW HAD
18 ABNORMAL LESIONS. IF YOU HAVE A LESS THAN 60 PERCENT
19 LESION, THIS PROGRESSED DRAMATICALLY. IF YOU HAD
20 MORE THAN A 60 PERCENT LESION, THIS PROGRESSED AS
21 WELL. SO IF YOU HAVE CORONARY DISEASE, IT
22 PROGRESSES, NOT SO BAD. IF YOU HAVE PERIPHERAL
23 VASCULAR DISEASE, IT PROGRESSES AND IT LOOKS LIKE
24 IT'S FAIRLY STRIKING.
25 AND SO, THIS IS THE RENAL ARTERY DATA.

00102

1 HOW ABOUT PROGRESSION AS ASSESSED BY GFR OR NEED FOR
2 END-STAGE RENAL DISEASE THERAPY RATHER THAN RENAL
3 ARTERY PATENCY, I.E., THE REAL DISEASE WE'RE TALKING
4 ABOUT TODAY, ISCHEMIC NEPHROPATHY. WELL, IT TURNS
5 OUT THAT IT AIN'T SO EASY TO PREDICT END-STAGE RENAL
6 DISEASE PROGRESSION THAT'S BASED ON GFR OR RENAL
7 ARTERY DIAMETERS WHEN ONE COMES INTO THE STUDY.
8 I'M GOING TO SHOW YOU A NUMBER OF STUDIES
9 OVER THE LAST FOUR OR FIVE YEARS. FOR THE MOST PART
10 THEY'RE SMALL, THEY'RE NOT LARGE, BUT THEY MAKE A
11 POINT THAT I WANT TO MAKE WITH YOU. AND SO, THESE
12 ARE INDIVIDUALS WITH GREATER THAN 50 PERCENT LESIONS,
13 WHO ARE -- SORRY, THESE ARE CONTROLLED INDIVIDUALS.
14 THESE ARE INDIVIDUALS WITH GREATER THAN 50 PERCENT
15 LESIONS. AND WHAT I WANT YOU TO SEE HERE IS IF YOU
16 LOOK AT SERUM CREATININE, CERTAINLY OVER THE FIRST
17 SIX YEARS OF THIS STUDY, WHETHER YOU DID OR DIDN'T
18 HAVE A 50 PERCENT LESION, IT DIDN'T LOOK LIKE THERE
19 WAS MUCH PROGRESSION. BETWEEN SIX AND EIGHT YEARS,
20 IT LOOKS LIKE THESE TWO GROUPS SEPARATED. IT WOULD
21 BE NICE TO KNOW WHAT THEY LOOKED AT THEREAFTER, BUT
22 WE DON'T HAVE THAT DATA.
23 IT TURNS OUT ALSO, AS YOU'VE HEARD
24 ALREADY, PROXIMAL NARROWING DOES NOT PREDICT GFR
25 EITHER AT THE BEGINNING OF THE STUDY OR THE

00103

1 FOLLOW-UP. AND SO HERE IS THE BEGINNING STUDY, THIS
2 IS AN INDEX OF LUMEN PATENCY GREATER THAN 1.5, AND IN
3 THESE INVESTIGATORS' STUDY WAS CONSIDERED LESS THAN A
4 25 PERCENT LESION, PROGRESSING DOWN TO LESS THAN 0.5
5 LUMEN PATENCY, THEIR MARKER. AND YOU CAN SEE,
6 WHETHER YOU HAD LESS THAN A 25 PERCENT LESION OR MORE
7 THAN ROUGHLY A 75 PERCENT LESION, OVER THE THREE TO
8 FIVE YEARS OF THIS STUDY, THERE WAS NO LOSS OR CHANGE
9 IN GFR OVER TIME.
10 THIS IS A VERY IMPORTANT STUDY, I THINK,
11 WHEN YOU THINK ABOUT THIS DISEASE, BECAUSE IT REALLY
12 GETS AT THE DIFFERENCE BETWEEN THE RENAL ARTERY
13 PER SE AND THE DEGREE OF HIDDEN DISEASE AS WELL.
14 THIS IS, TIME TO END-STAGE RENAL DISEASE IS NOT
15 RELATED TO CONTRALATERAL RENAL ARTERY ANATOMY. AND
16 THIS IS A STUDY THAT LOOKS AT INDIVIDUALS WHO COME IN
17 WITH UNILATERAL RENAL ARTERY STENOSIS, TIGHT STENOSIS
18 ON ONE SIDE. THE OTHER SIDE IS EITHER NORMAL, HAS
19 SIGNIFICANT RENAL ARTERY STENOSIS, MORE THAN A 50
20 PERCENT LESION, INSIGNIFICANT RENAL ARTERY STENOSIS,
21 OR RENAL ARTERY OCCLUSION.
22 AND SO IF YOU COME INTO THIS WITH ONE
23 KIDNEY DOWN AND THE OTHER KIDNEY NORMAL, THEN THE
24 ROUGHLY SIX OR SEVEN-YEAR FOLLOW-UP IS THAT YOUR
25 DIALYSIS FREE SURVIVAL IS PRETTY GOOD. IT AIN'T

00104

1 PERFECT, BUT IT'S PRETTY GOOD. IN CONTRAST, IF YOU
2 COME IN WITH ONE KIDNEY DOWN AND RENAL ARTERY
3 OCCLUSION, THEN YOU DON'T DO VERY WELL OVER THE NEXT
4 FIVE OR SIX YEARS.
5 IT'S THIS MIDDLE DATA THAT'S FASCINATING
6 TO US, AND THAT IS THESE ARE INDIVIDUALS WITH LESS
7 THAN A 50 PERCENT LESION. AND YOU CAN SEE, WITH LESS
8 THAN A 50 PERCENT LESION, THEY DID WORSE THAN THOSE
9 WITH A 50 PERCENT LESION. STATED DIFFERENTLY, IF ONE
10 LOOKED AT AN ANALYSIS OF THE CONTRALATERAL ANATOMY,
11 YOU'VE GOT A NORMAL KIDNEY, YOU SET THE RELATIVE RISK
12 AT ONE; INSIGNIFICANT RENAL ARTERY STENOSIS, THE RISK
13 WAS OVER THREE; SIGNIFICANT RENAL ARTERY STENOSIS,
14 NOT A LOT DIFFERENT THAN NORMAL. SO AGAIN, THE RENAL
15 ARTERY DIAMETER DOESN'T LOOK LIKE THE MAJOR PLAYER.
16 THESE ARE THE SAME INDIVIDUALS NOW, AND
17 NOW WHAT WE'RE GOING TO LOOK AT IS THE GFR ON THE
18 OTHER SIDE. THESE ARE INDIVIDUALS WITH A NORMAL GFR,
19 THESE ARE INDIVIDUALS WHO HAD A GFR GREATER THAN 25
20 MLS PER MINUTE, AND REMEMBER, THIS IS A SOLITARY
21 KIDNEY, THESE ARE INDIVIDUALS WITH GFR BETWEEN 10 AND
22 25, AND THESE ARE INDIVIDUALS WITH LOW GFR. AND YOU
23 GET THE SENSE HERE THAT IN THIS PARTICULAR STUDY, THE
24 ISSUE IS NOT RENAL ARTERY DIAMETER, BUT BASICALLY GFR
25 THAT REALLY DETERMINES IT. AND SO HERE ARE THE

00105

1 RELATIVE RISKS. SET AT ONE; 1.41 IF THE GFR GOES TO
2 25 TO 50; 10 TO 25 A FOURFOLD INCREASE; IF IT WAS
3 LESS THAN 10, A 30-FOLD INCREASE.
4 AND SO HERE'S THE ANATOMY DATA, THE GFR
5 DATA. HOW ABOUT IF YOU LOOK AT THE RENAL BIOPSY
6 SCORE IN INDIVIDUALS WITH RENAL ARTERY STENOSIS? A
7 SMALL STUDY, THERE ARE A COUPLE OF THESE SMALL
8 STUDIES, AND WHAT I WANT YOU TO SEE HERE IS OVER TIME
9 IF YOU LOOK AT CHANGE IN CREATININE CLEARANCE AND
10 SOME INDICATION OF RENAL DAMAGE OR FIBROSIS,
11 NEPHROSCLEROSIS, ET CETERA, YOU CAN SEE THAT OVER THE
12 TIME OF FOLLOW-UP, THAT IN FACT THERE WAS A TIME
13 RELATIONSHIP BETWEEN WHAT THE BIOPSY LOOKS LIKE AND
14 PROGRESSION. SO THE BEST PREDICTOR OF PROGRESSION IS
15 CLEARLY NOT RENAL ARTERY DIAMETER; IT'S GFR UPON
16 PRESENTATION AND/OR THE EXTENT OF RENAL FIBROSIS.
17 SO WHAT'S THE BEST TEST TO DIAGNOSE RENAL
18 ARTERY STENOSIS OR ISCHEMIC NEPHROPATHY? YOU'VE
19 HEARD THIS ALREADY. THERE ARE A WHOLE BUNCH OF TESTS
20 OUT THERE, BE IT ACEI-INDUCED INCREASES IN RENIN,
21 ACEI RENOGRAPHY, DUPLEX ULTRASOUND, MRAS, AND OF
22 COURSE THERE ARE OTHER STUDIES AS WELL. THE BOTTOM
23 LINE WHEN ONE LOOKS AT SENSITIVITY, SPECIFICITY OR
24 POSITIVE PREDICTIVE VALUE, WHETHER YOU USE ACEI
25 RENOGRAPHY, DUPLEX, MRA OR CAPTOPRIL RENOGRAM, IF YOU

00106

1 LOOK AT THIS DATA, IT'S ALL OVER THE PLACE AND ALL
2 LOOKS THE SAME. AND SO JUST BECAUSE IT'S CLOSEST TO
3 ME, THE POSITIVE PREDICTIVE VALUE CONSISTENTLY WAS
4 SOMEWHERE BETWEEN 70 AND 100 PERCENT WHEN WE LOOKED
5 AT THIS DATA.
6 AND SO HERE'S A PROBLEM WITH THE
7 NONINVASIVES. ANOTHER TELLING STUDY, THIS IS AN
8 INTERESTING STUDY BY THIS INVESTIGATOR, AND WHAT HE
9 WAS LOOKING FOR IS, HE WAS LOOKING FOR A FOUR-POINT
10 SCALE OF AGREEMENT, EITHER NOTHING, NO LESION, A LESS
11 THAN 50 PERCENT LESION, GREATER THAN 50 PERCENT
12 LESION, OR A GREATER THAN 80 PERCENT LESION AMONG SIX
13 TO SEVEN RADIOLOGISTS. NOW I WOULD HAVE THOUGHT THAT
14 THAT WOULD BE A NO-BRAINER, THAT THE RADIOLOGISTS
15 COULD GET THEIR ACT TOGETHER ON THIS ONE.
16 HERE'S THE DATA. WITH DSA, ABOUT 40
17 PERCENT AGREEMENT. WITH MRA IT LOOKS LIKE ABOUT 60
18 PERCENT AGREEMENT, FLOW STUDY, ABOUT 40 TO 50 PERCENT
19 AGREEMENT. SO HERE'S THE PROBLEM. IF THE
20 RADIOLOGISTS CAN'T AGREE ON THIS STUFF, HOW THE REST
21 OF US WHO ARE PRIMARY PROVIDERS ARE GOING TO AGREE,
22 IT'S TOUGH. AND SO WHEN ONE LOOKS AT ATHEROSCLEROTIC
23 RENAL ARTERY STENOSIS, THE BEST TEST REALLY IS CENTER
24 DEPENDENT, THE LITERATURE IS FAR BETTER THAN REALITY,
25 AND THE BOTTOM LINE, AT LEAST FOR US, IS THAT IF GFR

00107

1 IS OVER 50, ALL ARE ABOUT THE SAME; IF THE GFR IS
2 UNDER 50, I DON'T THINK WE HAVE THAT DATA TO TAKE A
3 STAND ON THE BEST TEST.
4 SO HERE'S THE CLINICAL DILEMMA. THE TESTS
5 WHICH WERE USEFUL IN DIAGNOSING RENAL ARTERY STENOSIS
6 ARE USEFUL IN DIAGNOSING RENAL ARTERY STENOSIS RATHER
7 THAN ISCHEMIC NEPHROPATHY. ISCHEMIC NEPHROPATHY IS
8 REALLY A PATHOLOGICAL DIAGNOSIS. ARE THERE ADEQUATE
9 SURROGATES FOR PATHOLOGY? THE RENAL ULTRASOUND FOR
10 SIZE AND DENSITY IS LIFE-CHANGER. THE RENAL DOPPLER
11 DETERMINATION OF RESISTIVE INDEX HAS BEEN FORWARDED
12 AS SOMETHING WE CAN UTILIZE, AND I'LL SHOW YOU WHAT
13 WE FEEL ABOUT THAT IN JUST A LITTLE BIT.
14 SO WHAT ARE THE RESULTS FOR BLOOD PRESSURE
15 AND PROGRESSION OF CKD FOR CURRENT THERAPY? DR. BALK
16 HAS SHOWN YOU THE TECHNICAL ANALYSIS. I WOULD REMIND
17 YOU THAT OVER THE LAST SEVERAL YEARS THE NUMBER, THE
18 VOLUME HAS INCREASED FROM ABOUT 7,000 UP TO 18,000,
19 AND THAT WAS THE YEAR 2000. MY SENSE IS IT PROBABLY
20 HAS DOUBLED OR MORE SO SINCE THEN.
21 WHAT ARE THE BENCHMARKS THAT DEFINE
22 SUCCESS? WE HAVE NOT BEEN VERY GOOD AT DEFINING
23 THAT. ARE WE TALKING ABOUT DEATH OR ARE WE TALKING
24 ABOUT RENAL OUTCOMES? AND IF WE'RE TALKING ABOUT
25 RENAL OUTCOMES, IS IT RENAL ARTERY PATENCY, LOSS OF

00108

1 GFR, OR NEED FOR RENAL REPLACEMENT THERAPY? WHAT ARE
2 THE CARDIOVASCULAR OUTCOMES, MI, STROKE, HEART
3 FAILURE, COMBINED OUTCOMES, ET CETERA? SO THE
4 CARDIOVASCULAR OUTCOMES, AS LANCE AND CHRIS COOPER
5 SAID BEFORE, WE REALLY DON'T HAVE PROSPECTIVE
6 STUDIES, WE'RE WAITING FOR THE CORAL STUDIES AS FAR
7 AS THOSE OUTCOMES ARE CONCERNED.
8 HOW ABOUT BLOOD PRESSURE AND RENAL
9 OUTCOMES? WELL, WHEN WE LOOKED AT THIS DATA, WE
10 THOUGHT IN A SUMMARY OF THE NINE STUDIES WE LOOKED
11 AT, THAT SOMEWHERE BETWEEN 15 AND 52 PERCENT IMPROVED
12 RENAL FUNCTION, 28 TO 81 PERCENT WERE STABLE, AND
13 MOST IMPORTANTLY, FOUR TO 54 PERCENT ACTUALLY WERE
14 REPORTED TO HAVE GOTTEN WORSE AFTER STENT PLACEMENT.
15 SO AS FAR AS STENT IS CONCERNED, OUR
16 CONCLUSIONS WERE IT PROBABLY IMPROVED BLOOD PRESSURE.
17 THERE ARE NO QUALITY COMPARATIVE TRIALS. COMPARED TO
18 ANGIOPLASTY ALONE, IT DOES LOOK LIKE THERE'S LESS
19 RESTENOSIS, BETTER PATENCY, BUT REMEMBER, THIS IS
20 ONLY SIX-MONTH DATA.
21 NOW HOW ABOUT SURGERY? THIS HAS BEEN
22 SHORT-SHRIFTED A LITTLE BIT TODAY AND I WANT TO SHOW
23 YOU A RECENT STUDY TO GIVE YOU SOME SENSE OF WHERE I
24 THINK WE ARE AS FAR AS SURGERY IS CONCERNED. THESE
25 ARE INDIVIDUALS WITH PRE-OP SERUM CREATININE LESS

00109

1 THAN 1.8, 1.8 TO ABOUT THREE, AND ABOVE THREE. AND
2 SO LOOK AT THIS WITH ME FOR A SECOND. IF YOUR
3 CREATININE WAS LESS THAN 1.8, ABOUT 30 PERCENT GOT
4 BETTER, 60 PERCENT NO CHANGE, AND STILL, SOME GOT
5 WORSE. IF YOUR CREATININE WAS BETWEEN 1.8 AND THREE,
6 ABOUT 54 PERCENT GOT BETTER IN THIS STUDY, ROUGHLY 40
7 PERCENT THE SAME, A FEW LESS GOT WORSE. AND THESE
8 ARE INDIVIDUALS WITH CREATININE OF THREE, AND THE
9 STUDY SHOWED THAT 58 PERCENT IMPROVED, 34 PERCENT HAD
10 NO CHANGE, AND ABOUT EIGHT PERCENT GOT WORSE.
11 SO THE BOTTOM LINE IN THIS SURGICAL STUDY
12 WAS, AGAIN, NO COMPARISONS, NOT RANDOMIZED, WAS THAT
13 THE RESULTS MAY BE A LITTLE BIT BETTER THAN WE'VE
14 HEARD AS FAR AS TODAY IS CONCERNED.
15 THIS IS DR. BALK'S SLIDE THAT YOU'VE SEEN
16 ALREADY AS FAR AS THE RESULTS OF INTERVENTION. I
17 DON'T WANT TO REPRODUCE THAT, I JUST WANT TO SAY IN
18 OUR OBSERVATION OR IN OUR STUDY THAT WE PUT TOGETHER
19 BEFORE THIS, WE CAME TO THE SAME CONCLUSIONS THAT
20 DR. BALK DID.
21 SO WHY DOESN'T SUCCESSFUL
22 REVASCULARIZATION IMPROVE RENAL FUNCTION? IF YOU'RE
23 FIXING THE RENAL ARTERY, KIND OF, WHY DOESN'T THAT?
24 AND THE REAL DEAL IS, AS DR. TEXTOR ALLUDED TO
25 BEFORE, THAT IT REALLY IS DOWNSTREAM RENAL ATROPHY,

00110

1 DOWNSTREAM RENAL FIBROSIS THAT'S THE NAME OF THE
2 GAME. SO HOW DO YOU ASSESS IT? YOU CAN ASSESS IT BY
3 KIDNEY SIZE AND ECHOGENICITY, KIND OF VERY, VERY SOFT
4 LIGHT CHANGERS. YOU CAN ASSESS IT BY RENAL BIOPSY,
5 PRETTY INVASIVE, YOU CAN'T BE DOING THAT IN MOST
6 PATIENTS. IT'S BEEN SAID TO BE ASSESSABLE BY MRA;
7 THERE'S A LOT OF ISSUES NOW WITH MRA IN THOSE WITH
8 ESTIMATED GFRS LESS THAN 60. AND THE NEW PLAYER OVER
9 THE LAST SEVERAL YEARS HAS BEEN THE DUPLEX DOPPLER
10 RESISTIVE INDEX.
11 THIS IS THE RADERMACHER STUDY THAT ALL OF
12 YOU ARE FAMILIAR WITH AND HAVE SEEN. THIS IS THAT
13 RESISTIVE INDEX PREDICTED CHANGE IN GFR AFTER
14 REVASCULARIZATION. THESE ARE INDIVIDUALS WITH LOW
15 RESISTIVE INDICES WHO HAD NO CHANGE IN GFR AFTER
16 REVASCULARIZATION. THESE ARE INDIVIDUALS WITH HIGH
17 RESISTIVE INDICES WHO DID POORLY AFTER
18 REVASCULARIZATION. THIS HAS BEEN KIND OF THE GOLD
19 STANDARD THAT MANY OF US WERE LOOKING FOR.
20 REPRODUCTION, WHEN THEY DID UNIVARIATE
21 ODDS RATIOS, WHEN THE RESISTIVE INDEX IS HIGH IT WAS
22 VERY HELPFUL. NO RESPONSE TO ACEI RENOGRAPHY, A
23 LITTLE LESS HELPFUL. LOWER GFR, PROTEIN EXCRETION,
24 ET CETERA, ET CETERA. THIS REALLY LOOKED TO BE VERY
25 PREDICTIVE AND VERY HELPFUL TO US, BUT IT TURNS OUT

00111

1 IT AIN'T QUITE AS CLEAN AS WE HAVE BEEN LED TO
2 BELIEVE.
3 NOW THIS IS A RELATIVELY SMALL STUDY BUT I
4 THINK A VERY IMPORTANT STUDY, THAT SAYS RESISTIVE
5 INDEX DOES NOT PREDICT CHANGES IN GFR AFTER
6 REVASCULARIZATION. THIS IS A STUDY THAT LOOKED AT
7 SERUM CREATININE BEFORE AND SHORTLY AFTER
8 REVASCULARIZATION. SO IT AIN'T PERFECT, BUT IT GIVES
9 YOU SOME SENSE THAT MAYBE IT'S NOT GREAT. THESE ARE
10 INDIVIDUALS WITH LOW RESISTIVE INDICES; THIS IS THE
11 CREATININE BEFORE AND AFTER REVASCULARIZATION, NO
12 PROBLEM. THESE ARE RESISTIVE INDICES BETWEEN .7
13 AND .8 THAT, YOU CAN SEE THAT ON AVERAGE, EVEN THOUGH
14 THE RESISTIVE INDEX WAS HIGH, SOME OF THESE
15 INDIVIDUALS GOT BETTER. THESE ARE INDIVIDUALS WITH
16 VERY HIGH RESISTIVE INDICES AND YOU CAN SEE THAT A
17 NUMBER OF THESE INDIVIDUALS GOT BETTER AFTER
18 REVASCULARIZATION. SO EVEN THE RESISTIVE INDEX THAT
19 WE ALL THOUGHT WAS GOING TO BE HELPFUL HAS SOME
20 PROBLEMS.
21 SO, WHICH PATIENTS WITH RENAL ARTERY
22 STENOSIS SHOULD BE STENTED, OR MAYBE OFFERED SURGERY?
23 AND SO AT LEAST FROM OUR PERCEPTION, NOT EVERYONE
24 WITH RENAL ARTERY STENOSIS. IF WE'RE DOING IT FOR
25 CARDIOVASCULAR PROTECTION, WE'RE AWAITING THE RESULTS

00112

1 OF THE CORAL STUDY. AT LEAST FOR RENAL PROTECTION
2 WHEN WE LOOK AT THIS DATA, WE THINK THAT THE PEOPLE
3 WHO ARE MOST LIKELY TO BENEFIT ARE THOSE WITH A
4 RECENT INCREASE IN CREATININE AND THOSE WITH A LOW
5 RESISTIVE INDEX. AND SO AT LEAST FROM THE RENAL SIDE
6 OF IT, THIS WOULD BE THE TARGET ORGAN, TARGET GROUP
7 WE WOULD BE SHOOTING AT, AND FOR CARDIOVASCULAR
8 PROTECTION, WE'RE EAGERLY AWAITING THE RESULTS OF THE
9 CORAL STUDY AS WELL. THANK YOU VERY MUCH.
10 DR. GARBER: THANK YOU, DR. LINAS. WE NOW
11 HAVE A SET OF SCHEDULED SPEAKERS AND THE FIRST
12 SPEAKER WILL BE DR. CHRISTOPHER WHITE.
13 DR. WHITE: THANK YOU VERY MUCH. IT'S A
14 PLEASURE TO BE HERE. I REPRESENT THE SOCIETY OF
15 CARDIAC ANGIOGRAPHY INTERVENTIONS, THEY PAID FOR MY
16 TRAVEL HERE TODAY. OTHER THAN THAT, I HAVE NO
17 FINANCIAL CONFLICTS RELATED TO THIS TOPIC.
18 I WOULD LIKE TO ADDRESS THE ISSUE OF
19 CORRELATION OF RENAL FUNCTION, AND THIS IS THE THIRD
20 DISPLAY, AS I'VE BEEN COUNTING, OF DR. TEXTOR'S DATA.
21 AND AGAIN, TO ME, THIS DATA SUGGESTS THAT THERE ARE
22 SIGNIFICANT PROBLEMS WITH THE NATURAL HISTORY OF
23 RENAL ARTERY DISEASE, AND CLEARLY FOR BILATERAL OR
24 SOLITARY RENAL ARTERY DISEASE.
25 AGAIN, THE THIRD OR FOURTH REPRESENTATION

00113

1 OF DR. CAPS' DATA. CLEARLY THE MORE SIGNIFICANT THE
2 DISEASE, THE MORE LIKELIHOOD OF THE CHANCE OF RENAL
3 ATROPHY. RENAL ATROPHY IS CLEARLY A SURROGATE, BUT I
4 THINK A VERY EFFECTIVE SURROGATE FOR THE LOSS OF
5 RENAL FUNCTION. SO THE MORE LIKELY THE PROGRESSION,
6 THE MORE SEVERE THE STENOSIS, THE MORE LIKELY
7 ATROPHY.
8 AND THEN FINALLY, DEMONSTRATION THAT IF
9 PATIENTS PROGRESS, THEY WILL LOSE RENAL FUNCTION.
10 THIS IS A TRIAL FROM DR. CROWLEY THAT LOOKED AT
11 PATIENTS ON FOLLOW-UP WHO HAD LESS THAN 50 PERCENT
12 RENAL ARTERY STENOSIS WITH NORMAL RENAL FUNCTION.
13 THOSE WHO PROGRESSED TO SEVERE RENAL ARTERY STENOSIS
14 HAD ABNORMAL RENAL FUNCTION. SO A PROGRESSION, IF IT
15 HAPPENS, IS ASSOCIATED WITH LOSS OF RENAL DISEASE.
16 THEY DO NOT NECESSARILY NEED TO PROGRESS TO OCCLUSION
17 TO HAVE THAT PROBLEM.
18 THIS IS DATA THAT REMINDS ME TO TELL YOU
19 THAT THERE'S A DIFFERENCE BETWEEN STENTS AND
20 ANGIOPLASTY. I FIND THAT PROVIDERS WHO ARE NOT IN
21 THE INTERVENTIONAL ARENA COMMONLY BLEND THE WORD
22 INTERVENTION, AND THINK THAT ANGIOPLASTY AND STENTS
23 ARE THE SAME, AND THEY CLEARLY ARE NOT. SO WHEN YOU
24 CONSIDER THIS DATA, YOU HAVE TO MAKE SURE YOU
25 SEPARATE STENT DATA FROM THE ANGIOPLASTY DATA BECAUSE

00114

1 THEY ARE DIFFERENT, AND THERE IS GOOD EVIDENCE THAT
2 STENT THERAPY DOES IMPACT POSITIVELY KIDNEY FUNCTION
3 IN MULTIPLE STUDIES. THESE ARE NOT CONTROLLED
4 STUDIES, THIS DOES NOT SAY THAT STENTS ARE BETTER
5 THAN MEDICAL THERAPY OR ANY OTHER THERAPY, BUT IT
6 DOES DEMONSTRATE TO YOU THAT THERE IS AN EFFECTIVE
7 CHANGE IN RENAL FUNCTION AFTER STENTING.
8 THIS IS A META-ANALYSIS OF DATA THAT
9 ADMITTEDLY, AS YOU'VE HEARD THIS MORNING, IS
10 RELATIVELY WEAK AND CONTAMINATED DATA. BUT THE
11 META-ANALYSIS ITSELF DEMONSTRATES THAT FOR RENAL
12 FUNCTION MEASURED BY SERUM CREATININE, IT FAVORS
13 BALLOON ANGIOPLASTY. IF WE LOOK AT CREATININE
14 CLEARANCE, IT FAVORS BALLOON ANGIOPLASTY,
15 STATISTICALLY SIGNIFICANT. AND IF WE LOOK AT
16 MEDICINES VERSUS BALLOON, AGAIN, NOT STENTED, THE
17 BALLOONS WOULD CONTROL HYPERTENSION, STATISTICALLY
18 SIGNIFICANT. THE META-ANALYSIS OF THESE TRIALS THAT
19 ARE ADMITTEDLY COMPROMISED AND FLAWED, BUT THE DATA
20 CURRENTLY SUGGESTS THAT INTERVENTION WITH BALLOON
21 ANGIOPLASTY STATISTICALLY IS BETTER THAN MEDICAL
22 THERAPY.
23 YOU'VE HEARD ABOUT THE DRASTIC TRIAL. THE
24 DRASTIC TRIAL IS SERIOUSLY FLAWED AGAIN, SINCE
25 CROSSOVER WAS ALMOST HALF THE PATIENTS. BUT WHAT

00115

1 ISN'T OFTEN LOOKED AT IS WHAT HAPPENED TO THOSE
2 PATIENTS AS THEIR OWN CONTROL. THE WAY THE DATA WAS
3 REPORTED WAS AS A COMPARISON BETWEEN THE GROUPS OF
4 INTERVENTION AND MEDICAL THERAPY, AND THERE WAS NO
5 DIFFERENCE AT BASELINE, THERE WAS NO DIFFERENCE AT
6 THREE MONTHS, AND THEN THE CROSSOVER OCCURRED. WHAT
7 THEY DON'T TELL YOU IS THAT IF YOU COMPARE EACH GROUP
8 AS ITS OWN CONTROL, THERE WAS STATISTICAL IMPROVEMENT
9 IN THE BLOOD PRESSURE OF THE INTERVENTIONAL BALLOON
10 ANGIOPLASTY GROUP COMPARED WITH THE MEDICAL GROUP.
11 IT WAS THEN CAUGHT UP WITH THE 44 PERCENT CROSSOVER
12 RATE.
13 THE SECOND RANDOMIZED CONTROLLED TRIAL,
14 THE EMMA TRIAL DID DEMONSTRATE A SIGNIFICANT BENEFIT
15 FOR DIASTOLIC BLOOD PRESSURE. YOU'VE HEARD THAT. IT
16 WOULD HAVE DEMONSTRATED A BLOOD PRESSURE IMPROVEMENT
17 FOR SYSTOLIC AS WELL IF THE NUMBER OF PATIENTS HAD
18 BEEN LARGE ENOUGH, BECAUSE THE DIFFERENCE IS
19 CERTAINLY LARGE.
20 AND THEN FOR BILATERAL DISEASED PATIENTS,
21 IN THE THIRD RANDOMIZED CONTROLLED TRIAL, THIS IS THE
22 SCOTTISH TRIAL, IT DID ACHIEVE STATISTICALLY
23 SIGNIFICANT DIFFERENCE IN THAT BILATERAL SUBGROUP.
24 SO THERE ARE THREE RANDOMIZED TRIALS, ALL
25 OF WHICH DEMONSTRATED STATISTICALLY SIGNIFICANT

00116

1 BENEFIT TO THE INTERVENTIONAL GROUP.
2 THIS IS A TRIAL THAT DEMONSTRATES THE
3 DIFFERENCE BETWEEN STENTS AND BALLOONS. AGAIN, THIS
4 WAS HAMPERED BY A 30 PERCENT CROSSOVER RATE IN THIS
5 TRIAL, BUT IT DEMONSTRATES A PROCEDURE SUCCESS.
6 THERE'S A SIGNIFICANT BENEFIT FOR STENTING OVER
7 ANGIOPLASTY. AND FOR RESTENOSIS, AS YOU'VE HEARD,
8 RESTENOSIS IS ALMOST 50 PERCENT FOR BALLOON
9 ANGIOPLASTY AND IS IN THE MIDDLE TEENS FOR STENTING.
10 THESE ARE TO ADDRESS THE ISSUES OF THE
11 DEFINITIONS. WE ACTUALLY SUBSCRIBE TO THE JNC-7.
12 FOR IMAGING METHODS AND TRANS-LESIONAL
13 GRADIENTS, YOU SAW DR. SOS REPRESENT THIS DATA. THIS
14 IS ELEGANT PHYSIOLOGY THAT DEMONSTRATES WHAT MANY OF
15 US KNOW, AND AS DR. SOS SAID, IF A 10 PERCENT
16 GRADIENT STARTS TO APPEAR, THEN RENIN IS INCREASED
17 FROM THE AFFECTED KIDNEY. WHAT IS VERY IMPORTANT IS
18 THAT THE UNAFFECTED KIDNEY ALSO SEES THIS SIGNAL AND
19 PRODUCES RENIN.
20 SURGERY HAS BEEN RECENTLY ADDRESSED.
21 SURGERY IS NOT THE PREFERRED TREATMENT FOR RENAL
22 ARTERY STENOSIS, AND SURGERY WOULD NOT BE A VERY
23 EFFECTIVE THERAPY IF WE WENT BACK TO OUR HOSPITALS
24 TODAY AND WERE NOT ABLE TO DO RENAL INTERVENTIONS.
25 SURGERY IS COMPLICATED BY INCREASED RISKS, ESPECIALLY

00117

1 IF THERE'S A NEED FOR AORTIC RECONSTRUCTION, IF
2 THERE'S PRE-OP RENAL FAILURE, OR AN AORTIC GRAFT IS
3 USED AS THE SOURCE, AND THERE ARE SOME PROBLEMS WITH
4 SURGERY.
5 THE LONG-TERM DURABILITY OF STENTS HAS
6 BEEN QUESTIONED. THERE ARE ACTUALLY TWO PAPERS THAT
7 HAVE REPORTED LONG-TERM DURABILITY. THIS IS A PAPER
8 BY HENRY IN 1999, WITH A PRIMARY PATENCY OF 78
9 PERCENT OUT MORE THAN FIVE YEARS AND A SECONDARY
10 PATENCY OF OVER 95 PERCENT. SO CLEARLY THE
11 DURABILITY OF STENTS AND THE RESTENOSIS RATE IS FAR
12 BETTER THAN IT IS FOR ANGIOPLASTY.
13 FOR DIAGNOSTIC TESTS, WE HAVE EVIDENCE TO
14 AGREE WITH WHAT DR. LINAS JUST SAID, AND THAT IS THAT
15 THE MORE RAPID A PATIENT'S RENAL DECLINE IS, THE MORE
16 LIKELY THEY WILL BENEFIT. WE'VE DONE SOME WORK AT
17 OUR INSTITUTION IN NEW ORLEANS THAT SUGGESTS THAT THE
18 RENAL FRACTIONAL FLOW RESERVE DOES PREDICT THE
19 PATIENTS WHO ARE LIKELY TO BENEFIT FROM BLOOD
20 PRESSURE, THEIR BLOOD PRESSURE WILL BENEFIT AFTER
21 INTERVENTION WITH A STATISTICALLY SIGNIFICANT BENEFIT
22 WITH FRACTIONAL FLOW RESERVE MEASURED IN THE RENAL
23 ARTERY.
24 AGAIN, PATIENTS WHO HAD A FRACTIONAL FLOW
25 RESERVE LESS THAN .8 HAD ALMOST A 90 PERCENT CHANCE

00118

1 OF BLOOD PRESSURE IMPROVEMENT. THIS IS A GREAT WAY
2 TO SEPARATE PATIENTS WHO ARE BORDERLINE FOR
3 INTERVENTION.
4 DR. GARBER: DR. WHITE, I'M GOING TO HAVE
5 TO ASK YOU TO STOP. THANK YOU. DR. JAFF, AND HE
6 WILL BE FOLLOWED BY DR. MISRA.
7 DR. JAFF: MR. CHAIRMAN, MEMBERS OF THE
8 PANEL, LADIES AND GENTLEMEN, THANK YOU FOR THE
9 OPPORTUNITY. MY NAME'S MICHAEL JAFF. I'M A VASCULAR
10 MEDICINE PHYSICIAN AT MASSACHUSETTS GENERAL HOSPITAL
11 IN BOSTON. I REPRESENT BOTH THE SOCIETY FOR VASCULAR
12 MEDICINE BIOLOGY AND THE VIVA PHYSICIANS GROUP. MY
13 TRAVEL TODAY WAS PAID FOR BY VIVA PHYSICIANS. I DO
14 HAVE CONFLICTS TO INFORM YOU OF. I DO HAVE STOCK
15 OWNERSHIP IN SQUARE ONE INCORPORATED AND PARAGON
16 MEDICAL, AND I HAVE BEEN IN THE PAST OR AM CURRENTLY
17 A CONSULTANT FOR CORDIS ENDOVASCULAR, BOSTON
18 SCIENTIFIC AND MEDTRONIC. I HAVE SPOKEN TO THE
19 SOCIETY FOR VASCULAR MEDICINE AND BIOLOGY, THE VIVA
20 GROUP, AND THE SOCIETY FOR CARDIAC ANGIOGRAPHY
21 INTERVENTION ABOUT THIS SPECIFIC MEETING PRIOR TO
22 THIS DISCUSSION TODAY.
23 WITH SOME BACKGROUND, THE SOCIETY FOR
24 VASCULAR MEDICINE AND BIOLOGY IS THE ONLY
25 PROFESSIONAL MEDICAL SOCIETY OF INTERNISTS WHO

00119

1 DIAGNOSE AND MEDICALLY MANAGE PATIENTS WITH ALL
2 ASPECTS OF VASCULAR DISEASE, INCLUDING RENAL ARTERY
3 DISEASE. VIVA PHYSICIANS IS A NOT-FOR-PROFIT
4 ORGANIZATION OF TEN SPECIALISTS IN VASCULAR DISEASE,
5 INCLUDING VASCULAR SURGERY, INTERVENTIONAL
6 CARDIOLOGY, INTERVENTIONAL RADIOLOGY AND VASCULAR
7 MEDICINE, ALL DEDICATED TO RESEARCH AND EDUCATION IN
8 VASCULAR DISEASE.
9 I PERSONALLY ACT AS THE MEDICAL DIRECTOR
10 OF THE VASCULAR ULTRASOUND CORE LABORATORY FOR THE
11 CORAL TRIAL, AND I AM A NONINTERVENTIONAL PHYSICIAN.
12 THEREFORE, MY INTEREST IN THIS FIELD IS IN THE
13 MANAGEMENT OF PATIENTS WITH RENAL ARTERY DISEASE.
14 ONE IMPORTANT POINT TO NOTE AS YOU'VE
15 HEARD DISCUSSIONS ABOUT MEDICAL THERAPY FOR RENAL
16 ARTERY DISEASE IS THAT THERE REALLY IS NO SPECIFIC
17 DATA DEMONSTRATING THE EFFICACY OF STATINS, ANTILIPID
18 AGENTS OR DIABETES CONTROL AGENTS IN PATIENTS
19 SPECIFICALLY WITH RENAL ARTERY DISEASE. IN ADDITION,
20 MANY PATIENTS WE CARE FOR IN MEDICINE IN THE FIELD OF
21 RENAL ARTERY DISEASE, CARDIOVASCULAR MEDICINE, AND
22 OUTSIDE OF THIS FIELD IN MEDICINE, ARE TREATED
23 WITHOUT LEVEL I RANDOMIZED CONTROLLED DATA, AND WE
24 MAKE DECISIONS AS PHYSICIANS BASED ON THE BEST
25 EVIDENCE THAT EXISTS.

00120

1 WE DO HAVE EXTENSIVE CLINICAL EXPERIENCE
2 IN THE SAFETY OF RENAL ENDOVASCULAR
3 REVASCULARIZATION. I AGREE WITH DR. WHITE AND OTHERS
4 THAT BALLOON ANGIOPLASTY IS NOT STATE OF THE ART
5 THERAPY FOR THIS DISORDER, AND FRANKLY, SHOULD NOT BE
6 CONTINUED IN DISCUSSIONS ABOUT THE TREATMENT OF
7 ATHEROSCLEROTIC RENAL ARTERY STENOSIS. IN ADDITION,
8 WE DO NOT BELIEVE THAT THERE IS ANY DRUG-ELUTING
9 STENT DATA IN RENAL ARTERY DISEASE THAT WOULD OFFER
10 ANY WORTHY DISCUSSION, AND THEREFORE, WE NOT CONTINUE
11 ON THAT EITHER.
12 REGARDING SURGICAL RENAL
13 REVASCULARIZATION, WE BELIEVE THAT THIS CARRIES
14 SIGNIFICANT PERIPROCEDURAL MORBIDITY AND MORTALITY,
15 AND EXCEPT FOR VERY SELECTIVE SCENARIOS, SHOULD NOT
16 BE USED AS A PRIMARY REVASCULARIZATION STRATEGY IN
17 2007 AND BEYOND. THIS IS NOT A SIMILAR DISCUSSION TO
18 THAT OF PROVIDED ENDARTERECTOMY VERSUS CAROTID
19 ENDOVASCULAR THERAPY, AND IN FACT I WOULD SUBMIT TO
20 YOU THAT THERE ARE MANY SKILLED VASCULAR SURGEONS,
21 NEUROSURGEONS AND EVEN OTHER SURGICAL SPECIALISTS,
22 WHO PERFORM EXCELLENT CAROTID ENDARTERECTOMY.
23 HOWEVER, I FEAR THAT AS THE NUMBER OF SURGICAL
24 REVASCULARIZATIONS FOR RENAL ARTERY DISEASE DECLINE,
25 THAT THE NUMBER OF TRAINEES COMING OUT OF

00121

1 INSTITUTIONS WITH EXCELLENT TRAINING PROGRAMS IN
2 VASCULAR SURGERY, WE WILL NOT BE ABLE TO SAY THE SAME
3 FOR RENAL ARTERY SURGERY REVASCULARIZATION.
4 WE STRONGLY SUPPORT THE ENROLLMENT IN THE
5 CORAL TRIAL. HOWEVER, THERE ARE IN FACT A NUMBER OF
6 PATIENTS WHO WOULD NOT BE ELIGIBLE TO PARTICIPATE IN
7 CORAL FOR A NUMBER OF REASONS, AND OTHER RANDOMIZED
8 PROSPECTIVE TRIALS. IN ADDITION, THERE ARE 100 SITES
9 THAT ARE PARTICIPATING IN THE CORAL TRIAL IN THE
10 UNITED STATES AND OUTSIDE THE UNITED STATES, AND THAT
11 DOES NOT ALLOW FOR WIDESPREAD USE IF THERE WERE ANY
12 CONSIDERATION TO RESTRICTING REIMBURSEMENT FOR
13 PATIENTS ONLY IN RANDOMIZED CLINICAL TRIALS.
14 IN AN EFFORT TO EXPAND THE KNOWLEDGE BASE,
15 VIVA PHYSICIANS IS ANNOUNCING THAT WE ARE WORKING ON
16 A PERFORMANCE GOAL INITIATIVE USING A MODERN DATABASE
17 OF OVER 500 PATIENTS THAT HAVE BEEN ENROLLED IN
18 PROSPECTIVE FDA-APPROVED CLINICAL TRIALS. WE CLEARLY
19 AGREE THAT WE NEED TO DO OUR BEST TO MANAGE THESE
20 COMPLEX PATIENTS WITH REFRACTORY AND RESISTANT
21 HYPERTENSION, GLOBAL RENAL ISCHEMIA WITH BASELINE
22 AZOTEMIA, DIALYSIS-DEPENDENT RENAL FAILURE DUE TO
23 RENAL ARTERY DISEASE, ESPECIALLY WITH RAPID
24 DETERIORATION OF RENAL FUNCTION, AND NOT PROPHYLACTIC
25 STENTING. WE SUPPORT DR. SOS'S COMMENTS.

00122

1 AND FINALLY, WE DO NOT BELIEVE THAT THERE
2 IS SIGNIFICANT DATA IN THE LITERATURE TO JUSTIFY ANY
3 CHANGE IN THE REIMBURSEMENT SCHEME FOR RENAL ARTERY
4 DISEASE, AND UNTIL THE CORAL TRIAL AND OTHERS
5 COMPLETE, WE WOULD URGE CONTINUED VIGILANCE IN THIS
6 FIELD. THANK YOU FOR THE OPPORTUNITY.
7 DR. GARBER: THANK YOU, DR. JAFF. NEXT,
8 DR. MISRA, AND HE WILL BE FOLLOWED BY DR. HIRSCH.
9 DR. MISRA: GOOD MORNING. I'M AN
10 INTERVENTIONAL RADIOLOGIST AT THE MAYO CLINIC. MY
11 TRAVEL HERE WAS PAID BY THE MAYO CLINIC AND I RECEIVE
12 AN HONORARIUM TO SERVE ON THE ADVISORY PANEL FOR
13 CORDIS.
14 WHAT I'M HERE TO TALK ABOUT TODAY IS SOME
15 DATA THAT HASN'T BEEN PUBLISHED, TALKING A LITTLE BIT
16 ABOUT HOW DO PATIENTS DO THAT HAVE ENDOVASCULAR
17 TREATMENT OF RENAL ARTERY STENOSIS IN A SETTING OF
18 RENAL SUFFICIENCY. THIS DATA STARTED ABOUT TWO YEARS
19 AGO, A DATABASE THAT WAS ACCUMULATED AT THE MAYO
20 CLINIC, AND I'M GOING TO GO THROUGH SOME OF THIS
21 RATHER QUICKLY SO I CAN ADHERE TO MY SIX MINUTES.
22 MOVING RIGHT INTO -- THE REASON WE STARTED
23 LOOKING AT THIS WAS, HERE'S A PATIENT WHO CAME INTO
24 THE CLINIC AND WAS SEEN BY MYSELF, A NEPHROLOGIST AND
25 OTHERS. AND THE QUESTION WAS, HE'S HYPERTENSIVE,

00123

1 HE'S ON THREE MEDICATIONS, HE'S GOT PROGRESSIVE RENAL
2 SUFFICIENCY, HE'S GOT DIABETES, HE'S GOT PERIPHERAL
3 ATHEROSCLEROTIC DISEASE, AND I'LL SHOW YOU TWO MRAS
4 FOUR YEARS APART WHICH BASICALLY SHOW THAT HE'S GOT
5 BILATERAL RENAL ARTERY STENOSIS.
6 NOW WHAT WAS THE BEST MANAGEMENT FOR THIS
7 GENTLEMAN? IN 2003 HE HAD A GFR ESTIMATED AT THAT
8 TIME OF ABOUT 40. FOUR YEARS LATER, THE SAME GFR.
9 WHAT'S INTERESTING IS IF YOU LOOKED AT HIS URINE, AND
10 I KNOW THERE'S A LOT OF NEPHROLOGISTS HERE, THE
11 PROTEINURIA CHANGED. IN 2003 HE HAD A MILD AMOUNT OF
12 PROTEINURIA, ABOUT 300 MILLIGRAMS IN 24 HOURS. BY
13 2007 THAT HAD PROGRESSED TO MORE THAN A GRAM.
14 SO WHAT'S INTERESTING TO ME AS A
15 RADIOLOGIST IS THAT OVER THE LAST TWO YEARS, THE
16 CHRONIC KIDNEY INITIATIVE HAS RECLASSIFIED LOOKING AT
17 CHRONIC KIDNEY DISEASE, AND THESE NUMBERS ARE NOT
18 ACCURATE, THEY SHOULD BE 90 HERE AND 90 HERE, BUT I
19 WANT TO FOCUS OUR ATTENTION ON STAGE 3, 4 AND 5
20 DISEASE, AND THIS IS WHAT WE WANTED TO LOOK AT. IF
21 YOU HAVE STAGE 3, 4 AND 5 DISEASE AND YOU HAVE RENAL
22 ARTERY STENOSIS AND WE STENTED YOU, WHAT WERE YOUR
23 OUTCOMES?
24 AND HOW DID WE GET AT THIS? WE REVIEWED
25 OUR EXPERIENCE AT SCOTTSDALE, JACKSONVILLE AND

00124

1 ROCHESTER FROM '96 TO 2005, AND CLASSIFIED EVERYBODY
2 INTO A STAGE FOR CHRONIC KIDNEY DISEASE, BASICALLY 1,
3 2, 3, 4 AND 5. AND THE OUTCOMES THAT I WAS MOST
4 INTERESTED IN, AND MANY OF YOU HAVE ALLUDED TO IT, IS
5 WHAT'S MOST IMPORTANT TO ME WAS DID YOU DIE, DID YOU
6 GET TRANSPLANTED, OR DID YOU GO INTO DIALYSIS. THE
7 WAY OUR PRACTICE RUNS, IT'S A VERY TRANSIENT
8 PRACTICE, PEOPLE COME AND GET TREATED AND GO BACK
9 HOME. WE'VE SENT FOR THE U.S. RENAL DATA SYSTEM WITH
10 DIALYSIS TRANSPLANTATION DATA, AND WE'VE GOT THE
11 DEATHS FROM THE SOCIAL SECURITY DATABASE, AND WE
12 LOOKED THROUGH ALL THE ANGIOGRAPHIC CLINICAL DATA
13 SETS. THE OTHER THING WE DID WAS WE CLASSIFIED
14 EVERYBODY INTO A STAGING PHASE BASED ON A
15 MODIFICATION OF DIET RENAL DISEASE FORMULA, AND ALSO
16 DETERMINED THE 24-HOUR PROTEINURIA.
17 WE HAVE TREATED IN THIS TIME PERIOD
18 APPROXIMATELY 1,500 PATIENTS. WE HAD 700 PATIENTS
19 THAT FELL INTO THIS GROUPING, AND THE DATA THAT I'M
20 GOING TO SHOW YOU IS BASED ON LIFE TABLE ESTIMATES
21 AFTER MULTIVARIATE-UNIVARIATE ANALYSIS ON 552
22 PATIENTS. THE REST OF IT IS PENDING.
23 THIS IS WHAT THE BREAKDOWN WAS. WE
24 DIVIDED STAGE 3, I FOUND IT TO BE TOO LARGE OF A
25 STAGE, INTO 3-A AND 3-B. AND WE HAD ABOUT 165

00125

1 PATIENTS, 190, IN STAGE 4 AND STAGE 5. WHAT WE FOUND
2 WAS BASED ON STAGING AND PROTEINURIA AND DIABETES, WE
3 HAD DIFFERENT OUTCOMES. WHAT I'M GOING TO SHOW YOU
4 IS BASICALLY FIVE-YEAR SURVIVAL ESTIMATES FROM THIS
5 DATA.
6 SO THESE WERE THE COMORBIDITIES. I'M
7 GOING TO FLY THROUGH HERE SO I DON'T GET CUT OFF.
8 AND THIS WAS OUR FIRST SLIDE. THERE WAS SIGNIFICANT
9 SURVIVAL DIFFERENCE, AND THIS WAS FOR A COMPOSITE OF
10 DEATH AND FREEDOM FROM DIALYSIS OR TRANSPLANTATION
11 FOR FIVE YEARS. THERE'S A P VALUE. THE PEOPLE DID
12 DIFFERENTLY IF YOU CAME IN WITH DIFFERENT GFRS. SO
13 WE BASICALLY KNEW THAT, OR WE HAD A GOOD IDEA OF
14 THAT.
15 BUT IF YOU LOOKED AT DIFFERENCES IN
16 DIABETICS VERSUS NONDIABETICS, WE HAD A SMALL GROUP
17 OF DIABETICS HERE, THERE WASN'T A DIFFERENCE. BUT
18 WHEN YOU GOT INTO STAGE 3-B, DIABETICS VERSUS
19 NONDIABETICS, THERE WAS A DIFFERENCE, AGAIN,
20 SIGNIFICANT VALUE BY P VALUE AT FIVE YEARS, AND THIS
21 IS THE STAGING.
22 NOW LOOKING AT LOW AND HIGH PROTEINURIA,
23 WE DEFINED LOW PROTEINURIA AS 300 MILLIGRAMS IN 24
24 HOURS OR LESS, AND THERE WERE DIFFERENCES. SAME
25 HERE, 3-A AND 3-B. SO DEPENDING ON GFR, PROTEINURIA

00126

1 WAS A TRUMP CARD AND SO WAS DIABETES. YOU CAN MOVE
2 IN AND LOOK AT THESE CURVES, AND WE'VE SUPERIMPOSED
3 DIABETES WITH LOW AND HIGH PROTEINURIA, NONDIABETICS
4 WITH LOW AND HIGH PROTEINURIA. THE P VALUES,
5 FIVE-YEAR ESTIMATES FOR ALL THREE SURVIVAL, FOR
6 DEATH, DIALYSIS FREE SURVIVAL, TRANSPLANTATION, WHAT
7 A DIFFERENCE.
8 MOVING TO STAGE 4, NOT A LOT OF DIFFERENCE
9 BETWEEN DIABETES AND NONDIABETES, AND IN PART WE HAD
10 LOW NUMBERS OF DIABETICS. THIS WAS AGAIN A
11 RETROSPECTIVE STUDY. YOU CAN SEE WHAT THE SURVIVAL
12 CURVES ARE. FOR GFR BETWEEN LOW AND HIGH
13 PROTEINURIA, AGAIN, SIGNIFICANT DIFFERENCES IF YOU
14 WERE DROPPING PROTEIN. AND THIS IS WHAT THE CURVES
15 LOOKED LIKE SUPERIMPOSED WITH DIABETES WITH LOW AND
16 HIGH PROTEINURIA, SIGNIFICANT DIFFERENCES.
17 FINALLY, STAGE 5, A SMALL GROUP, WE HAD
18 ABOUT 40 PATIENTS. THESE WERE ALL PEOPLE THAT WERE
19 NOT ON DIALYSIS YET. NO DIFFERENCE IN SURVIVAL BASED
20 ON DIABETES OR NONDIABETES. MOVING TO LOW AND HIGH
21 PROTEINURIA, NOT A BIG DIFFERENCE BECAUSE THE N WAS
22 SMALL.
23 SO I THINK, YOU KNOW, WHAT I'VE TAKEN AWAY
24 FROM THIS DATA IS, ONE, AN APPRECIATION FOR PICKING
25 THE PATIENTS. BASELINE GFR IS A STRONG PREDICTOR,

00127

1 PROTEINURIA IS A STRONG PREDICTOR, DIABETES IS A
2 STRONG PREDICTOR FOR A COMPOSITE SURVIVAL, FIVE-YEAR
3 ESTIMATES FOR THIS.
4 ONE OF THE WEAKNESSES OF OUR DATA IS THAT
5 WE DON'T HAVE A CONTROL STUDY. WE'RE SUPPOSED TO BE
6 GETTING ABOUT 400 TO 500 PATIENTS FROM ENGLAND FROM
7 DR. KALERA, WHO HAS FOLLOWED PATIENTS WITH SIMILAR
8 OUTCOMES, AND WE WILL TRY TO MATCH THEM UP IN A CASE
9 CONTROL SETTING. THANK YOU.
10 DR. GARBER: THANK YOU, DR. MISRA. NEXT
11 WILL BE DR. HIRSCH, AND HE WILL BE FOLLOWED BY
12 DR. ZWOLAK.
13 DR. HIRSCH: PANEL AND COLLEAGUES, THANK
14 YOU FOR THE OPPORTUNITY TO PRESENT THE VIEWS OF THE
15 AMERICAN HEART ASSOCIATION. AND FOR INTRODUCTION, MY
16 NAME IS DR. ALAN HIRSCH. I SERVE AS PROFESSOR OF
17 EPIDEMIOLOGY AND COMMUNITY HEALTH AT THE UNIVERSITY
18 OF MINNESOTA SCHOOL OF PUBLIC HEALTH, AND DIRECTOR OF
19 ABBOTT NORTHWESTERN VASCULAR CENTER IN MINNEAPOLIS,
20 MINNESOTA. I HAVE SERVED AS CHAIR OF THE ACC/AHA
21 WRITING COMMITTEE TO DEVELOP GUIDELINES FOR THE
22 MANAGEMENT OF PATIENTS WITH PERIPHERAL ARTERIAL
23 DISEASE.
24 IN THE INTEREST OF FULL DISCLOSURE, AHA
25 RECEIVES LESS THAN ONE PERCENT OF ITS REVENUE FROM

00128

1 PHARMACEUTICAL AND MEDICAL DEVICE INDUSTRIES.
2 PERSONALLY I SERVE AS AN ACTIVE INVESTIGATOR IN A
3 NUMBER OF CARDIOVASCULAR CLINICAL RESEARCH STUDIES,
4 INCLUDING THE CORAL STUDY. HOWEVER, I DO NOT SERVE
5 IN ANY CONSULTING CAPACITY NOR RECEIVE FINANCIAL
6 SUPPORT FROM ANY STENT MANUFACTURING COMPANY.
7 NEITHER THE ASSOCIATION NOR I RECEIVED ANY SPECIFIC
8 FUNDING TO PARTICIPATE IN TODAY'S MEETING.
9 MY TESTIMONY IS BASED PRIMARILY ON THE
10 ACC/AHA 2005 PRACTICE GUIDELINES FOR THE MANAGEMENT
11 OF PATIENTS WITH PERIPHERAL ARTERIAL DISEASE,
12 INCLUDING LOWER EXTREMITY, RENAL, MESENTERIC, AND
13 ABDOMINAL AORTIC DISEASE, AND MY COMMENTS WILL BE
14 OBVIOUSLY MUCH ABBREVIATED FROM THE MARCH 28 LETTER
15 SUBMITTED TO CMS.
16 THESE GUIDELINES HAVE BEEN CO-DEVELOPED IN
17 A PROCESS BEGINNING OVER 25 YEARS AGO IN 1980. IT
18 INVOLVES A RIGOROUS SYSTEMATIC REVIEW OF THE BEST
19 PRINTED SCIENTIFIC EVIDENCE. A BRIEF OVERVIEW OF THE
20 GUIDELINES DEVELOPMENT PROCESS IS PRESENTED IN THIS
21 SLIDE, AND THE GUIDELINE THAT I WILL DISCUSS TODAY
22 WAS CHARTERED IN ORDER TO ASSIST HEALTHCARE PROVIDERS
23 WITH THE CLINICAL DECISION-MAKING, WHICH IS COMPLEX,
24 REQUIRED FOR MAKING THE DIAGNOSIS, MANAGING AND
25 PREVENTING THE THREE MAJOR CLINICAL MANIFESTATIONS OF

00129

1 PAD, INCLUDING ATHEROSCLEROTIC RENAL ARTERY STENOSIS.
2 THESE GUIDELINES FOR RENAL ARTERY STENOSIS
3 IN PAD WERE DEVELOPED BY ACC AND THE AHA IN
4 COLLABORATION WITH THE SOCIETY FOR VASCULAR SURGERY,
5 THE SOCIETY FOR CARDIOVASCULAR ANGIOGRAPHY
6 INTERVENTION, THE SOCIETY FOR VASCULAR MEDICINE AND
7 BIOLOGY, THE SOCIETY OF INTERVENTIONAL RADIOLOGY, AND
8 AGAIN, NOT FOCUSED ON THIS SLIDE, AS WELL AS THESE
9 ADDITIONAL FIVE ORGANIZATIONS WHICH PERFORMED A CLOSE
10 PEER REVIEW AND ENDORSED THIS GUIDELINE, INCLUDING
11 THE NATIONAL HEART, BLOOD AND LUNG INSTITUTE.
12 THESE WERE THE FIRST MAJOR NATIONAL
13 TREATMENT GUIDELINES FOR RENAL ARTERY STENOSIS EVER
14 PUBLISHED, AND THEY DO REPRESENT THE WIDEST
15 PROFESSIONAL ENDORSEMENT AND CONSENSUS EVER ACHIEVED
16 FOR ANY VASCULAR CARE EVIDENCE-BASED GUIDELINE.
17 MANY OF YOU WILL BE FAMILIAR WITH THE
18 METHODS USED FOR THESE GUIDELINES SUMMARIZED IN THIS
19 SLIDE. IN CONSIDERING APPROACHES TO IDENTIFYING
20 PATIENTS WITH RENAL ARTERY STENOSIS WHO WOULD BENEFIT
21 FROM TREATMENT, THE GUIDELINES ASSIGN A
22 CLASSIFICATION OF EACH RECOMMENDATION. A CLASS I
23 RECOMMENDATION, WHICH INDICATES THAT THERE IS
24 EVIDENCE AND/OR GENERAL AGREEMENT THAT A GIVEN
25 PROCEDURE OR TREATMENT IS BENEFICIAL, USEFUL AND

00130

1 EFFECTIVE, IS THE HIGHEST LEVEL OF EVIDENCE.
2 CLASS II RECOMMENDATIONS ARE OBVIOUSLY NOT AS STRONG
3 AND MAY REPRESENT CONFLICTING EVIDENCE OR DIVERGENCE
4 OF OPINIONS. AND CLASS III RECOMMENDATIONS CLEARLY
5 CAN DEMONSTRATE AREAS WHERE THERE IS GENERAL
6 AGREEMENT THAT A PROCEDURE IS NOT BENEFICIAL OR MAY
7 BE HARMFUL.
8 AND THEN EACH CLASS IS OF COURSE
9 IDENTIFIED WITH A SPECIFIC LEVEL OF EVIDENCE UPON
10 WHICH THE RECOMMENDATION IS BASED. LEVEL A BEING THE
11 HIGHEST LEVEL, REPRESENTING INFORMATION FROM MULTIPLE
12 RANDOMIZED TRIALS, LEVEL B INDICATING A SINGLE
13 RANDOMIZED TRIAL OR NONRANDOMIZED STUDIES, AND
14 LEVEL C REPRESENTING GENERALLY OPINION OF EXPERTS,
15 CASE STUDIES, OR THE CURRENT STANDARD OF CARE.
16 NOW BASED ON THE EVIDENCE CURRENTLY
17 AVAILABLE, THE GUIDELINES MADE THE FOLLOWING CLASS I
18 AND IIA RECOMMENDATIONS FOR THE TREATMENT OF
19 ATHEROSCLEROTIC RENAL ARTERY STENOSIS, AND I WILL TRY
20 TO BE BRIEF IN SUMMARIZING THESE. THESE ARE
21 OBVIOUSLY AVAILABLE TO THE PANEL FOR THEIR REVIEW.
22 THE GUIDELINES ENDORSE THE PHARMACOLOGIC TREATMENT
23 FOR ALL INDIVIDUALS WITH ATHEROSCLEROTIC RENAL ARTERY
24 STENOSIS, INCLUDING EACH OF THE VARIOUS CLASS OF
25 MEDICATIONS THAT HAS ALREADY BEEN REVIEWED BY THE

00131

1 PRIOR PRESENTERS. WE DO BELIEVE THAT CLINICIANS
2 SHOULD CONSIDER MEDICAL THERAPY FOR THE TREATMENT OF
3 HYPERTENSION ASSOCIATED WITH ALL PATIENTS WITH
4 UNILATERAL RENAL ARTERY STENOSIS.
5 AND WE KNOW THAT THESE ARE CLASS I
6 RECOMMENDATIONS, WITH THE EXCEPTION OF THAT FOR
7 ANGIOTENSIN RECEPTOR BLOCKERS, WHICH WAS BASED ON
8 DATA FROM A SINGLE TRIAL OR STUDY. BEYOND THAT, ALL
9 THE RECOMMENDATIONS FOR MEDICAL THERAPY WERE BASED ON
10 DATA FROM MULTIPLE RANDOMIZED CLINICAL TRIALS OR
11 META-ANALYSES.
12 FOR ANGIOPLASTY AND STENTING, WE DID
13 RECOGNIZE A MUCH MORE LIMITED DATABASE FOR THE
14 TREATMENT OF ATHEROSCLEROTIC RENAL ARTERY STENOSIS BY
15 ENDOVASCULAR APPROACHES. BUT WE DID RESPECT THE
16 STILL SUBSTANTIAL EVIDENCE SUPPORTING ITS EFFICACY.
17 THE CURRENT EVIDENCE BASE, ALTHOUGH LIMITED, DOES
18 SUGGEST THAT REVASCULARIZATION COULD BENEFIT SELECTED
19 PATIENTS WITH ATHEROSCLEROTIC RAS. FOR EXAMPLE, THE
20 GUIDELINE DOES SUGGEST THAT PHYSICIANS CONSIDER
21 PERCUTANEOUS REVASCULARIZATION IN PATIENTS WITH
22 HEMODYNAMICALLY SIGNIFICANT RAS WHOSE STENOSIS IS
23 ASSOCIATED WITH RECURRENT, UNEXPLAINED CONGESTIVE
24 HEART FAILURE, SUDDEN UNEXPLAINED PULMONARY EDEMA, OR
25 UNSTABLE ANGINA.

00132

1 WE ALSO RECOGNIZED IN THIS GUIDELINE THAT
2 PHYSICIANS CONSIDER PERCUTANEOUS REVASCULARIZATION IN
3 PATIENTS IN WHOM THERE IS A PHYSIOLOGICALLY
4 SIGNIFICANT RAS AND ACCELERATED, RESISTANT, OR
5 MALIGNANT HYPERTENSION, WELL DEFINED IN THE WRITTEN
6 TEXT, HYPERTENSION WITH UNEXPLAINED SMALL UNILATERAL
7 KIDNEY, AS WELL AS INDIVIDUALS WITH HYPERTENSION
8 INTOLERANT TO MEDICATION, OR PATIENTS WITH
9 PROGRESSIVE CHRONIC KIDNEY DISEASE AND BILATERAL
10 ATHEROSCLEROTIC RAS, AS WELL AS INDIVIDUALS WITH
11 ATHEROSCLEROTIC RAS IN A SOLITARY FUNCTIONING KIDNEY.
12 THESE RECOMMENDATIONS WERE ALSO ALL
13 CLASS I OR IIA, LEVEL OF EVIDENCE B, AND BASED ON THE
14 EVIDENCE AVAILABLE, WE WOULD SUGGEST THAT THESE
15 SPECIFIC PATIENT GROUPS ARE CURRENTLY QUITE
16 APPROPRIATE FOR COVERAGE OF RENAL PTA.
17 SURGICAL REVASCULARIZATION IS ALSO AN
18 EFFECTIVE, IF MORE INVASIVE, TREATMENT AND SHOULD BE
19 CONSIDERED FOR PATIENTS IN A NUMBER OF SITUATIONS,
20 INCLUDING THOSE OUTLINED IN THIS SLIDE. FMD WITH
21 CLINICAL INDICATIONS FOR INTERVENTIONS AS DEFINED
22 ABOVE, AND THOSE AS OUTLINED IN THESE THREE BULLET
23 POINTS EXHIBITING COMPLEX LESIONS EXTENDING INTO THE
24 RENAL SEGMENTAL ARTERIES AND THOSE IN INDIVIDUALS
25 HAVING MACROANEURYSMS, INDIVIDUALS WITH MULTIPLE

00133

1 SMALL RENAL ARTERIES OR EARLY PRIMARY BRANCHING OF
2 THE MAIN RENAL ARTERY, AND INDIVIDUALS WHO HAVE
3 UNDERGONE PARARENAL AORTIC RECONSTRUCTION FOR
4 TREATMENT OF ANEURYSMS OR SEVERE AORTOILIAC DISEASE.
5 ALL THREE REPRESENT CLASS I
6 RECOMMENDATIONS SUPPORTED BY LEVEL OF EVIDENCE B OR
7 C, AND WE STRONGLY SUPPORT COVERAGE FOR THESE CLASS I
8 RECOMMENDATIONS.
9 DR. GARBER: DR. HIRSCH, I'LL HAVE TO ASK
10 YOU TO STOP. THANK YOU VERY MUCH, BUT YOUR TIME IS
11 UP. BUT LET ME JUST POINT OUT THAT I BELIEVE THE
12 MEMBERS OF THE PANEL HAVE THIS IN THEIR BOOKS AND
13 ALSO IN THE HANDOUTS FROM TODAY.
14 DR. HIRSCH: MAY I JUST MAKE THE STATEMENT
15 THAT WE OBVIOUSLY SUPPORT ALIGNMENT OF INCENTIVES FOR
16 CLINICAL TRIAL PARTICIPATION. THAT'S IMPORTANT AND
17 YOU HAVE THAT IN YOUR BOOKS. THANK YOU VERY MUCH.
18 DR. GARBER: THANK YOU. DR. ZWOLAK WILL
19 BE FOLLOWED BY DR. KELLEY.
20 DR. ZWOLAK: THANKS VERY MUCH. I'M BOB
21 ZWOLAK. I CHAIR THE HEALTH POLICY COMMITTEE FOR THE
22 SOCIETY FOR VASCULAR SURGERY. I HAVE NO CONFLICTS,
23 BUT SVS PAID FOR MY TRANSPORTATION HERE, AND A
24 DELIGHTFUL EVENING LAST NIGHT AT THE HOLIDAY INN.
25 THE SVS REPRESENTS 2,300 PHYSICIANS IN THE

00134

1 UNITED STATES WHO HAVE BEEN TREATING RENOVASCULAR
2 DISEASE FOR 40 YEARS. SVS IS IN A UNIQUE POSITION TO
3 COMMENT ON RENAL ARTERY PDA AND STENTING, GIVEN OUR
4 COMMUNITY'S HISTORY OF TREATING THIS PROCESS. WHILE
5 OPEN SURGICAL REVASCULARIZATION IS NOT THE CENTRAL
6 FOCUS OF THIS SESSION, A BRIEF REVIEW OF THE
7 REFERENCES SVS SUBMITTED MAKES THE POINT THAT
8 SURGICAL REVASCULARIZATION REALLY HAS BEEN THE
9 STANDARD OF TREATMENT FOR THIS DISORDER FOR MANY
10 YEARS, BUT THAT STANDARD IS CHANGING.
11 SINCE EIGHT TO 15 PERCENT OF PATIENTS WHO
12 DEVELOP END-STAGE RENAL DISEASE HAVE ATHEROSCLEROTIC
13 RENOVASCULAR DISEASE AS THE ONLY DOCUMENTED
14 PATHOLOGY, WE BELIEVE TREATMENT OF THIS ENTITY IS
15 COMPELLING. NATURAL HISTORY STUDIES HAVE SHOWN THAT
16 ATHEROSCLEROTIC RENAL DISEASE TENDS TO PROGRESS OVER
17 TIME, KIDNEYS WITH STENOTIC RENAL ARTERIES UNDERGO
18 ATROPHY OR DETERIORATION OF RENAL FUNCTION. WHILE WE
19 CAN CONTROL BLOOD PRESSURE SUCCESSFULLY IN ALMOST
20 EVERY PATIENT NOW, THE UNFORTUNATE END POINT OF
21 ATHEROSCLEROTIC RENAL DISEASE IS END-STAGE RENAL
22 FAILURE IN A SUBSTANTIAL PROPORTION OF PATIENTS. THE
23 KDOQI GUIDELINES STRESSED THE IMPORTANCE OF RENAL
24 PRESERVATION AND THE BENEFITS ARE CLEAR AND NUMEROUS.
25 THE OPEN SURGICAL DATA HAVE BEEN NICELY

00135

1 SUMMARIZED BY HANSEN, CAMBRIA AND OTHERS AND ARE IN
2 THE RECORDS THAT WE SUPPLIED. THE SURGICAL
3 LITERATURE HAS SHOWN EXCELLENT DURABILITY OF OPEN
4 SURGICAL REVASCULARIZATION IN STABILIZING OR
5 IMPROVING RENAL FUNCTION, BUT THIS IS DERIVED AT A
6 SIGNIFICANT COST IN TERMS OF PERIOPERATIVE MORBIDITY
7 AND MORTALITY. NEVERTHELESS, AT CENTERS OF
8 EXCELLENCE, HYPERTENSION CAN BE CURED OR IMPROVED IN
9 85 PERCENT OF ATHEROSCLEROTIC ADULTS, WITH RENAL
10 FUNCTION AMONG PATIENTS WITH ISCHEMIC NEPHROPATHY
11 DEMONSTRATING A 20 PERCENT OR GREATER INCREASE IN GFR
12 IN APPROXIMATELY 60 PERCENT OF PATIENTS. HANSEN'S
13 SERIES IN FACT INCLUDED 28 OF 35 PATIENTS WHO WERE
14 PERMANENTLY REMOVED FROM HEMODIALYSIS BY SURGICAL
15 REVASCULARIZATION.
16 SO WHERE DOES PERCUTANEOUS INTERVENTION
17 FIT BETWEEN MEDICAL THERAPY AND SURGICAL
18 REVASCULARIZATION? STUDIES SUCH AS THE CORAL WILL
19 PROVIDE INSIGHT BUT RECRUITMENT HAS BEEN SLOW, AND
20 THAT BRINGS ABOUT ITS OWN SET OF ISSUES. I THINK
21 IT'S IMPORTANT TO CITE THE DIFFERENCE IN APPROACH BY
22 VASCULAR SURGEONS NOW COMPARING CAROTID STENTING WITH
23 RENAL STENTING. AFTER TREATING RENOVASCULAR DISEASE
24 FOR DECADES WITH OPEN SURGERY, THE VASCULAR SURGICAL
25 COMMUNITY HAS EMBRACED THE BENEFITS OF RENAL STENTING

00136

1 COMPARED TO THE MAJOR OPEN OPERATIONS NECESSARY TO
2 TREAT RENAL ARTERY STENOSIS. THE DIFFERENCE IN
3 ATTITUDE BETWEEN CAROTID STENTING AND RENOVASCULAR
4 DISEASE RELATES TO THE MAGNITUDE OF THE SURGERY FOR
5 RENOVASCULAR DISEASE, AND IT'S SUBSTANTIAL.
6 SO WHAT SHOULD THE INDICATIONS BE FOR
7 STENTING? THE STANDARD INDICATIONS FOR OPEN SURGERY
8 FOR MANY YEARS HAVE INCLUDED POORLY CONTROLLED
9 HYPERTENSION ON THREE MEDICATIONS, OR PROGRESSIVE
10 ISCHEMIC NEPHROPATHY IN THE PRESENCE OF A SEVERE
11 RENAL ARTERY STENOSIS. IF THREE-DRUG HYPERTENSION IS
12 AN INDICATION FOR OPEN SURGERY, WHAT SHOULD
13 CONSTITUTE AN APPROPRIATE INDICATION FOR STENT
14 PLACEMENT? PROBABLY LESS THAN THAT, BUT STUDIES SUCH
15 AS CORAL MAY HELP US DECIDE THAT.
16 SVS DOES NOT SUPPORT, HOWEVER, WHAT'S BEEN
17 DESCRIBED THIS MORNING AS PROPHYLACTIC STENTING.
18 WHILE I AND MANY OF MY COLLEAGUES ARE VERY SKILLED AT
19 PERFORMING RENAL ARTERY BYPASS, WE WOULD TODAY
20 RECOMMEND RENAL STENT PLACEMENT OVER RENAL BYPASS IN
21 A PATIENT WITH POORLY CONTROLLED HYPERTENSION OR
22 PROGRESSIVE RENAL NEPHROPATHY WITH A SEVERE PROXIMAL
23 RENAL ARTERY STENOSIS.
24 NOW FOR MY LAST FEW MINUTES, I'D LIKE TO
25 ADDRESS SPECIFICALLY SOME OF THE QUESTIONS. MANY OF

00137

1 THESE STUDIES HAVE BEEN CITED ALREADY. FIRST, IS
2 THERE A CORRELATION BETWEEN PERCENT RENAL ARTERY
3 STENOSIS AND RENAL FUNCTION? THE OBVIOUS ANSWER IS
4 YES. IN THE CAPS STUDY, WHICH WAS A PROSPECTIVE
5 NATURAL HISTORY STUDY UNDERTAKEN AT THE UNIVERSITY OF
6 WASHINGTON, 170 PATIENTS WITH RENAL ARTERY STENOSIS
7 GREATER THAN 60 PERCENT WERE FOLLOWED FOR A MEAN OF
8 33 MONTHS. HEMODYNAMIC PROGRESSION OF DISEASE WAS
9 SEEN IN 31 PERCENT OF THE 295 ARTERIES STUDIED. NINE
10 OF THE 295, OR THREE PERCENT, PROGRESSED TO COMPLETE
11 OCCLUSION. THE INCIDENCE OF RENAL ATROPHY AT TWO
12 YEARS, HOWEVER, WAS MUCH MORE SUBSTANTIAL; 21 PERCENT
13 OF THE KIDNEYS WITH GREATER THAN 60 PERCENT STENOSIS
14 DEMONSTRATED RENAL ATROPHY.
15 A STATISTICALLY SIGNIFICANT ASSOCIATION
16 WAS NOTED BETWEEN THE NUMBER OF KIDNEYS PER PATIENT
17 THAT SHOWED ATROPHY AND THE OBSERVED CHANGE IN THE
18 SERUM CREATININE CONCENTRATION. THE MEAN CHANGE OF
19 SERUM CREATININE LEVEL WAS ABOUT 0.1 MILLIGRAMS PER
20 DECILITER PER YEAR AMONG PATIENTS WITH ATROPHY
21 DETECTED IN ONLY ONE KIDNEY, BUT IT WAS SUBSTANTIALLY
22 GREATER, MORE THAN 0.3 MILLIGRAMS PER DECILITER PER
23 YEAR FOR THOSE PATIENTS WHERE ATROPHY DEVELOPED IN
24 BOTH KIDNEYS.
25 REGARDING THE ROLE OF TREATMENT CHOICE

00138

1 BASED ON THE PATIENT'S EXISTING CONDITION AND
2 COMORBIDITIES, OPEN SURGICAL REVASCULARIZATION AS
3 IDENTIFIED BY MARONE AND CAMBRIA IDENTIFIED
4 REVASCULARIZATION AS CLINICALLY BENEFICIAL IN THOSE
5 PATIENTS WITH RAPID DECLINE IN EXCRETORY RENAL
6 FUNCTION, AND ALSO THOSE PATIENTS WITH A DUPLEX
7 ULTRASOUND THAT IDENTIFIED NORMAL RENAL RESISTIVE
8 INDICES, AND I'LL SPEAK ABOUT THAT AGAIN IN A SECOND.
9 THESE WERE LONG-TERM CLINICAL MARKERS OF SUCCESS IN
10 THIS RETROSPECTIVE REVIEW OF 235 PATIENTS PERFORMED
11 AT THE MASSACHUSETTS GENERAL HOSPITAL.
12 REGARDING DISCUSSION QUESTION 2, THE USE
13 OF INTERMEDIATE OR SURROGATE OUTCOMES SUCH AS BLOOD
14 PRESSURE IMPROVEMENT WITH NUMBER OF MEDICATIONS
15 VERSUS HARD HEALTH OUTCOMES SUCH AS MORTALITY,
16 DECREASED MI AND STROKE, SVS BELIEVES THAT BOTH OF
17 THESE FORMS OF OUTCOMES ARE INEXTRICABLY LINKED.
18 YOU'VE SEEN ALL THOSE DATA ALREADY PRESENTED AND
19 THEY'RE BOTH IMPORTANT MEASURES.
20 WITH REGARD TO THE CURRENT STATE OF
21 PRIMARY SURGICAL DIRECTION IN RENAL ARTERY
22 RECONSTRUCTION FOLLOWING STENTING, THE DATA ARE
23 SUBSTANTIAL IN TERMS OF THE PERIOPERATIVE DEATH RATE.
24 PERIOPERATIVE DEATH RATE FOR OPEN RENAL ARTERY
25 REVASCULARIZATIONS IS IN THE THREE TO SIX PERCENT

00139

1 RANGE, ALTHOUGH OFTENTIMES THESE DEATHS OCCURRED IN
2 PATIENTS UNDERGOING SIMULTANEOUS AORTIC AND/OR OTHER
3 REVASCULARIZATION PROCEDURES, OR THEY OCCURRED IN
4 PATIENTS WITH EXTREMELY DIFFUSE ATHEROSCLEROSIS. AS
5 SEEN FROM THE PREVIOUS PRESENTERS, THE PERIPROCEDURAL
6 DEATH RATE FOR RENAL STENTING IS SUBSTANTIALLY LESS,
7 PERHAPS A THIRD TO A HALF OF THAT OF THE SURGICAL
8 TREATMENT OPTION.

9 NUMBER TWO --

10 DR. GARBER: DR. ZWOLAK, I'M SORRY, I'M
11 GOING TO HAVE TO ASK YOU TO STOP. YOUR TIME'S UP.

12 DR. ZWOLAK: OKAY. THANKS VERY MUCH.

13 DR. GARBER: THANK YOU. DR. KELLEY, TO BE
14 FOLLOWED BY DR. MURPHY.

15 DR. KELLEY: GOOD MORNING. THANK YOU FOR
16 THE OPPORTUNITY AND ALLOWING ME TO PRESENT HERE. AS
17 THE SOLE REPRESENTATIVE I THINK FROM INDUSTRY, IT
18 SPEAKS TO THE DIFFICULTY IN PLAYING TO THIS
19 ENVIRONMENT, AND I WAS A LITTLE SURPRISED TO SEE THAT
20 IN THE LISTING THIS MORNING. SO THIS IS, I'M A
21 VASCULAR SURGEON WHO IS PRESENTLY THE MEDICAL
22 DIRECTOR FOR ALL THE PERIPHERAL PRODUCTS AT BOSTON
23 SCIENTIFIC. FORTUNATELY, I ACTUALLY TRAINED UNDER
24 BOB ZWOLAK, SO I CAN ATTEST TO HIS SKILL IN OPEN
25 PROCEDURES, AND IT IS REMARKABLE FOR ME TO HEAR HIM

00140

1 SAY THAT RENAL ARTERY STENTING ACTUALLY HAS A VERY
2 STRONG PLACE IN PATIENT CARE.
3 QUICK OBJECTIVES, I'LL GO THROUGH THIS
4 QUICKLY SO WE CAN MOVE FORWARD, AND SIX MINUTES GOES
5 BY QUICKLY. OUR OBJECTIVE HERE IS TO SUPPORT
6 MAINTENANCE OF COVERAGE OR CURRENT MEDICARE COVERAGE
7 FOR RENAL ARTERY STENTING. I'M GOING TO PROVIDE YOU
8 SOME OF THE RENAISSANCE CLINICAL DATA THAT IS
9 AVAILABLE NOW OUT TO TWO YEARS FOR RENAL ARTERY
10 STENTING IN PATIENTS, AND THEN ALSO TOUCH UPON SOME
11 OF THE CORAL TRIAL. AS YOU'VE HEARD FROM DR. COOPER,
12 AND I'M VERY ENCOURAGED TO SEE AN UP RAMP IN THE
13 ENROLLMENT FOR CORAL, BECAUSE I THINK FROM A
14 SCIENTIFIC POINT OF VIEW IT IS THE RIGHT STUDY TO DO.
15 I THINK FROM AN INDUSTRY PERSPECTIVE IT'S A VERY
16 CHALLENGING STUDY TYPE TO DO, AND IT PRESENTS SOME
17 ETHICAL CHALLENGES IN TERMS OF ENROLLMENT.
18 JUST SO YOU'RE AWARE, THE CORAL TRIAL IS
19 THE ONLY RENAL ARTERY STENTING TRIAL THAT'S GOING ON
20 IN THE UNITED STATES. THERE'S NO INDUSTRY-SPONSORED
21 TRIAL GOING ON AT THIS TIME, SO CORAL IS IT. SO IF
22 MEDICARE COVERAGE IS LIMITED TO PARTICIPATION IN
23 CLINICAL TRIALS, YOU'RE GOING TO LIMIT PATIENTS TO BE
24 REQUIRED TO BE IN A RANDOMIZED CLINICAL TRIAL, AND
25 THAT PUTS A CHALLENGE ON PATIENTS THEMSELVES.

00141

1 I'M NOT GOING TO GO THROUGH THIS. SUFFICE
2 IT TO SAY THAT THE VARIOUS CLINICAL ORGANIZATIONS
3 HAVE ALL COME OUT IN SUPPORT OF RENAL ARTERY
4 STENTING. THE BIASES ARE DIFFERENT. CLEARLY I WAS A
5 VASCULAR SURGEON WHO HAD AN ACADEMIC PRACTICE WHO DID
6 RENAL ARTERY BYPASS, RENAL ARTERY STENTING, AND HAD A
7 VERY LARGE DIALYSIS PRACTICE. AND I CAN TELL YOU,
8 THE PASSION FOR RENAL ARTERY STENTING COMES FROM THE
9 DESIRE TO PREVENT DIALYSIS IN A MAJORITY OF PEOPLE.
10 THE LIFESTYLE OF A DIALYSIS PATIENT IS MISERABLE AND
11 IF YOU CAN PREVENT THAT, THAT'S, AT LEAST FROM MY
12 POINT OF VIEW AND MANY PHYSICIANS' POINT OF VIEW, A
13 DESIRE TO PREVENT THAT.
14 NOW WE KNOW FROM THE PREVIOUS STUDIES THAT
15 THERE'S NOT ALWAYS A CORRELATION, AND I CANNOT
16 EMPHASIZE ENOUGH THAT WE ARE ADVOCATING FOR
17 APPROPRIATE PATIENT SELECTION FOR RENAL ARTERY
18 STENTING.
19 RENAL ARTERY STENTING IS INCREASING IN
20 VOLUME. AS YOU CAN SEE HERE IN 2005, 35,000 RENAL
21 ARTERY STENTING PROCEDURES.
22 WHAT WAS THE RENAISSANCE TRIAL? AS
23 DR. COOPER POINTED OUT, THESE REGISTRY TYPE, REGISTRY
24 NONRANDOMIZED TRIALS ALL HAD THEIR PROBLEMS. IT WAS
25 A PROSPECTIVE, MULTICENTER, SINGLE-ARM TRIAL

00142

1 EVALUATING THE SAFETY AND EFFICACY OF AN EXPRESS SD
2 STENT IN SUBJECTS WITH RENAL ARTERY STENOSIS. THE
3 THING ABOUT THE RENAISSANCE TRIAL THAT'S DIFFERENT
4 FROM SOME OF THE THINGS POINTED OUT IS PATIENTS HAD
5 TO HAVE A GREATER THAN 70 PERCENT STENOSIS, PATIENTS
6 HAD TO HAVE ALSO FAILED MEDICAL MANAGEMENT THERAPY.
7 OUR PATIENTS ALL WERE ON ASPIRIN, OVER 85 PERCENT
8 WERE ON STATIN DRUGS, AND OVER 99 OF THE HUNDRED
9 PATIENTS WERE CONSIDERED HYPERTENSIVE AND
10 UNCONTROLLED HYPERTENSION, ON THREE OR MORE
11 MEDICATIONS.
12 WE DID, AS WAS SAID, LOOK AT A SURROGATE
13 MARKER OF NINE-MONTH PRIMARY RESTENOSIS, WITH A
14 PRIMARY EFFICACY ENDPOINT ALSO, LOOKING AT IF THERE
15 WAS A WAY TO FOLLOW UP THESE PATIENTS WITH A
16 NONINVASIVE DUPLEX STUDY. AND THESE WERE THE
17 NINE-MONTH SIGNIFICANT OUTCOMES. WE USED AN OPC OF
18 40 PERCENT, WHICH WAS DERIVED FROM THE LITERATURE.
19 MOST OF THAT LITERATURE HAS BEEN PRESENTED TO YOU
20 TODAY. THE EXPRESS SP CAME IN AT 21.3 PERCENT,
21 STATISTICALLY SIGNIFICANT.
22 IN ADDITION, WE ALSO SHOWED CONCORDANCE
23 BETWEEN DUPLEX ULTRASOUND AND ANGIOGRAPHY. WE DID
24 HAVE HYPERTENSION, IMPROVEMENT IN SYSTOLIC
25 HYPERTENSION, AND I'LL GO THROUGH THAT BRIEFLY HERE.

00143

1 WE DO NOT SEE ANY CHANGE WITH DIASTOLIC FUNCTION. WE
2 ALSO HAD MAINTENANCE OF SERUM CREATININE LEVELS, AND
3 NO PATIENT IN THE ENTIRE STUDY WENT ON TO REQUIRE
4 RENAL REPLACEMENT THERAPY TO TWO YEARS, DESPITE THE
5 FACT THAT THESE ARE PATIENTS WHO HAD ALL FAILED
6 MEDICAL MANAGEMENT.
7 LOW RATE OF MAJOR ADVERSE EVENTS. AS YOU
8 CAN SEE, MOST OF THE ADVERSE EVENTS WERE TARGETED TO
9 LEAD TO REVASCULARIZATION, MOST OF THOSE WERE DUPLEX
10 TRIGGERED AS THE PROTOCOL STATEMENT.
11 SO IN CONCLUSION, RENAL ARTERY STENTING
12 WITH THE EXPRESS SD STENT SUCCESSFULLY TREATS OSTIAL
13 RENAL ARTERY STENOSIS, IT DEMONSTRATED STABILIZATION
14 OF HYPERTENSION, AND A FREEDOM FROM RENAL REPLACEMENT
15 THERAPY FOR TWO YEARS. WE HOPE AND NEED -- WE HAVE
16 GONE THROUGH THE PMA SUBMISSION PROCESS. HE HOPE
17 THAT WE WILL HAVE A PMA APPROVAL TO ALLOW THE U.S.
18 MARKET TO HAVE A PURPOSE-FILLED RENAL STENT AVAILABLE
19 TO YOU THAT IS FDA-APPROVED, WHICH CURRENTLY DOES NOT
20 EXIST AT THIS TIME.
21 SO IN CONCLUSION, CONTINUED COVERAGE FOR
22 RENAL ARTERY STENTING FOR INDICATED PATIENTS IS
23 REASONABLE AND NECESSARY. THE CURRENT PRACTICE,
24 AVAILABLE DATA, AND SOCIETY GUIDELINES IS CONSISTENT
25 SPECIALTIES AND SUPPORTS MAINTENANCE OF ONGOING

00144

1 COVERAGE. WHILE CORAL IS VERY IMPORTANT AND SHOULD
2 BE ALLOWED TO CONTINUE, THE RESTRICTION OF RENAL
3 ARTERY STENTING TO PATIENTS ENROLLED IN THE ONLY
4 RENAL ARTERY STENTING TRIAL IN THE UNITED STATES HAS
5 ETHICAL CONSIDERATIONS WHEN YOU'RE RESTRICTING
6 APPLICATIONS, AND OUR RECOMMENDATION IS TO MAINTAIN
7 CURRENT COVERAGE FOR RENAL ARTERY STENTING. THANK
8 YOU VERY MUCH FOR YOUR TIME.
9 DR. GARBER: THANK YOU. DR. MURPHY.
10 DR. MURPHY: GOOD MORNING, AND THANK YOU
11 FOR THE OPPORTUNITY TO ADDRESS YOU TODAY. I'M TIM
12 MURPHY, I'M AN INTERVENTIONAL RADIOLOGIST AT RHODE
13 ISLAND HOSPITAL IN PROVIDENCE, AND A PROFESSOR OF
14 RADIOLOGY AT BROWN MEDICAL SCHOOL. I'M SPEAKING TO
15 YOU TODAY ON BEHALF OF THE SOCIETY OF INTERVENTIONAL
16 RADIOLOGY. SIR IS A 5,000-MEMBER ORGANIZATION OF
17 INTERVENTIONAL RADIOLOGISTS, A SPECIALTY THAT
18 DESCRIBED CATHETER-BASED DIAGNOSTIC PROCEDURES,
19 ANGIOPLASTY AND STENT PLACEMENT IN THE 1950S AND THE
20 1960S.
21 I HAVE A NUMBER OF DISCLOSURES. I'M
22 CURRENTLY SERVING AS CO-PI OF THE CORAL STUDY. THE
23 SOCIETY, OF COURSE, RECEIVES A TREMENDOUS AMOUNT OF
24 INDUSTRY SUPPORT. I HAVE RECEIVED RESEARCH GRANTS
25 FROM THE NATIONAL HEART, LUNG AND BLOOD INSTITUTE,

00145

1 AND SUPPLEMENTS FOR NIH STUDIES FROM A NUMBER OF
2 INDUSTRY PARTNERS INCLUDING BOSTON SCIENTIFIC,
3 CORDIS, GUIDANT AND OTSUKA PHARMACEUTICALS. BUT I
4 DON'T RECEIVE RESEARCH EDUCATION HONORARIA FOR
5 ADVISORY PANELS, ET CETERA, ET CETERA, AND I'M NOT
6 BEING PAID TO SPEAK WITH YOU TODAY, I PAID FOR MY OWN
7 WAY HERE.
8 I'M GOING TO SKIP OVER THE REVIEW BECAUSE
9 IT'S BEEN COVERED IN A LOT OF DETAIL. I THINK
10 EVERYBODY APPRECIATES THAT THE NUMBER OF STUDIES THAT
11 HAVE BEEN DONE SO FAR LOOKING AT RENAL ARTERY
12 INTERVENTIONAL PROCEDURES IS SMALL AND THERE ARE A
13 NUMBER OF METHODOLOGICAL FLAWS, AND IT'S HARD TO DRAW
14 CONCLUSIONS. THE STUDIES SEEM TO SHOW LITTLE BENEFIT
15 OF STENTING OR ANGIOPLASTY, OR LITTLE BENEFIT, BUT I
16 BELIEVE THAT THOSE STUDIES ARE REALLY SO PROFOUNDLY
17 METHODOLOGICALLY FLAWED THAT THEIR CREDIBILITY IS
18 SEVERELY UNDERMINED. I WOULD SAY AT THIS POINT WE'RE
19 IN A PERIOD OF NOT HAVING A LOT OF EVIDENCE.
20 WE HEARD ABOUT THE GROWTH AND NOW IT HAS
21 BEEN EXTRAPOLATED OUT TO 2005 WITH A CONTINUING
22 FAIRLY STEEP UP-CURVE, AND I THINK THAT GIVES
23 EVERYBODY A LOT OF CONCERN, PHYSICIANS AND PATIENTS
24 ALIKE.
25 AS FAR AS WHAT WE KNOW CURRENTLY, THE

00146

1 STUDIES THAT WE HAVE ARE FEW IN NUMBER AND FLAWED.
2 WE NEED DATA. THE CORAL STUDY IS A KEY STUDY TO HELP
3 PROVIDE THAT.
4 IN THE BIGGEST MEDICAL THERAPY, THE
5 BIGGEST STUDY COMPARING MEDICAL THERAPY AND
6 ANGIOPLASTY, AGAIN, WE HEARD THAT STENTING WASN'T
7 USED, DRUG THERAPY WAS RESTRICTED FOR THE STENT
8 ANGIOPLASTY GROUP, AND 44 PERCENT OF PATIENTS CROSSED
9 OVER FROM MEDICAL TO ANGIOPLASTY AND STILL WERE
10 ANALYZED ACCORDING TO INTENTION TO TREAT AS PART OF
11 THE MEDICAL GROUP.
12 HOWEVER, AGAIN, POINTING OUT SOME OF THE
13 METHODOLOGIC FLAWS OF SOME OF THESE STUDIES, IN THIS
14 BIGGEST STUDY, RANDOMIZED TRIAL, WE NOTE FROM THE
15 AUTHORS' MANUSCRIPT THAT PATIENTS ARE MORE LIKELY TO
16 HAVE IMPROVEMENT IN THEIR BLOOD PRESSURE CONTROL WHEN
17 THEY WERE TREATED WITH ANGIOPLASTY, MORE LIKELY TO BE
18 CURED, AND LESS LIKELY TO HAVE WORSENING OF EITHER
19 BLOOD PRESSURE CONTROL OR PROGRESSION TO RENAL ARTERY
20 CONCLUSION. SO THERE ARE DATA IN THOSE STUDIES THAT
21 SUGGEST HOW RENAL ARTERY INTERVENTIONS ARE
22 BENEFICIAL, AND I THINK MOST OF US IN CLINICAL
23 PRACTICE HAVE CLEARLY SEEN PATIENTS WHO HAVE
24 BENEFITED FROM THE PROCEDURE.
25 THESE ARE THE COVERAGE ISSUES THAT I'D

00147

1 LIKE TO ADDRESS IN THE NEXT COUPLE OF MINUTES. THE
2 ISSUE OF ANGIOPLASTY AND/OR STENTING, WHEN IS IT
3 APPROPRIATE TO HAVE BOTH OF THOSE CODES, IF EVER.
4 INITIAL MANAGEMENT USING ANGIOPLASTY OR STENTING, OR
5 SHOULD PEOPLE UNDERGO MEDICAL MANAGEMENT.
6 I'D LIKE TO DISCUSS SOME OF THE DOUBTERS
7 TO CLINICAL TRIAL FOR A MOMENT, THE ISSUE OF DISTAL
8 INVOLVED PROTECTION, IS IT NECESSARY, AND THEN THE
9 ISSUE OF PROPHYLACTIC PTRAS, OR RENAL ANGIOPLASTY
10 STENT PLACEMENT FOR RENAL PRESERVATION.
11 FIRSTLY, SIR DEVELOPED THE CODES FOR BOTH
12 RENAL ANGIOPLASTY AND PERIPHERAL STENT PLACEMENT.
13 WHEN THEY WERE FIRST IMPROVED BY A CPT EDITORIAL
14 COMMITTEE IN 1992, IT WAS NEVER THE INTENTION THAT
15 THEY WOULD BOTH BE USED TOGETHER. SIR RECOMMENDS
16 THAT PROVIDERS BE REIMBURSED FOR EITHER RENAL
17 ANGIOPLASTY IF NO STENT IS PLACED, OR THE RENAL CODE
18 IF THE STENT IS PLACED, BUT NOT BOTH, AS WE HAVE SEEN
19 IS OFTEN THE PRACTICE FOR THE SAME PATIENT ON THE
20 SAME DAY OF SERVICE.
21 AT WHAT TIME DURING THE PATIENT'S DISEASE
22 HISTORY IS RENAL ANGIOPLASTY OR STENT PLACEMENT
23 INDICATED? GIVEN THE CURRENT KNOWLEDGE BASE, WE
24 BELIEVE THAT RENAL ARTERY REVASCULARIZATION IS RARELY
25 INDICATED AS THE DE NOVO TREATMENT FOR RENAL ARTERY

00148

1 STENOSIS AND CLINICAL SEQUELA. PATIENTS SHOULD
2 UNDERGO A DEDICATED, SYSTEMATIC TRIAL OF MEDICAL
3 MANAGEMENT BY A MEDICAL SPECIALIST FOLLOWING
4 PUBLISHED GUIDELINES PRIOR TO REFERRAL FOR
5 INTERVENTIONS. THAT GOES ALONG WITH THE PRINCIPLE OF
6 FIRST DO NO HARM, AND MEDICAL MANAGEMENT OBVIOUSLY IS
7 LOWER RISK THAN INTERVENTION, SO MEDICAL MANAGEMENT
8 SHOULD HAVE A TRIAL FIRST.
9 WE'VE HEARD A LITTLE BIT ABOUT THE
10 IMPORTANCE OF THE CORAL STUDY AND HOW IT IS A
11 METHODOLOGICALLY SOUND, WELL FUNDED NIH STUDY THAT
12 WILL BE DEFINITIVE IN PROVIDING ANSWERS FOR THIS
13 DISEASE, ANSWERS THAT WE SORELY LACK. WE NOTE THAT
14 THERE ARE ECONOMIC DISINCENTIVES TO INVESTIGATIVE
15 PARTICIPATION AND ENROLLMENT IN THE U.S. HAS BEEN
16 LACKLUSTER ALMOST UNIVERSALLY ACROSS THE BOARD,
17 PARTICULARLY IN STUDIES THAT COMPARE CONSERVATIVE
18 VERSUS INVASIVE MANAGEMENT. AND WE IMPLORE MEDICARE
19 TO COME UP WITH A PROGRAM THAT WILL AT LEAST
20 ELIMINATE OR BLUNT THESE ECONOMIC DISINCENTIVES TO
21 GETTING THE ANSWERS THAT WILL FORM SOUND COVERAGE
22 DECISIONS.
23 DISTAL PROTECTION, THERE'S LITTLE EVIDENCE
24 OF THE BENEFIT OF DISTAL PROTECTION. WE DON'T
25 BELIEVE THAT DISTAL PROTECTION SHOULD BE REQUIRED FOR

00149

1 REIMBURSEMENT. SEPARATE PROFESSIONAL REIMBURSEMENT
2 IF USED IS NOT SUPPORTED AT THIS TIME, THERE'S JUST
3 SIMPLY NO EVIDENCE TO SHOW THAT IT DOES ANY MORE
4 BENEFIT THAN HARM.
5 FINALLY TO ADDRESS PROPHYLACTIC PTRAS,
6 AGAIN, GETTING BACK TO THE NEED FOR CLINICAL
7 MANIFESTATIONS OF THE DISEASE, WE BELIEVE THAT RENAL
8 ARTERY STENOSIS WITHOUT REFRACTORY HYPERTENSION OR
9 CHRONIC KIDNEY DISEASE SHOULD NOT BE AN INDICATION
10 FOR REVASCULARIZATION OF THE KIDNEY ARTERIES. THANK
11 YOU.
12 DR. GARBER: THANK YOU VERY MUCH.
13 IMPRESSIVE TIMING THERE.
14 ALL RIGHT. WE NOW HAVE THREE OPEN PUBLIC
15 SPEAKERS WHO HAVE SIGNED UP TO SPEAK. LET ME ALSO
16 THANK ALL OF THE SCHEDULED SPEAKERS, AND I HOPE THAT
17 YOU WILL ALL STICK AROUND AFTER LUNCH, BECAUSE I'M
18 SURE THE PANEL WILL HAVE A NUMBER OF QUESTIONS FOR
19 YOU AT THAT TIME.
20 SO WE WILL BEGIN WITH DR. CAMBRIA -- YOU
21 HAVE THREE MINUTES EACH. HE WILL BE FOLLOWED BY
22 DR. ROSENFELD, THEN DR. GERHARD-HERMAN.
23 DR. CAMBRIA: THANK YOU, MR. CHAIRMAN. MY
24 NAME IS RICHARD CAMBRIA, I'M A PROFESSOR OF SURGERY
25 AT THE HARVARD MEDICAL SCHOOL AND CHIEF OF THE

00150

1 DIVISION OF VASCULAR AND ENDOVASCULAR SURGERY AT THE
2 MASSACHUSETTS GENERAL HOSPITAL IN BOSTON. I'VE BEEN
3 LECTURING ABOUT OR WRITING ABOUT THIS DISEASE PROCESS
4 FOR OVER 20 YEARS ON A CIRCUIT THAT HAS OFTEN
5 INCLUDED MANY OF THE SPEAKERS THAT YOU HAVE HEARD
6 THIS MORNING. MY OWN PERSPECTIVE IS THAT OF A
7 VASCULAR SURGEON. I AM HERE ON BEHALF OF THE SOCIETY
8 FOR VASCULAR SURGERY, WHO I CERTAINLY HOPE WILL
9 REIMBURSE MY TRAVEL EXPENSES.
10 I AGREE WITH MUCH THAT HAS BEEN SAID BY MY
11 PREDECESSORS. AS A VASCULAR SURGEON, I HAVE
12 PERFORMED MANY, MANY OPEN SURGICAL REPAIRS OF RENAL
13 ARTERY LESIONS AND I HAVE PERSONALLY LOOKED INTO THE
14 INSIDE OF LITERALLY THOUSANDS OF RENAL ARTERY OSTIA.
15 THERE IS NO QUESTION THAT EVEN VASCULAR SURGEONS HAVE
16 ACCEPTED THE MIGRATION OF THE PRIMARY FORM OF
17 INTERVENTIONAL THERAPY FROM OPEN SURGERY TO RENAL
18 ARTERY STENTING, AND THIS IS FOR THE VERY OBVIOUS
19 REASONS OF THE SIGNIFICANT DIFFERENCE IN THE
20 MORBIDITY OF THE TWO PROCEDURES.
21 THAT BEING SAID, I CERTAINLY AGREE THAT IT
22 IS ILLOGICAL AND IRRELEVANT TO USE THE ANALOGY WITH
23 CAROTID ANGIOPLASTY AND STENTING AND OPEN CAROTID
24 SURGERY. THE TWO ARE FUNDAMENTALLY DIFFERENT DISEASE
25 PROCESSES AND THE SURGICAL INTERVENTION IN TERMS OF

00151

1 MORBIDITY ARE VASTLY DIFFERENT.
2 WE HAVE BEEN TEACHING OUR VASCULAR SURGERY
3 TRAINEES SINCE THE INCEPTION OF OUR SPECIALTY
4 EXAMINATIONS THAT THE APPROPRIATE POSTURE TOWARDS A
5 "ASYMPTOMATIC RENAL ARTERY LESION," THAT IS, ONE IN
6 THE ABSENCE OF HYPERTENSION OR ANY EVIDENCE OF
7 ISCHEMIC NEPHROPATHY, SHOULD BE CONSERVATIVE. THAT
8 REMAINS THE APPROPRIATE ANSWER WHEN WE EXAMINE OUR
9 FELLOWSHIP APPLICANTS EVEN TODAY.
10 YES, THERE CLEARLY ARE PATIENTS WHO DO
11 BENEFIT, EVEN DRAMATICALLY, FROM RENAL ARTERY
12 INTERVENTION. AND OUR OWN EFFORTS AND PUBLICATIONS
13 OVER THE PAST 20 YEARS HAVE FOCUSED ON THE PREDICTION
14 OF THE FUNCTIONAL RESPONSE TO REVASCULARIZATION. I
15 CAN TELL YOU THAT PERSONALLY I HAVE PERFORMED NO MORE
16 GRATIFYING VASCULAR INTERVENTION THAN TO RETRIEVE A
17 PATIENT FROM RENAL REPLACEMENT THERAPY. THESE
18 PATIENTS ARE NOT COMMON BUT THEY DO REPRESENT THE
19 DRAMATIC FAR END OF THE SPECTRUM OF THE BENEFIT OF
20 RENAL ARTERY INTERVENTIONS.
21 THE PROBLEM OF COURSE IS THE LARGE MASS OF
22 PATIENTS WHO, AS YOU HAVE HEARD, ARE INCREASINGLY
23 BEING OFFERED RENAL ARTERY INTERVENTIONS WITH VERY
24 SOFT INDICATIONS. I APPRECIATE THE AGENCY'S DILEMMA
25 IN THIS REGARD. HOWEVER, I WOULD LIKE TO CLOSE BY

00152

1 STATING THAT THERE ARE DISTINCT PATIENT AND ANATOMIC
2 SUBSETS WHEREIN THE BENEFITS OF INTERVENTION BASED ON
3 AVAILABLE EVIDENCE, ALBEIT NOT LEVEL I, IS CLEAR.
4 I WOULD PARENTHETICALLY ADD THAT THERE ARE
5 ADDITIONAL CIRCUMSTANCES AS VASCULAR INTERVENTIONS
6 EVOLVE, AND I WOULD USE THE EXAMPLE OF CONCOMITANT
7 RENOVASCULAR DISEASE IN PATIENTS BEING TREATED WITH
8 AORTIC PATHOLOGY. THESE DAYS THE PRESENCE OF EVEN AN
9 ASYMPTOMATIC RENAL ARTERY STENOSIS MAY BENEFIT FROM
10 STENTING IN THE CONTEXT OF AN OTHERWISE INVASIVE
11 PROCEDURE FOR AORTIC PATHOLOGY, MOST NOTICEABLY STENT
12 GRAFT REPAIR OF ABDOMINAL AORTIC ANEURYSM. I THANK
13 YOU FOR YOUR ATTENTION.
14 DR. GARBER: THANK YOU, DR. CAMBRIA.
15 NEXT, DR. ROSENFELD.
16 DR. ROSENFELD: MR. CHAIRMAN AND
17 PANELISTS, THANK YOU FOR THE PRIVILEGE OF SPEAKING.
18 MY NAME IS KEN ROSENFELD, AND I'M THE HEAD OF THE
19 SECTION OF VASCULAR MEDICINE AND INTERVENTION AT MASS
20 GENERAL HOSPITAL IN BOSTON. YOU'RE GETTING A LOT OF
21 US TODAY. MY TRAVEL HERE WAS SUPPORTED BY THE SCA&I.
22 RELEVANT CONFLICTS ARE OUTLINED IN YOUR PAMPHLETS,
23 AND THESE INCLUDE THE FACT THAT I AND MY INSTITUTION
24 HAVE RECEIVED RESEARCH AND/OR EDUCATIONAL GRANTS FROM
25 VARIOUS INDUSTRY SPONSORS, AND I HAVE SERVED AS A

00153

1 PAID ADVISOR OR CONSULTANT TO SEVERAL COMPANIES.
2 I'M A CLINICIAN THAT HAS BEEN INVOLVED IN
3 CARING FOR PATIENTS WITH RENOVASCULAR DISEASE FOR 20
4 YEARS. I CURRENTLY SERVE AS CHAIRPERSON OF THE AHA
5 CARDIOVASCULAR CATHETERIZATION COMMITTEE, THE PRIOR
6 CHAIR OF THE PERIPHERAL VASCULAR DISEASE COMMITTEE OF
7 THE ACC, AND THE CURRENT CHAIR OF THE PVD COMMITTEE
8 FOR THE SCA&I. I WAS THE NATIONAL PI OF THE ASPIRE
9 II TRIAL, WHICH WAS THE FIRST STUDY THAT OBTAINED FDA
10 APPROVAL FOR RENAL STENT DEPLOYMENT IN THE UNITED
11 STATES, AND I'VE ALSO BEEN INVOLVED IN THE CORAL
12 TRIAL FROM ITS OUTSET, SERVING AS THE CHAIRMAN OF THE
13 CORAL SITE SELECTION COMMITTEE.
14 I WOULD LIKE TO SPECIFICALLY NOTE THAT I
15 AM HERE TODAY SPEAKING ON BEHALF OF SCA&I AND ITS
16 NEARLY 4,000 MEMBER CLINICIANS WHO CARE FOR PATIENTS
17 WITH CARDIOVASCULAR AND VASCULAR DISEASE. FIRST, MY
18 COLLEAGUES IN THE SCA&I WOULD LIKE TO EMPHASIZE THAT
19 WE SUPPORT THE ACCRUAL OF ADDITIONAL EVIDENCE TO
20 REFINE PATIENT SELECTION FOR RENAL ANGIOPLASTY AND
21 STENTING, AND WE SUPPORT THE CORAL TRIAL. WHILE THIS
22 IS OUR POSITION, THE SCA&I DOES NOT BELIEVE THAT
23 EVIDENCE DEVELOPMENT SHOULD OCCUR AT THE COST OF
24 RESTRICTING ACCESS TO IMPORTANT THERAPIES THAT CAN
25 REDUCE MORBIDITY OR MORTALITY IN A GIVEN PATIENT.

00154

1 CARE SHOULD BE TAKEN NOT TO THROW OUT THE BABY WITH
2 THE BATH WATER.
3 WE DO NEED MORE INFORMATION AS TO WHICH
4 PATIENTS ARE MORE OR LESS LIKELY TO BENEFIT FROM THIS
5 THERAPY. HOWEVER, LIMITING COVERAGE TO PATIENTS
6 ENROLLED IN THE CORAL OR OTHER TRIAL WOULD BE A
7 DISSERVICE TO THE MEDICARE BENEFICIARIES IN THE 21
8 STATES, FOR EXAMPLE, WHERE THERE ARE NO CORAL SITES,
9 AND FOR MANY PATIENTS WHO ARE NOT ELIGIBLE FOR
10 ENROLLMENT. MEDICARE AND OTHER PATIENTS WHO STAND TO
11 BENEFIT FROM AND CURRENTLY HAVE ACCESS TO RENAL
12 REVASCULARIZATION BY STENTING CANNOT BE RELEGATED
13 SOLELY TO MEDICAL THERAPY OR TO HIGHER RISK SURGICAL
14 REVASCULARIZATION.
15 WHILE MOST HAVE TODAY FOCUSED ON EVIDENCE
16 FOR OR AGAINST RENAL STENTING, EVIDENCE SUPPORTING
17 MEDICAL THERAPY FOR THIS DISEASE IS NO MORE ROBUST
18 AND MAY BE LESS SO THAN THAT FOR OPENING THE NARROW
19 VESSEL. LIKewise THE COST, BOTH FINANCIAL AND
20 LIFESTYLE, OF PROLONGED LIFETIME ADMINISTRATION OF
21 MEDICATIONS CAN EXCEED THAT OF REVASCULARIZATION.
22 IT IS IMPORTANT TO POINT OUT THAT WHILE
23 HAVING A ROBUST EVIDENCE BASE IS ALWAYS DESIRABLE,
24 ABSENCE OF A CONCLUSIVE EVIDENCE BASE DOES NOT MEAN
25 THAT A THERAPY IS INEFFECTIVE AND SHOULD NOT BE

00155

1 APPLIED. MOST OF THE DECISIONS, INDEED, THAT WE MAKE
2 IN CARING FOR OUR PATIENTS ARE MADE WITHOUT THE
3 BENEFIT OF A CONCLUSIVE BODY OF DATA. WERE LEVEL I
4 OR IIA EVIDENCE TO BE REQUIRED FOR ALL DECISIONS WE
5 MAKE, WE WOULD ALL BE PARALYZED AS CLINICIANS. WE AS
6 CLINICIANS MUST TAKE INTO ACCOUNT THE WEIGHT OF THAT
7 EVIDENCE AS IT PERTAINS TO THE INDIVIDUAL PATIENT WHO
8 IS BEFORE US.
9 I SERVED ON THE ACC/AHA/SVS/SVMB
10 GUIDELINES DOCUMENT WRITING GROUP WHICH YOU'VE HEARD
11 ABOUT. THE ASSIGNMENT TO CLASS IIB FOR CERTAIN
12 INDICATIONS FOR RENAL STENTING BY A GROUP OF EXPERTS
13 WAS NOT INTENDED TO RESTRICT ACCESS, BUT RATHER TO
14 INFORM PHYSICIANS AND THEIR PATIENTS THAT THESE
15 PARTICULAR INDICATIONS WERE ONES FOR WHICH THERE WAS
16 AN EVOLVING AND SOMETIMES CONFLICTING EVIDENCE BASE,
17 AND THAT CLINICIANS SHOULD FACTOR THAT IN WHEN
18 DECIDING UPON THERAPY FOR AN INDIVIDUAL PATIENT.
19 THAT DESIGNATION WAS INTENDED TO LEAVE THE ULTIMATE
20 DECISION-MAKING IN THE HANDS OF A PATIENT AND HIS OR
21 HER CAPABLE AND COMPETENT PHYSICIAN.
22 DR. GARBER: DR. ROSENFELD, I'M SORRY,
23 BUT YOUR TIME IS UP.
24 DR. ROSENFELD: THANK YOU.
25 DR. GARBER: DR. GERHARD-HERMAN.

00156

1 DR. GERHARD-HERMAN: THANK YOU FOR THE
2 OPPORTUNITY TO SPEAK. I'M THE CURRENT CHAIR OF THE
3 ACC PVD COMMITTEE AND I'M A NONINTERVENTIONAL
4 CARDIOLOGIST.
5 THE TWO POINTS THAT WE WANTED TO RAISE
6 FROM THE PERSPECTIVE OF OUR GROUP IN THE AMERICAN
7 COLLEGE OF CARDIOLOGY, ONE IS THAT THERE ARE
8 SUBPOPULATIONS OF PATIENTS WHERE THERE IS CLEAR
9 BENEFIT TO INTERVENTION IN THE SETTING OF RENAL
10 ARTERY STENOSIS. THAT'S ALREADY BEEN DISCUSSED BUT
11 WE JUST WANTED TO SAY IT AGAIN. THOSE ARE THE
12 PATIENTS WITH BILATERAL RENAL ARTERY STENOSIS AND
13 RENAL ARTERY STENOSIS IN THE SETTING OF A SOLITARY
14 KIDNEY.
15 BUT IT HAS ALREADY BEEN DISCUSSED THAT
16 THERE'S A HUGE NUMBER OF PATIENTS WHO HAVE RENAL
17 ARTERY STENOSIS THAT DON'T FIT IN THOSE CATEGORIES,
18 AND WE WOULD SAY WE HAVE INSUFFICIENT EVIDENCE TO
19 DECIDE WHAT TO DO WITH THOSE PATIENTS. AND I THINK
20 AT THIS POINT WE ALL STAND TOGETHER IN CONTINUING TO
21 SUPPORT THE ACC AND AHA GUIDELINES FOR BOTH LEVEL I
22 AND LEVEL II RECOMMENDATIONS IN TERMS OF TREATMENT OF
23 RENAL ARTERY STENOSIS, AND WE ENCOURAGE CONTINUED
24 SUPPORT OF THE CLINICAL TRIALS.
25 AND THE LAST POINT IS THAT WHILE WE

00157

1 ENCOURAGE SUPPORT OF ENROLLMENT IN THE CORAL TRIAL,
2 THERE ARE A LOT OF PATIENTS WHO WON'T HAVE ACCESS TO
3 A CORAL SITE THAT WE TOO DO NOT WISH TO DEPRIVE FROM
4 RENAL INTERVENTION. THANK YOU.
5 DR. GARBER: THANK YOU VERY MUCH. WE HAVE
6 A GUEST HERE WHO I WONDER IF WE COULD ASK TO JUST
7 MAKE A FEW BRIEF COMMENTS, AND THAT'S DR. KENT
8 CAVANAUGH FROM THE FDA, WHO WASN'T REALLY PREPARED TO
9 SPEAK TODAY. I'D ASK HIM IF HE COULD JUST MENTION
10 THE CURRENT STATUS OF FDA APPROVAL FOR DEVICES USED
11 TO STENT RENAL ARTERIES.
12 DR. CAVANAUGH: SURE, THANK YOU, AND I
13 WILL BE BRIEF SO WE CAN HAVE ABOUT 35 MINUTES FOR
14 LUNCH TODAY.
15 MY NAME IS KENT CAVANAUGH, I'M A
16 SCIENTIFIC REVIEWER WITHIN THE DIVISION OF
17 CARDIOVASCULAR DEVICES AT THE FOOD AND DRUG
18 ADMINISTRATION. I'D JUST LIKE TO PROVIDE A BRIEF
19 REGULATORY OVERVIEW OF RENAL ARTERY STENTING FROM OUR
20 PERSPECTIVE.
21 IN OUR REGULATORY CLASSIFICATION SCHEME WE
22 CONSIDER RENAL ARTERY STENTS TO BE CLASS III DEVICES
23 FOR WHICH A PREMARKET APPROVAL APPLICATION IS
24 APPROPRIATE. TO SUPPORT THAT TYPE OF APPLICATION,
25 THE DEVICE NEEDS TO HAVE REASONABLE ASSURANCE OF

00158

1 SAFETY AND EFFECTIVENESS FOR ITS INTENDED USE PRIOR
2 TO APPROVAL OF THAT MARKETING APPLICATION.
3 TO DATE THERE HAVE BEEN TWO PMAS APPROVED
4 FOR RENAL ARTERY STENTS FOR ANY INDICATION, ONE IN
5 2002 AND ONE IN 2003, I BELIEVE. THE APPROVED
6 INDICATIONS FOR BOTH DEVICES ARE SIMILAR AND THAT IS,
7 THEY ARE INDICATED FOR USE FOLLOWING FAILED OR
8 SUBOPTIMAL PERCUTANEOUS TRANSLUMINAL RENAL
9 ANGIOPLASTY, BALLOON ANGIOPLASTY, AS DEFINED BY
10 CERTAIN LESION AND HEMODYNAMIC CHARACTERISTICS.
11 THERE ARE NO STENTS APPROVED SO FAR TO TREAT RENAL
12 ARTERY STENOSIS AS A PRIMARY TREATMENT OPTION.
13 BY THE SAME TOKEN, WHILE INVOLVED
14 PROTECTION DEVICES ARE REGULATED SOMEWHAT
15 DIFFERENTLY, THERE ARE NONE CURRENTLY MARKETED WITH A
16 RENAL ARTERY INDICATION, THEY ARE ONLY MARKETED WITH
17 INDICATIONS FOR USE IN CAROTID ARTERIES AND BYPASS
18 GRAFTS. THAT BEING SAID, WHILE I WON'T GET INTO
19 RECOMMENDATIONS FOR STUDY DESIGNS HERE, I WILL SAY
20 THAT TO SUPPORT SUCH AN INDICATION LIKE THIS, FDA
21 WOULD ENCOURAGE DEVICE MANUFACTURERS AND ACADEMIC
22 GROUPS TO CONDUCT NEW STUDIES, GATHER ADDITIONAL
23 CLINICAL DATA TO SUPPORT INDICATIONS LIKE THIS OR ANY
24 INDICATION FOR WHICH -- THERE ARE NO APPROVED
25 DEVICES, BUT FOR WHICH DEVICE USE MAY CURRENTLY

00159

1 REPRESENT CLINICAL PRACTICES. THANK YOU.
2 DR. GARBER: THANK YOU, DR. CAVANAUGH. WE
3 WILL TAKE OUR BREAK FOR LUNCH NOW. WE ARE RIGHT ON
4 SCHEDULE, ACCORDING TO MY WATCH, AND WE WILL RESUME
5 THE MEETING AT 12:05.
6 (LUNCH RECESS.)
7 DR. GARBER: SOME OF THE PRESENTERS ARE
8 DRIFTING IN, SO ACTUALLY BEFORE WE GET STARTED WITH
9 QUESTIONS TO THE PRESENTERS, I JUST WANTED TO SUGGEST
10 THAT WHEN YOU LOOK AT THE QUESTIONS, I KNOW THAT NOT
11 ALL OF YOU WERE ON THE CONFERENCE CALL ABOUT THE
12 LOGISTICS OF THE MEETING, BUT THE INITIAL DISCUSSION
13 QUESTIONS ARE THINGS THAT WE NEED TO KEEP IN MIND
14 WHEN WE ANSWER THE VOTING QUESTIONS, BUT WE DON'T
15 HAVE TO NECESSARILY GO THROUGH EACH OF THESE AS A
16 GROUP DELIBERATING. BUT YOU ARE CERTAINLY WELCOME TO
17 ASK OF THE PRESENTERS OR MAKE STATEMENTS ABOUT THESE
18 QUESTIONS AT THIS POINT. IT'S INTENDED TO SORT OF
19 SENSITIZE US TO WHAT THE ULTIMATE SCIENTIFIC AND
20 CLINICAL ISSUES ARE WITH REGARD TO THE MAIN
21 QUESTIONS, AS WELL AS TO THE INTERPRETATION OF THE
22 STUDIES THAT WE'VE DISCUSSED TODAY.
23 DOES ANYBODY WANT TO MAKE ANY STATEMENTS
24 THEN? AND WE CAN ASK QUESTIONS OF PRESENTERS NOW.
25 PRESENTERS, WHEN YOU ANSWER THE QUESTIONS, I WILL ASK

00160

1 YOU TO BE AS SUCCINCT AS POSSIBLE, BECAUSE THERE ARE
2 MANY PEOPLE WHO BOTH MIGHT HAVE QUESTIONS OR MIGHT
3 WANT TO ANSWER A QUESTION. WHEN YOU ANSWER A
4 QUESTION, PLEASE COME UP TO THE MIKE THAT'S IN THE
5 FRONT OF THE ROOM HERE ON THE STAND. ALEX.
6 DR. KRIST: I HAVE A QUESTION IF WE'RE
7 GOING TO START WITH QUESTIONS CLARIFYING THINGS, AND
8 DR. COOPER IS HERE, SO THE QUESTION IS ACTUALLY FOR
9 YOU. I JUST WANT TO LEARN A LITTLE BIT MORE ABOUT
10 THE CORAL STUDY, BECAUSE ONE OF THE THINGS WE'RE
11 ASKED TO THINK ABOUT IS LIMITING COVERAGE TO
12 PARTICIPATING IN A RESEARCH STUDY, AND I WAS HOPING
13 YOU COULD JUST TALK A LITTLE BIT ABOUT KIND OF THE
14 INCLUSION AND EXCLUSION CRITERIA AND, BASED ON YOUR
15 STUDY DESIGN, WHAT TYPES OF PATIENTS WHO MIGHT HAVE
16 AN INDICATION FOR AN INTERVENTION FOR RENAL ARTERY
17 STENOSIS MIGHT NOT BE INCLUDED IN YOUR STUDY. THAT
18 WOULD BE THE FIRST PART.
19 AND THEN THE SECOND PART I'M INTERESTED IN
20 IS IF YOU LOOK AT SOME OF THE OTHER STUDIES LIKE IN
21 DRASTIC, THEY QUOTED THAT 1,205 PATIENTS WERE
22 REFERRED FOR CONSIDERATION OF INCLUSION AND THEN THAT
23 ENDED UP WITH 106 PEOPLE BEING RANDOMIZED, SO ABOUT
24 EIGHT PERCENT OF THOSE OR LESS THAT THEY WERE
25 THINKING ABOUT INCLUDING WERE ACTUALLY INCLUDED. AND

00161

1 THEN YOU REPORTED TODAY THAT YOU'VE ENROLLED ABOUT
2 240 PATIENTS, AND I WAS JUST CURIOUS IF YOU HAD ANY
3 TYPE OF COROLLARY NUMBER TO WHAT DRASTIC HAD AS TO
4 HOW MANY PEOPLE MIGHT HAVE BEEN CONSIDERED OR
5 EVALUATED TO GET THAT 240 FOR INCLUSION.
6 DR. GARBER: COULD I JUST ADD TO ALEX'S
7 QUESTION, SINCE IT'S KIND OF AN EXPANSION OF ONE OF
8 HIS POINTS, IT WOULD BE USEFUL TO KNOW WHICH PATIENT
9 TYPES WERE EXCLUDED BECAUSE YOU AND THE OTHER
10 INVESTIGATORS THOUGHT THAT THERE WAS SUCH COMPELLING
11 NEED FOR STENTING THAT THEY SHOULD NOT BE RANDOMIZED.
12 DR. DWORKIN: I'M LANCE DWORKIN AND I'LL
13 TAKE THAT ONE FOR CHRIS, IF YOU DON'T MIND, BECAUSE
14 I'M THE STUDY CHAIR FOR CORAL. REGARDING WHAT TYPES
15 OF PATIENTS WERE EXCLUDED, THE ENTRANCE CRITERIA FOR
16 CORAL REQUIRED PATIENTS TO HAVE EITHER HYPERTENSION
17 THAT REQUIRES TWO MEDICATIONS, OR CHRONIC KIDNEY
18 DISEASE WITH A GFR LESS THAN 60, ARE THE MAIN
19 INCLUSION CRITERIA, AND THEN DOCUMENTED RENAL ARTERY
20 STENOSIS WHICH IS DETERMINED EITHER ANGIOGRAPHICALLY
21 OR NOW NONINVASIVELY. THOSE ARE THE ONLY INCLUSION
22 CRITERIA, SO IT'S A FAIRLY BROAD SWEEP IN TERMS OF
23 THE POSSIBLY AFFECTED PATIENTS, AND PEOPLE DON'T HAVE
24 TO BE HYPERTENSIVE IF THEY HAVE KIDNEY DISEASE.
25 IN TERMS OF EXCLUSION CRITERIA, THERE

00162

1 REALLY AREN'T THAT MANY. THERE IS A CREATININE
2 CUTOFF OF THREE, THAT WAS SOMETHING THAT WAS DEBATED,
3 SO PATIENTS WITH A CREATININE ABOVE THREE CAN'T
4 ENTER. AND THAT WAS SOMETHING DEBATED, AND THE
5 REASON THAT IT WAS SET UP THAT WAY, BECAUSE THERE WAS
6 ACTUALLY A FEELING PRIMARILY AMONG THE
7 INTERVENTIONALISTS, I THINK, THAT PATIENTS WITH
8 CREATININES ABOVE THREE WERE LESS LIKELY TO BENEFIT
9 AND, THEREFORE, THE STUDY MIGHT BE BIASED AGAINST THE
10 INTERVENTION IF THOSE PATIENTS WERE LET IN.
11 YOU KNOW, IN DESIGNING THE TRIAL, I THINK
12 WE TRIED TO BE VERY, VERY INCLUSIVE BECAUSE WE FELT
13 THAT IN FACT THERE WERE ALMOST NO TYPES OF PATIENTS
14 WITH RENOVASCULAR DISEASE FOR WHOM THE DATA IS CLEAR
15 THAT ONE APPROACH OR ANOTHER IS SUPERIOR. AND IN
16 FACT, YOU KNOW, A CRITICAL SESSION, I THINK, THAT WE
17 HAD WAS AT ONE POINT WE WERE IN A ROOM WITH ABOUT 30
18 DIFFERENT PEOPLE THAT WERE INVOLVED IN DESIGNING THE
19 TRIAL. AND I POSED THE QUESTION TO THE GROUP,
20 DESCRIBE A SET OF CRITERIA, CLINICAL, LABORATORY OR
21 OTHERWISE, WHERE YOU FEEL THAT IT'S DEFINITELY KNOWN
22 THAT A PATIENT REQUIRES REVASCULARIZATION AS COMPARED
23 TO MEDICAL THERAPY, AND THERE WAS SILENCE. SO NOBODY
24 FELT COMFORTABLE REALLY PUTTING FORTH ANY SET OF
25 CRITERIA FOR WHICH REVASCULARIZATION WAS REQUIRED

00163

1 AND, THEREFORE, THOSE PATIENTS SHOULDN'T BE ENROLLED
2 IN CORAL.
3 SO WE HAVE PATIENTS WITH UNILATERAL AND
4 BILATERAL DISEASE, PATIENTS WITH PRETTY SEVERE KIDNEY
5 DYSFUNCTION, PATIENTS WITH A WHOLE VARIETY OF
6 COMORBIDITIES, BECAUSE WE FELT AT LEAST THAT FOR MOST
7 OF THESE CATEGORIES, THE INFORMATION WASN'T CLEAR.
8 THE ONLY DEFINED GROUP THAT ARE SUPPOSED TO GET A
9 STENT ARE PATIENTS THAT DEVELOP ACUTE RENAL FAILURE
10 WHERE IT'S DOCUMENTED BY IMAGING THAT THEY HAVE
11 GLOBAL RENAL ISCHEMIA, MEANING VERY HIGH GRADE
12 STENOSIS, OR OCCLUSION TO ALL OF THEIR RENAL
13 ARTERIES, AND THAT'S THE ONLY GROUP FOR WHOM THE
14 STUDY DICTATES THAT THEY MUST BE REVASCULARIZED.
15 OTHERWISE, THEY CAN BE RANDOMIZED.
16 DR. GARBER: THANK YOU.
17 DR. LEWIS: CAN I ASK A QUESTION REGARDING
18 THAT AS WELL? BECAUSE THEN IT CONFLICTS WITH THE
19 ISSUES WITH RESPECT TO THE AMERICAN HEART ASSOCIATION
20 GUIDELINES IN TERMS OF THE CLASS I INDICATIONS FOR
21 PEOPLE WHO HAVE FLASH PULMONARY EDEMA, UNSTABLE
22 ANGINA. AND SO IF THAT'S THE CASE, CAN WE TRY TO
23 RESOLVE THAT CONFLICT A LITTLE BIT AS WELL?
24 DR. DWORKIN: I CAN'T REALLY SPEAK TO THE
25 GUIDELINES SPECIFICALLY, I WASN'T PARTY TO WRITING

00164

1 THOSE. I MEAN, I THINK IF A CLASS I, TO MY MIND
2 ANYWAY, IF A CLASS I INDICATION MEANS THAT THERE IS
3 PROSPECTIVE RANDOMIZED CONTROLLED TRIAL DATA THAT
4 DOCUMENTS THAT ONE APPROACH IS SUPERIOR TO ANOTHER, I
5 DON'T THINK THAT EXISTS FOR ALMOST ANY CLINICAL
6 SCENARIO THAT YOU CAN DESCRIBE. I JUST DON'T THINK
7 THE DATA ARE THAT GOOD.
8 AND I THOUGHT THAT THAT WAS ALSO, YOU
9 KNOW, THE AHRQ REVIEW THAT WAS COMMISSIONED, I
10 THOUGHT THAT WAS THEIR CONCLUSION AS WELL. I DIDN'T
11 THINK THEY --
12 DR. GARBER: THAT WAS EITHER A GRADE B OR
13 GRADE C LEVEL OF EVIDENCE, I THINK.
14 DR. DWORKIN: YEAH, I DON'T KNOW WHAT IT
15 WAS. I MEAN, I PROBABLY SHOULDN'T BE TALKING TO THIS
16 SINCE I DIDN'T WRITE THE GUIDELINES, BUT IF YOU HAVE
17 GRADE B EVIDENCE, THEN HOW DO YOU GET TO A CLASS I
18 INDICATION? THAT SEEMS TO ME TO BE SORT OF A
19 METHODOLOGIC ISSUE.
20 DR. LEWIS: WELL, THE OTHER QUESTION IS,
21 OR AN ADDITIONAL QUESTION IS THAT CORAL DOES EXCLUDE
22 PEOPLE WITH HEART FAILURE AND LOW EJECTION FRACTIONS
23 AS WELL AS --
24 DR. DWORKIN: IN THE REVISED PROTOCOL,
25 THERE'S NO EXCLUSION FOR EJECTION FRACTION. THAT WAS

00165

1 SOMETHING THAT WAS PUT IN THERE INITIALLY WHICH WAS
2 DROPPED. I MEAN, THE ONLY HEART FAILURE EXCLUSION IS
3 IF SOMEBODY HAS BEEN ADMITTED WITHIN, I THINK IT'S
4 THE LAST 30 DAYS, FOR CONGESTIVE HEART FAILURE. YOU
5 KNOW, PART OF THIS IS JUST KEEPING PEOPLE OUT OF THE
6 TRIAL THAT ARE SO ILL.
7 SO ONE OF THE THINGS WE WERE CONCERNED
8 ABOUT IS THAT ACTUALLY AMONG THE COMPOSITE ENDPOINTS
9 WHICH INCLUDES, THE PRIMARY ENDPOINT IS A COMPOSITE
10 IN CORAL, WHICH INCLUDES, AMONG ONE OF THE ENDPOINTS
11 IS ADMISSION TO THE HOSPITAL FOR CONGESTIVE HEART
12 FAILURE. AND WE WERE A LITTLE BIT CONCERNED THAT
13 THERE WERE PATIENTS WHO WERE ADMITTED VERY FREQUENTLY
14 LIKE THAT, AND THEN IF WE ALLOWED PATIENTS LIKE THAT
15 TO BE ENROLLED, THAT THAT PARTICULAR OUTCOME MIGHT
16 DRIVE THE WHOLE OUTCOME OF THE TRIAL.
17 BUT I THINK IT'S FAIRLY STANDARD IN MANY
18 CLINICAL TRIALS TO EXCLUDE PATIENTS THAT HAD AN MI
19 WITHIN THE LAST 30 DAYS, OR A STROKE WITHIN A CERTAIN
20 AMOUNT OF TIME, SO PART OF IT IS JUST THAT. YOU
21 DON'T WANT PEOPLE THAT ARE IN THE MIDST OF AN ACUTE
22 ILLNESS COMING INTO A LONG-TERM PROSPECTIVE TRIAL
23 LIKE THIS WHERE YOU'RE TRYING TO LOOK AT THE IMPACT
24 OF THESE TWO APPROACHES ON THOSE OUTCOMES. SO WE
25 WERE TRYING TO GET A GROUP OF PATIENTS WHO AT LEAST

00166

1 WITH REGARD TO THE VARIOUS COMPONENTS OF THE PRIMARY
2 ENDPOINT WERE RELATIVELY STABLE AT THE TIME THAT THEY
3 WERE ENROLLED AND NOT ACUTELY ILL, IN THOSE
4 CATEGORIES.
5 AND THAT'S REALLY THE ONLY REASON, OR THE
6 PRIMARY REASON FOR THAT EXCLUSION. IT WASN'T THAT WE
7 FELT THAT PATIENTS WITH HEART FAILURE WERE A GROUP
8 FOR WHOM IT WAS CLEAR THAT ONE APPROACH WAS SUPERIOR
9 TO THE OTHER. I DON'T THINK WE FELT THAT AT ALL.
10 DR. CHARYTAN: BUT THERE WAS A SECOND PART
11 TO THE QUESTION THAT DR. KRIST HAD ASKED, AND THAT
12 WAS HOW MANY PATIENTS WERE SCREENED TO COME UP WITH
13 THE 200 PATIENTS THAT YOU ENDED UP WITH.
14 DR. DWORKIN: WE ARE KEEPING SCREENING
15 LOGS. THE PROBLEM WITH LOOKING AT THE SCREENING LOGS
16 LIKE THAT IS THAT WHAT PEOPLE RECORD AS A SCREENED
17 PATIENT IS VERY VARIABLE, YOU KNOW, FROM INSTITUTION
18 TO INSTITUTION. SO SOMETIMES A SCREENED PATIENT
19 MIGHT BE SOMEBODY THAT HAS HYPERTENSION AND THE
20 CREATININE OF 1.2, WHO GETS A DUPLEX ULTRASOUND
21 ORDERED AND IT DOESN'T SHOW RENOVASCULAR DISEASE. SO
22 THAT COULD BE A SCREENING FAILURE, BUT THAT'S NOT
23 REALLY SOMEBODY WITH RENAL ARTERY STENOSIS OR
24 RENOVASCULAR DISEASE WHO WAS NOT BEING ENTERED INTO
25 THE TRIAL.

00167

1 AND I DON'T KNOW, CHRIS, DO WE KNOW THE
2 PERCENTAGE OF PATIENTS THAT HAVE, ACTUALLY HAVE
3 DOCUMENTED HIGH GRADE RENAL ARTERY STENOSIS OR
4 STENOSIS THAT WOULD QUALIFY THEM FOR ENTRY THAT WERE
5 BEING SCREENED AND NOT ENTERED? DO YOU HAVE A --
6 DR. COOPER: I'M LOOKING IT UP. I DON'T
7 KNOW WHAT THE EXACT NUMBER IS.
8 DR. DWORKIN: I MEAN, CLEARLY THERE ARE
9 PATIENTS LIKE THAT THAT ARE NOT GETTING ENTERED, AND
10 THERE'S A VARIETY OF REASONS WHY THAT HAPPENS.
11 PATIENTS DECLINE, YOU KNOW, AFTER THEY READ THE
12 CONSENT FORM, OR, YOU KNOW, FOR ONE OTHER REASON OR
13 ANOTHER. BUT I DON'T KNOW THE EXACT NUMBERS.
14 DR. CHARYTAN: BUT AGAIN, I THINK THAT'S
15 PERTINENT TO THE POINT THAT IF THERE WERE ABOUT 18 OR
16 20,000 PROCEDURES BEING DONE BY 2000, AND I HEARD A
17 NUMBER BEING RECENTLY MENTIONED THAT IT MIGHT BE UP
18 TO 30,000 OR 40,000 BY 2005, THEN CLEARLY IN
19 RESTRICTING COVERAGE TO JUST PATIENTS, A THOUSAND
20 PATIENTS WHO ARE GOING TO BE IN THE STUDY, EVEN
21 THOUGH MANY PATIENTS MAY BE GETTING PROCEDURES, THAT
22 WOULD BE EXCLUDING POTENTIALLY A SIGNIFICANT NUMBER
23 OF PATIENTS WHO MIGHT CONCEIVABLY BENEFIT. AND I
24 THINK ONE COULD ARGUE THAT THERE IS A PROBLEM WITH
25 THAT APPROACH.

00168

1 DR. DWORKIN: YEAH. I DON'T DISAGREE WITH
2 THAT. I MEAN, I CAN'T REALLY SPEAK FOR CORAL AS A
3 STUDY BECAUSE WE'RE A GROUP OF INDIVIDUALS, BUT I
4 DON'T THINK AS A GROUP WE'VE REALLY ADVOCATED THAT
5 POSITION. I THINK WHAT WE'VE BEEN CONCERNED ABOUT IS
6 THAT ENROLLMENT HAS BEEN VERY SLOW DESPITE THE FACT
7 THAT THERE ARE OBVIOUSLY, YOU KNOW, TREMENDOUS
8 NUMBERS OF THESE PROCEDURES BEING DONE. AND YOU
9 KNOW, WE'RE JUST TRYING TO ADDRESS EVERY POTENTIAL
10 BARRIER TO GET THE PATIENTS INTO THE STUDY.
11 THERE CLEARLY IS, I THINK IT SEEMS OBVIOUS
12 TO ME, A LITTLE BIT OF A FINANCIAL DISINCENTIVE IF A
13 PATIENT GETS ENROLLED, BECAUSE YOU ONLY HAVE A 50
14 PERCENT CHANCE OF ACTUALLY BEING ABLE TO DO THE
15 PROCEDURE. IT'S IMPOSSIBLE FOR ME TO SAY HOW MUCH
16 THAT DISINCENTIVE IS INFLUENCING ENROLLMENT, BUT IT
17 JUST IS A CONCERN. AND YOU KNOW, WE HAVE BEEN
18 STRUGGLING WITH THE FACT THAT IF THERE ARE REALLY
19 50,000 PROCEDURES BEING DONE IN THE UNITED STATES AND
20 WE'RE ENROLLING A HUNDRED PATIENTS A YEAR IN CORAL,
21 OR NOT MUCH MORE THAN THAT, THAT WE'RE GETTING .1
22 PERCENT OF ALL THE PROCEDURES, AND IT IS AN ISSUE FOR
23 US.
24 BUT I THINK IT APPLIES NOT ONLY TO CORAL,
25 IT APPLIES TO CLINICAL STUDIES IN GENERAL IN THIS

00169

1 COUNTRY WHERE ENROLLMENT HAS TENDED TO BE LOW. BUT
2 WE CERTAINLY HAVEN'T SUGGESTED AS A GROUP OR AS THE
3 CORAL TRIAL, THAT FUNDING ONLY BE LIMITED TO PATIENTS
4 ENROLLED IN THE CORAL STUDY.
5 DR. GARBER: WE WILL BE GETTING INTO A
6 DISCUSSION OF THIS WHEN WE GET TO VOTING QUESTION
7 NUMBER 4, AND HOPEFULLY THE SPEAKERS WILL STILL BE
8 HERE TO ADDRESS QUESTIONS SPECIFICALLY ON THAT POINT.
9 ANY OTHER QUESTIONS FOR THE PRESENTERS? STEVE?
10 DR. TEXTOR: I WONDER IF I COULD ASK
11 DR. HIRSCH TO COMMENT A LITTLE BIT MORE ON THE
12 GUIDELINES FROM THE AMERICAN HEART OR ACC,
13 SPECIFICALLY AS TO THE ISSUE OF THE CLASS I
14 RECOMMENDATION ABOUT PATIENTS WITH PULMONARY EDEMA,
15 AND REALLY THE SERIES OF RECOMMENDATIONS BASICALLY
16 ARGUING THAT IT'S REASONABLE TO UNDERTAKE
17 REVASCULARIZATION FOR HYPERTENSION, PRESERVATION OF
18 RENAL FUNCTION BASICALLY, GIVEN THE IIA
19 RECOMMENDATION. THEY SEEM TO ME OPTIMISTIC COMPARED
20 TO THE AHRQ RECOMMENDATIONS. HOW WOULD YOU RECONCILE
21 THAT?
22 DR. HIRSCH: WELL, I WON'T TRY TO SPEAK
23 DIRECTLY TO THE RECOMMENDATIONS THEMSELVES, BUT THE
24 GUIDELINE WRITING COMMITTEE DID FEEL THAT THE CASE
25 SERIES THAT EXISTED, THE LEVEL OF EVIDENCE A FOR

00170

1 THOSE INDICATIONS WERE NOT ADEQUATE TO ACHIEVE A
2 CLASS I INDICATION, SO I CAN'T SPEAK MORE IN DETAIL
3 TO THAT.
4 BUT I WOULD LIKE TO MAKE A COMMENT IF I
5 COULD, THAT FOR THOSE CLASS I INDICATIONS AND THE IIA
6 INDICATIONS, WE DO FEEL THERE IS COMPELLING EVIDENCE
7 THAT MANY INDIVIDUALS IN OUR COUNTRY WOULD BENEFIT
8 FROM MAINTAINING REIMBURSEMENT, THAT THERE IS AN
9 ETHICAL STANDARD THAT CAN BE SUSTAINED THAT PERMITS
10 THESE INTERVENTIONS TO IMPROVE HEALTH.
11 BUT YOU'RE RIGHT, THE EVIDENCE BASE IS
12 INCOMPLETE AND I WOULD HAVE COMPLETED THAT WITH MY
13 OTHER COMMENTS. WAS THERE AN ADDITIONAL QUESTION?
14 DR. TEXTOR: THE OTHER QUESTION, IT WAS
15 ALLUDED THERE WAS SOME SORT OF MAJOR ETHICAL CONCERN,
16 AND PERHAPS A REPRESENTATIVE FROM BOSTON SCIENTIFIC
17 WOULD COMMENT ON THEIR ETHICAL RESERVATIONS ABOUT
18 ENTERING PEOPLE IN THE CORAL TRIAL.
19 DR. GARBER: DR. KELLEY, CAN YOU COME UP
20 TO THE MIKE, PLEASE?
21 DR. KELLEY: I THINK IT'S NOT ETHICAL IN
22 THE SETTING OF THE TRIAL ITSELF, IT'S ETHICAL IN
23 ASKING PATIENTS. IF YOU DECIDE UPON A COVERAGE THAT,
24 YOU CAN ONLY HAVE A RENAL STENT IF YOU'RE PART OF A
25 CLINICAL TRIAL, AND THE ONLY TRIAL IS A RANDOMIZED

00171

1 CLINICAL TRIAL, THAT PUTS PATIENTS IN A TOUGH
2 POSITION, BECAUSE THEN THEY HAVE TO DECIDE WHETHER,
3 A, YOU KNOW, IN THE INFORMED CONSENT THEY HAVE TO
4 PARTICIPATE IN A CLINICAL TRIAL, AGAINST A TREATMENT
5 THAT HAS BEEN OFFERED FOR THE LAST, YOU KNOW,
6 TEN-PLUS YEARS.
7 DR. TEXTOR: REMIND ME WHAT THE ETHICAL
8 BIND IS.
9 DR. GARBER: ARE YOU SAYING THAT IT IS
10 KNOWN THAT THE TREATMENT IS EFFECTIVE, OR JUST BY
11 VIRTUE OF HISTORY IT HAS BEEN AVAILABLE, AND
12 THEREFORE IT'S POTENTIALLY UNETHICAL TO ONLY PROVIDE
13 THE CONTEXT OF THE TRIAL. I THINK FROM MANY PEOPLE'S
14 UNDERSTANDING OF ETHICS, IT'S ONE THING TO DENY A
15 KNOWN EFFECTIVE THERAPY. IT'S QUITE ANOTHER TO DENY
16 AN UNPROVEN THERAPY. AND I BELIEVE THAT THE
17 RATIONALE FOR THE TRIAL IS THAT IT'S UNKNOWN WHETHER
18 THIS IS EFFECTIVE.
19 DR. KELLEY: AND I AGREE ENTIRELY, AND I
20 THINK THE COMMENTS THAT WERE MADE BY PEOPLE THAT IT'S
21 NOT UNKNOWN IF IT'S THE RIGHT -- IT'S THE PATIENT
22 SELECTION THAT POTENTIALLY IS NOT UNKNOWN, WHO ARE
23 THE BEST PATIENTS TO BENEFIT FROM THIS THERAPY.
24 DR. GARBER: DR. HIRSCH, DID YOU WANT TO
25 MAKE A COMMENT?

00172

1 DR. HIRSCH: THAT'S A VERY INTERESTING
2 QUESTION, AND MANY PEOPLE IN THE AUDIENCE I THINK
3 COULD SPEAK TO THAT. I THINK THAT WE MIGHT MAKE
4 METAPHORS OF OTHER DISEASES WHERE WE HAVE AN
5 INCOMPLETE EVIDENCE BASE, WHICH IS TRUE OF MANY
6 CANCERS, FOR EXAMPLE, WHERE WE HAVE SOME EVIDENCE OF
7 EFFICACY, IT'S INCOMPLETE, AND THE WRITING COMMITTEE
8 ACKNOWLEDGED THAT. AND SOME PATIENTS REALLY DON'T
9 HAVE ACCESS TO IT BASED ON REIMBURSEMENT FOR
10 MEDICATIONS, ACCESS TO THEIR PHYSICIANS, TO PURE
11 MEDICAL THERAPY ALONE.
12 SO I THINK THAT, ALAN, ONE CAN MAKE THE
13 CASE THAT WHEN THERE IS A POTENTIAL THERAPEUTIC
14 CHOICE BETWEEN TWO OR THREE DIFFERENT INDICATIONS,
15 DIFFERENT TREATMENTS, AND IN A SENSE PATIENTS MAY
16 ONLY HAVE ACCESS TO ONE OR THE OTHER PREFERENTIALLY,
17 WE DO SET UP INHERENT BIASES BY REIMBURSING ONE
18 VERSUS THE OTHER. SO PATIENTS END UP IN VERY UNIQUE
19 CIRCUMSTANCES AND THE CLINICIAN WHO'S TREATING THE
20 PATIENT DOES HAVE TO MAKE THAT BALANCE.
21 THERE'S SOME TREATMENT OFFERED. THESE
22 ARE, AFTER ALL, DISEASES. ATHEROSCLEROTIC RENAL
23 ARTERY STENOSIS HAS A VERY, VERY HIGH SHORT-TERM
24 EVENT RATE. SO YOU LEAVE PATIENTS POTENTIALLY
25 UNTREATED, IN A SENSE COERCED INTO NO TREATMENT IF

00173

1 YOU HAVE NO EQUIPOISE FOR REIMBURSEMENT. I HOPE THAT
2 HELPS.
3 DR. GARBER: OKAY. THESE ARE INTERESTING
4 POINTS. WE'RE GOING TO HAVE TO MOVE ON TO SOME MORE
5 SPECIFIC QUESTIONS THAT ARE FACING US. YES?
6 DR. PRESSMAN: CONSIDERING WE'VE HEARD A
7 FEW MINUTES AGO ABOUT THE SMALL NUMBER OF PEOPLE THAT
8 ARE BEING RECRUITED TO STUDY, IT SEEMS TO ME WE
9 SHOULD BE CONSIDERING APPROPRIATE CRITERIA FOR
10 PERFORMING THESE PROCEDURES ON PATIENTS WHO ARE NOT
11 RECRUITED FOR A STUDY, IF WE'RE GOING TO CONTINUE TO
12 PAY FOR IT IN ANY FORMAT. AND I WOULD LIKE TO ASK
13 DR. MURPHY, WHO REFERRED TO THAT EARLIER IN HIS
14 COMMENTS, WHETHER OR NOT HE HAD ANY SUGGESTIONS OF
15 SOME SORT OF INCLUSION CRITERIA FOR THE NON-CORAL
16 STUDY PATIENTS.
17 DR. MURPHY: YEAH. THAT'S A GREAT
18 QUESTION AND I THINK IS THE FUNDAMENTAL REASON FOR
19 BEING HERE. THE GROWTH IN THE PROCEDURES IS SORT OF
20 PARADOXICAL WHEN WE LOOK AT THE LITERATURE THAT CAME
21 OUT DURING THE TIME PERIOD OF GROWTH, WHICH SUGGESTED
22 THAT THE PROCEDURES DON'T PROVIDE A LOT OF BENEFIT.
23 SO THE QUESTION IS, FOR THOSE OF US WHO DO THE
24 PROCEDURES AND KNOW THAT WE'VE HAD PATIENTS WHO'VE
25 GOTTEN BETTER, WHAT'S DISTINCT ABOUT THOSE INDIVIDUAL

00174

1 PATIENTS THAT WOULD ALLOW US TO CONTINUE TO OFFER
2 SERVICES TO THOSE PATIENTS, ASSUMING THAT THERE'S
3 GOING TO BE SOME COVERAGE FOR THE INTERVENTION IN
4 GENERAL, WHICH I THINK THERE HAS TO BE. I DON'T
5 THINK IT'S REASONABLE TO PULL THE RUG OUT FROM UNDER
6 THE PROCEDURE IN TOTO AT THIS POINT IN TIME, BUT
7 THERE HAS TO BE POTENTIALLY SOME GUIDELINES OR SOME
8 REINING IN, SO THAT IT'S CLEAR AS TO WHO IS ELIGIBLE
9 FOR THE PROCEDURE.
10 NUMBER ONE, I THINK THE PROPHYLACTIC STUFF
11 IS POORLY JUSTIFIED. I THINK PEOPLE NEED SOME TYPE
12 OF CLINICAL INDICATIONS. ALMOST ALWAYS THAT'S
13 REFRACTORY BLOOD PRESSURE, CHRONIC KIDNEY DISEASE,
14 AND IN SOME CASES HEART FAILURE, AND I'LL TALK MORE
15 ABOUT THAT IN A MINUTE. BUT THE HYPERTENSION AS AN
16 INDICATION SHOULD BE IN MY OPINION QUALIFIED BY
17 HAVING PEOPLE UNDERGO FIRST DEDICATED MEDICAL
18 MANAGEMENT ACCORDING TO THE JNC PROGRAM. AND IF THE
19 BLOOD PRESSURE CAN'T BE CONTROLLED WITH THAT, AGAIN
20 GETTING BACK TO THE PRINCIPLE OF FIRST DO NO HARM,
21 TRY THE LESS INVASIVE MEANS FIRST AND EXHAUST THAT
22 AVENUE. AND IF THAT DOESN'T WORK, THEN THE PERSON
23 CAN BE CONSIDERED FOR INTERVENTION. SO THERE WOULD
24 POTENTIALLY BE SOME PREQUALIFICATION BASED ON MEDICAL
25 MANAGEMENT OF HYPERTENSION FAILING.

00175

1 AND ALSO, TO THROW IN WITH THAT, THERE HAS
2 TO BE SOME THRESHOLD OF ANATOMY. A RENAL ARTERY
3 STENOSIS OF 50 PERCENT WITH NO GRADIENT AND FAILED
4 MEDICAL MANAGEMENT PROBABLY DOESN'T QUALIFY SOMEBODY.
5 A STENOSIS OF, SAY, FOR EXAMPLE, 60 OR 70 PERCENT OR
6 GREATER, PERHAPS WITH A PRESSURE GRADIENT AND
7 REFRACTORY ON MEDICAL MANAGEMENT, WOULD BE A STRONG
8 INDICATION FOR REIMBURSEMENT.
9 ON THE CHRONIC KIDNEY DISEASE SIDE, AN
10 INDICATION OF CHRONIC KIDNEY DISEASE WOULD BE
11 SUPPORTED IF THE PERSON HAD BILATERAL SEVERE STENOSES
12 OR A SINGLE KIDNEY AND A SEVERE STENOSIS. ALSO, IT
13 SHOULD BE A LONG-TERM OR AT LEAST SOME PERIOD OF
14 TIME, IT SHOULDN'T BE A TRANSIENT KIDNEY FAILURE
15 RELATED TO STATIN, ACE, OR DEHYDRATION OR SOME
16 EPISODE OF SEPSIS OR WHATEVER THE CASE MAY BE.
17 AND THE LAST CLINICAL INDICATION WOULD BE
18 THE HEART FAILURE INDICATION WHICH PATIENTS IN MY
19 EXPERIENCE WOULD HAVE A STRONG CLINICAL BENEFIT FROM
20 THE PROCEDURE, BUT ALMOST ALL OF THOSE HAVE BILATERAL
21 DISEASE OR A SINGLE KIDNEY WITH SEVERE STENOSIS, AND
22 THEY ALSO HAVE ELEMENTS OF CHRONIC KIDNEY DISEASE.
23 SO IF YOU'RE LOOKING FOR A LIST OF
24 INDICATIONS FROM WHICH TO RUN THIS IN AS SORT OF A
25 LITMUS TEST FOR A FIRST PASS AT A COVERAGE POLICY, I

00176

1 THINK REFRACTORY HYPERTENSION AFTER DEDICATED MEDICAL
2 MANAGEMENT WITH A SEVERE STENOSIS OR CHRONIC KIDNEY
3 DISEASE WITH BILATERAL OR A SINGLE KIDNEY WITH SEVERE
4 STENOSIS WOULD BE A GOOD PLACE TO START.
5 DR. GARBER: OKAY, THANK YOU. THIS IS
6 ONLY NATURAL, IT HAPPENS ALL THE TIME, BUT WE'RE
7 BORDERING INTO THE DISCUSSION OF THE VOTING
8 QUESTIONS. SO, COULD I ASK THE SENSE OF THE PANEL,
9 ARE WE READY TO GO?
10 DR. FENDRICK: ONE MORE.
11 DR. GARBER: GO AHEAD, MARK.
12 DR. FENDRICK: AND THIS BEING YOUR LAST
13 PANEL, I THINK IT'S IMPORTANT FOR US TO THINK ABOUT
14 THE INSTITUTIONAL HISTORY OF SEEING A NUMBER OF VERY
15 PROMISING NONPHARMACEUTICAL INTERVENTIONS THAT HAVE A
16 LOT OF INCREDIBLY TALENTED AND PASSIONATE
17 INVESTIGATORS, AND WE'RE ALWAYS ASKING FOR MORE
18 EVIDENCE. THE NAME OF THIS PANEL ACTUALLY CHANGED
19 FROM THE MEDICARE COVERAGE ADVISORY COMMITTEE TO THE
20 MEDICARE EVIDENCE DEVELOPMENT AND COVERAGE ADVISORY
21 COMMITTEE, AND I THINK THAT WE WILL ALL BE ABLE TO
22 TALK AT THE END OF THE DAY ABOUT THE LIMITATIONS OF
23 RANDOMIZED TRIALS.
24 BUT I AM SOMEWHAT SURPRISED, GIVEN THAT
25 EVERY ONE OF THE MAJOR PROFESSIONAL ORGANIZATIONS IS

00177

1 HERE AND REPRESENTED, AND THE FACT THAT THERE IS NOW
2 SEVERAL THOUSAND PROCEDURES A YEAR, THAT THERE HAS
3 NOT BEEN CREATED AT LEAST A WELL-RUN REGISTRY THAT
4 COULD AT LEAST GIVE US AN INFERENCE TO WHAT A
5 RANDOMIZED TRIAL MIGHT SHOW. AND I JUST SAY THAT
6 BECAUSE OF THE FACT THAN IN MOST OF THE OTHER MCACS I
7 SAT ON, WE PUSHED FOR RCT, AND YOU PUSHED BACK SAYING
8 THERE AREN'T ENOUGH SITES, IT TAKES TOO LONG,
9 PATIENTS WON'T DO IT. BUT AT A MINIMUM, MANY OTHER
10 INTERVENTIONAL FIELDS HAVE AT LEAST COME UP WITH, OF
11 THE 30,000 FOLKS THAT HAVE BEEN STENTED OVER THE LAST
12 FIVE YEARS -- I WOULD IMAGINE THERE ARE STILL A FEW
13 PEOPLE IN AMERICA WITH RENAL ARTERY STENOSIS THAT
14 HAVE NOT GOTTEN IT DONE, ALTHOUGH PROBABLY NOT IN
15 MASSACHUSETTS OR TOLEDO, OHIO. BUT AT LEAST IN RHODE
16 ISLAND, THERE'S PROBABLY A FEW FOLKS WITH RENAL
17 ARTERY STENOSIS THAT HAVE NOT BEEN INTERVENED UPON.
18 SO I WOULD REALLY -- I'M NOT PICKING ON
19 ANY ONE INDIVIDUAL, BUT I'VE SEEN ENOUGH NODDING
20 DURING MY COMMENTS THAT YOU DISCUSSED IT. AND SHORT
21 OF RANDOMIZED TRIALS, AND MOST OF US DON'T WANT TO
22 WAIT UNTIL 2010, THERE ARE ENOUGH SKILLED
23 INVESTIGATORS AMONG YOU AND PEOPLE AT YOUR
24 INSTITUTIONS WITH ABILITIES, METHODOLOGIC AND OTHER
25 EXPERTISE, TO GIVE YOU REASONABLE ANSWERS TO AT LEAST

00178

1 GET US A MAJOR STEP FORWARD FROM WHERE WE ARE NOW.
2 DR. GARBER: LET ME JUST ADD ONE POINT OF
3 INFORMATION TO WHAT MARK SAID. OUR VOTING QUESTION 4
4 DOES NOT SAY THAT MEDICAL NATIONAL COVERAGE SHOULD BE
5 LIMITED TO PATIENTS ENROLLED IN CLINICAL TRIALS. IT
6 SAYS IN QUALIFIED CLINICAL RESEARCH STUDIES, SO IN
7 FACT THIS DOES NOT MEAN THAT -- THEY ARE NOT ASKING
8 US TO SAY EVERYONE WOULD NEED TO BE ENROLLED IN CORAL
9 IN ORDER TO BE ELIGIBLE FOR REIMBURSEMENT. AGAIN,
10 WE'LL GET TO THAT WHEN WE DISCUSS VOTING QUESTION 4.
11 DR. FENDRICK: THERE IS NO REGISTRY -- I
12 SHOULD ASK THE QUESTION. AS FAR AS THE COUNTRY'S
13 EXPERTS KNOW, THERE IS NO REGISTRY IN PLACE NOW.
14 DR. COOPER: AT THE DINGLE CENTER, YES.
15 DR. GARBER: THERE'S NO NATIONAL REGISTRY.
16 DR. HIRSCH: AND THERE'S NO REGISTRY THAT
17 INCLUDES MEDICAL THERAPY EITHER.
18 DR. KRIST: I HAVE A CLARIFICATION
19 QUESTION, NOT FOR ANYONE IN PARTICULAR. BUT WHEN WE
20 SEE THE ONGOING STUDIES, THINKING ABOUT WHAT EVIDENCE
21 DO WE HAVE, I SEE HERE FIVE OR SIX ONGOING STUDIES,
22 BUT STAR, RAVE, ASTRAL AND NITER ARE ALL SUPPOSED TO
23 BE DONE, AT LEAST LOOKING AT THE TIME LINES THAT I
24 SEE. DO WE HAVE ANY INDICATION OF RESULTS OR WHEN WE
25 MIGHT KNOW RESULTS, OR DOES ANYONE KNOW THIS?

00179

1 DR. COOPER: I HAVE BEEN IN CONTACT WITH
2 THE HEAD OF THE STAR NETWORK AND ALSO THE ASTRAL
3 NETWORK. I KNOW THAT STAR SOMETIME NEXT YEAR
4 PROBABLY WILL PRESENT THEIR PRELIMINARY DATA. ASTRAL
5 HAS FINISHED ENROLLMENT IN THEIR RANDOMIZED PHASE AND
6 IS CONTINUING SOME OF THEIR CARDIAC REGISTRIES, AND I
7 SUSPECT PROBABLY NEXT FALL WILL HAVE SOME RESULTS
8 THERE.
9 RAVE IS A REGISTRY, I BELIEVE A SINGLE
10 CENTER REGISTRY. I DON'T THINK THAT YOU'RE GOING TO
11 GET EARTH-SHAKING NEWS FROM THAT.
12 DR. EDWARDS: DR. GARBER, COULD I SUBMIT
13 ONE BRIEF COMMENT BEFORE WE -- I DON'T KNOW IF WE'RE
14 READY TO PROCEED TO VOTING QUESTIONS, BUT IF IT'S
15 OKAY, AS FAR AS THE VOTING QUESTIONS, BEFORE WE
16 PROCEED TO THAT, I WANTED TO MAKE ONE POINT CLEAR
17 THAT HAS BEEN ALLUDED TO BY MANY BUT NEVER OVERTLY
18 STATED. AND THAT WOULD BE THE FACT THAT WE ARE VERY
19 LIKELY DEALING WITH SPLIT CATEGORIES OF PATIENTS WHO
20 MAY HAVE VERY DIFFERENT RESPONSES TO THERAPY, AND THE
21 VOTING QUESTIONS DON'T BREAK THAT DOWN. I KNOW THAT
22 WOULD CREATE A LIST OF ABOUT 25 QUESTIONS, I
23 UNDERSTAND THAT.
24 BUT I THINK THAT A LOT OF DATA WHICH HAS
25 BEEN ALLUDED TO BY SEVERAL OF THE PRESENTERS BUT

00180

1 EXCLUDED FROM THE WONDERFUL ANALYSIS BY THE TUFTS
2 GROUP BECAUSE IT IS MOSTLY RETROSPECTIVE DATA, I
3 THINK THERE IS STILL INFORMATION WITHIN ALL THOSE
4 SCIENTIFIC STUDIES WHICH HAS SOME MERIT IN AT LEAST
5 STATING THAT AND USING IT TO SORT OF SEPARATE THESE
6 GROUPS, BECAUSE I THINK IT'S IMPORTANT TO
7 THEORETICALLY UNDERSTAND THAT THERE ARE VERY
8 DIFFERENT PATIENT POPULATIONS.
9 ONE IS THE FACT THAT EVEN IN ALL THE
10 RETROSPECTIVE WORK THAT'S BEEN DONE OVER THOUSANDS OF
11 PATIENTS, EVEN WITH VERY PRONOUNCED BLOOD PRESSURE
12 DECREASES IN SOME OF THE SURGICAL GROUPS IN TERMS OF
13 ABSOLUTE BLOOD PRESSURE DECREASE, BLOOD PRESSURE
14 RESPONSE IN AND OF ITSELF HAS NEVER BEEN ASSOCIATED
15 WITH A DECREASE IN ADVERSE EVENTS AND MORTALITY IN
16 THE LIMITED NUMBER OF STUDIES THAT THAT'S BEEN LOOKED
17 AT.
18 ALSO, AS MANY HAVE ALLUDED TO, SEVERE
19 HYPERTENSION IS BECOMING A MORE INCREASINGLY RARE
20 PHENOMENON BECAUSE OF THE INCREASE IN EFFICACY IN
21 ANTIHYPERTENSIVE AGENTS. RENAL FUNCTION, ON THE
22 OTHER HAND, HAS BEEN SHOWN BY SEVERAL INVESTIGATORS
23 TO BE A FAIRLY ROBUST PREDICTOR AFTER INTERVENTION.
24 IN OTHER WORDS, IF YOU HAD A GOOD RENAL FUNCTION
25 RESPONSE, YOUR SUBSEQUENT FREEDOM FROM ADVERSE EVENTS

00181

1 AND SURVIVAL ARE BETTER. AND NOT ONLY THAT, BUT YOUR
2 RESPONSE HAS SOMETHING TO DO WITH INITIAL FUNCTION.
3 AND WHAT I MEAN THERE IS THERE'S SOME WORK
4 THAT WAS DONE BY ONE OF MY MENTORS, I'VE NOT SEEN IT
5 REPRODUCED BY ANYONE ELSE, BUT SAYING THAT IF YOU
6 HAVE SEVERE RENAL INSUFFICIENCY, IF YOU IMPROVED TO
7 ENJOY BETTER SURVIVAL THAN THOSE WHO WERE LEFT
8 QUOTE-UNQUOTE STABILIZED, UNCHANGED OR WORSENERED -- AS
9 A MATTER OF FACT, THOSE LATTER TWO COHORTS, THEIR
10 SURVIVAL ANALYSES WERE OVERLAPPING. HOWEVER,
11 PATIENTS WITH LESSER DEGREES OF RENAL DYSFUNCTION OR
12 NORMAL RENAL FUNCTION, THE ONLY GROUP THAT WAS
13 SIGNIFICANTLY IMPACTED IN TERMS OF SURVIVAL WERE
14 THOSE WORSENERED.
15 AND I THINK THAT'S AN IMPORTANT POINT WHEN
16 WE TALK ABOUT ANGIOPLASTY AND STENTING BECAUSE AS IT
17 HAS BEEN ALLUDED TO, OVER THE SHORT HAUL, NOT
18 NECESSARILY PERIPROCEDURALLY, BUT ANGIOPLASTY AND
19 STENTING HAS BEEN ASSOCIATED WITH, PROBABLY
20 CONSERVATIVELY, A 10 TO 20 PERCENT RATE OF HARMING
21 RENAL FUNCTION, OR AT LEAST ASSOCIATED WITH
22 DETERIORATING RENAL FUNCTION OVER SHORT-TERM
23 FOLLOW-UP. AND IT IS UNKNOWN WHETHER THAT IS
24 SECONDARY TO THE PROCEDURE, BUT A LOT OF PEOPLE,
25 INCLUDING MYSELF, SUSPECT THAT IT IS.

00182

1 AND THAT APPLICATION OF PEOPLE WITH NORMAL
2 RENAL FUNCTION AND HYPERTENSION, IF RENAL FUNCTION
3 RESPONSE IS A BIG PREDICTOR OF OUTCOME, THAT'S BAD.
4 WE MAY BE ACTUALLY HURTING PEOPLE WITH THE BEST OF
5 INTENTIONS OF HELPING THEM.
6 NOW GIVEN ALL THAT INFORMATION, OUR GROUP
7 IN PARTICULAR AND A LOT OF GROUPS, I THINK THE MAYO
8 CLINIC GROUP AS WELL, HAVE REALLY STARTED TO SHIFT
9 THEIR FOCUS TO PATIENTS WITH DECLINING RENAL FUNCTION
10 AND SEVERE RENAL INSUFFICIENCY. AND THAT BRINGS ME
11 BACK TO THE POINT THAT I THINK THERE ARE VERY
12 DIFFERENT CATEGORIES. I THINK WITHIN HYPERTENSION
13 THERE IS A REFRACTORY HYPERTENSION GROUP, BUT THEY
14 PROBABLY NEED TO BE STUDIED SEPARATELY. THERE IS THE
15 COMPLICATED HYPERTENSION GROUP, THOSE WITH FLASH
16 PULMONARY EDEMA AND ALTERED CARDIAC DISTURBANCE
17 SYNDROMES. AND THEN THERE'S THE PEOPLE WITH
18 DECLINING RENAL FUNCTION.
19 I WOULD ALSO POINT OUT AS A LAST POINT
20 THAT EVEN THOUGH DR. WEIBULL'S STUDY OF ANGIOPLASTY
21 VERSUS SURGERY HAS BEEN QUOTED, WE ALL HAVE TO
22 UNDERSTAND THAT THAT STUDY WAS DESIGNED, ITS
23 ENDPOINTS WERE DESIGNED WITH AN INCREMENTAL INFERIOR
24 RESULT OF ANGIOPLASTY AND STENTING BEING CONSIDERED
25 EQUIVALENT TO SURGERY.

00183

1 NOW PLEASE DON'T GET ME WRONG. I'M NOT AT
2 ALL CRYING FOR RETURN TO SURGERY, BUT WHAT I'M SAYING
3 IS, I THINK IF YOU LOOK AT THE AGGREGATE LITERATURE,
4 THE OUTCOMES IN TERMS OF RENAL FUNCTION RESPONSE WERE
5 BETTER WITH SURGERY AND LESSER WITH ANGIOPLASTY AND
6 STENTING, AND WE HAVE TO FIND OUT WHY THAT IS.
7 BECAUSE FINDING THAT OUT WILL PROBABLY SHED A LOT
8 MORE LIGHT ON, A, WHAT'S HAPPENING, AND B, WHAT ARE
9 THE IMPORTANT PREDICTORS OF GOOD RESPONSES FOR FOLKS
10 AFTER WE INTERVENE UPON THEM.
11 DR. GARBER: YOU MADE A NUMBER OF
12 EXCELLENT POINTS. LET ME JUST SUGGEST A PROCEDURE SO
13 THAT WE MAKE SURE THEY DON'T GET LOST IN OUR
14 DISCUSSION AND VOTING PROCESS. QUESTIONS 1, 3 AND 4,
15 VOTING QUESTIONS 1, 3 AND 4 ARE QUESTIONS, AND
16 POSSIBLY ALSO 2, ARE QUESTIONS THAT COULD BE DIVIDED
17 UP BY INDICATION. AND AS MATT SUGGESTED, I THINK
18 THIS WAS NEVER CONSIDERED SERIOUSLY BECAUSE OF THE
19 EFFECT IT WOULD HAVE ON THE LENGTH OF OUR
20 DELIBERATION, SO IT'S NOT MEANT TO BURY ANY IMPORTANT
21 FACTS.
22 SO WHAT I WANT TO SUGGEST AS A STARTING
23 POINT FOR PROCEDURE IS IF YOU FEEL, FOR EXAMPLE, IN
24 QUESTION 1 THAT IT IS IMPORTANT TO DISTINGUISH SOME
25 PARTICULAR SUBGROUP OF PEOPLE, SAY FOR EXAMPLE IF YOU

00184

1 THINK THAT THE EVIDENCE IS INADEQUATE GENERALLY BUT
2 THERE'S A GROUP OF PEOPLE LIKE PEOPLE WITH DECLINING
3 RENAL FUNCTION FOR WHICH THE EVIDENCE IS ADEQUATE,
4 THEN YOU SHOULD STATE THAT AND AS A PANEL WE COULD
5 DECIDE TO VOTE SEPARATELY ON THE QUESTIONS.
6 AN ALTERNATIVE, YOU WILL BE ASKED TO
7 EXPLAIN THE WAY YOU VOTED AND YOU CAN STATE THAT YOU
8 VOTED THIS WAY BECAUSE YOU WERE CONSIDERING SOME
9 GROUP LIKE THAT.
10 INCIDENTALLY, ONE OF THE REASONS FOR NOT
11 HAVING GONE THE ROUTE OF LISTING A BUNCH OF
12 INDICATIONS IS THERE WAS NO CONSENSUS GOING INTO
13 THIS, OR AT LEAST THAT WAS THE IMPRESSION OF STAFF,
14 AND ALEX AND ME, THAT IF THERE'S NO CONSENSUS, IT'S
15 GOING TO BE KIND OF HARD TO DECIDE WHICH CATEGORIES
16 TO VOTE ON, AT LEAST BEFORE WE HAVE A DISCUSSION IN
17 THE MEETING. BUT THAT SHOULD NOT PRECLUDE CREATING
18 SOME CATEGORIES NOW IF ANYBODY FEELS STRONGLY ABOUT
19 THAT.
20 SO I WOULD SUGGEST THAT WHEN WE GET TO
21 QUESTION 1, AND ALSO QUESTIONS 3 AND 4 WHERE I THINK
22 THIS IS RELEVANT, THAT WE HAVE A DISCUSSION, AND IF
23 PEOPLE FEEL THAT THEY WANT TO DISTINGUISH SOME
24 SUBGROUP, WE CAN VOTE SEPARATELY ON THAT.
25 I WANTED TO CHECK WITH MICHELLE WHETHER

00185

1 THAT'S FEASIBLE. OKAY. SO, DOES THAT ADDRESS YOUR
2 CONCERNS IF WE GO THAT ROUTE?
3 DR. EDWARDS: ABSOLUTELY. I WASN'T TRYING
4 TO CHANGE PROCEDURES, I JUST WANTED THE THOUGHT OUT
5 THERE, BECAUSE I THINK IT IS IMPORTANT THAT WE THINK
6 ABOUT THAT.
7 DR. GARBER: YEAH. BUT IF YOU DO THINK
8 THERE IS A GROUP THAT'S REALLY DIFFERENT IN TERMS OF
9 LEVEL OF EVIDENCE AND SO FORTH, THAT REALLY NEEDS TO
10 COME OUT FROM OUR DELIBERATIONS TODAY.
11 DR. TEXTOR: COULD I ASK ONE EXTENSION OF
12 THAT? IT STRIKES ME THAT PEOPLE ASKED ABOUT EARLY
13 OUTCOMES FROM NITER AND THE STAR TRIAL. SEVERAL OF
14 THOSE ARE BASED ON RENAL FUNCTIONAL END POINTS, AND I
15 WANTED TO ASK DR. LINAS TO COMMENT. I THINK THERE
16 ARE SOME MYTHS INVOLVED IN THE BASIS FOR SOME OF
17 THESE TRIALS, MYTHS MEANING WIDELY VARYING ESTIMATES
18 OF HOW MANY PEOPLE REACH END-STAGE RENAL DISEASE
19 (INAUDIBLE). CAN YOU HELP CLARIFY, STU, HOW MANY
20 PEOPLE WITH END-STAGE DISEASE ARE THERE BECAUSE OF
21 RENOVASCULAR DISEASE, IN YOUR VIEW?
22 DR. LINAS: THANKS, STEVE, FOR ASKING THAT
23 QUESTION. I THINK, CONSERVATIVELY SPEAKING, LOOKING
24 AT THE USRDS DATA, THE NUMBER IS SOMEWHERE AROUND SIX
25 OR SEVEN PERCENT. BUT OUR SENSE IS THAT THAT MAY BE

00186

1 HIGH AS WELL. IN THAT WHEN ONE LISTS A CAUSE OF
2 END-STAGE RENAL DISEASE IN A PATIENT ENTERING A
3 DIALYSIS PROGRAM, THERE ARE SOME DIAGNOSES THAT ARE
4 PRETTY EASY. THAT IS, TYPE 2 DIABETES THAT HAS A
5 PROTEINURIOPATHY, YOU CAN DO IT. SOMEONE WHO'S HAD
6 AN EPISODE OF LUPUS NEPHRITIS, YOU CAN DO IT.
7 AND THEN THERE COMES DOWN A LIST OF I
8 DON'T KNOW WHY THIS PATIENT HAS END-STAGE RENAL
9 DISEASE, THEY DON'T HAVE A, B, C, D AND E. BY
10 DEFAULT, THEY'VE BEEN HYPERTENSIVE. MAYBE THERE'S
11 SOME RACE ISSUES HERE, AFRICAN-AMERICANS AREN'T SAID
12 TO GET RENAL ARTERY STENOSIS, WHITE AMERICANS ARE.
13 THEY DON'T HAVE PROTEINURIC RENAL DISEASE. THEY HAVE
14 NOTHING THAT'S OBVIOUS, SO I'M GOING TO CHECK OFF THE
15 BOX THAT SAYS RENAL ARTERY STENOSIS. SO THE DATA
16 SAYS ABOUT SIX OR SEVEN PERCENT, BUT IN REALITY I
17 THINK WE WOULD SAY IT'S PROBABLY HALF OF THAT IN
18 REALITY.
19 BUT AFTER TELLING YOU THAT, KIND OF THE
20 PROBLEM IS THE CORAL STUDY. EVEN IF THEY DON'T HAVE
21 END-STAGE RENAL DISEASE, THEY ARE PRESUMABLY, IF THE
22 DATA'S GOOD, AT RISK FOR CARDIOVASCULAR OUTCOMES, AND
23 SO KNOWING WHETHER AN INTERVENTION IN THAT GROUP OF
24 PATIENTS WOULD HAVE MADE A DIFFERENCE
25 CARDIOVASCULARLY, WE DON'T KNOW.

00187

1 DR. SCHWARTZ: AND ALAN, THAT'S THE
2 QUESTION I HAVE. I'M NOT SURE HOW TO PUT IT, BUT I
3 THINK IN VOTING WE NEED TO BE CLEAR ABOUT WHY THIS
4 PROCEDURE IS BEING DONE. IT SEEMS TO ME IT EVOLVES
5 INTO ONE OF TWO CATEGORIES. ONE IS SALVAGE OR
6 IMPROVEMENT OF RENAL FUNCTION, AND THE OTHER IS
7 CARDIOVASCULAR EVENTS. I MEAN, THE REASON AS A
8 GENERAL INTERNIST, I'M INTERESTED IN HYPERTENSION
9 BECAUSE IT INCREASES CARDIOVASCULAR RISKS, EITHER MI
10 OR STROKE OR THINGS LIKE THAT, AND THEY'RE VERY
11 DIFFERENT. MOST OF THE EVENTS ARE GOING TO BE
12 CARDIOVASCULAR EVENTS.
13 BUT THERE MAY BE SEPARATE INDICATIONS FOR
14 RENAL FUNCTION, AND I THINK BY NOT SEPARATING THEM
15 OUT, WE LEAD TO A MUDDINESS THAT FEELS A LITTLE
16 UNCOMFORTABLE. SO I WONDER, AS WE GO THROUGH THESE,
17 IF WE NEED TO JUST MAKE THOSE TWO DISTINCTIONS ON A
18 BROAD BASIS THROUGHOUT.
19 DR. GARBER: I THINK WHAT, WE'LL DO THIS
20 QUESTION BY QUESTION, AND IT WILL BECOME APPARENT
21 WHETHER PEOPLE FEEL A NEED TO CARRY THROUGH ACROSS
22 ALL THE QUESTIONS.
23 MY GUESS IS THAT THERE'S A DISTINCTION
24 WE'RE NOT MAKING AT THIS POINT THAT'S GOING TO BECOME
25 IMPORTANT LATER, WHICH IS, THERE'S A BELIEF ABOUT

00188

1 WHICH INDICATIONS ARE THE MOST PROMISING INDICATIONS.
2 AND THERE'S ANOTHER ABOUT HOW MUCH
3 EVIDENCE EXISTS. SO YOU MIGHT NOT FEEL THE SAME
4 DISTINCTION IS NECESSARY FOR QUESTION 1 THAT YOU
5 MIGHT THINK IS IMPORTANT, FOR EXAMPLE, FOR QUESTION
6 3. I DON'T WANT TO PRESUPPOSE HOW PEOPLE ARE GOING
7 TO VOTE, BUT THE FIRST ONE IS PURELY A LEVEL OF
8 EVIDENCE QUESTION.
9 DR. SCHWARTZ: THE OTHER THING I THINK WE
10 NEED TO PUT IN QUESTION 1, MAYBE AS A 1.B, YOU COULD
11 STILL HAVE A CERTAIN LEVEL OF CONFIDENCE FOR THE
12 THREE CATEGORIES OR THREE PROCEDURAL AREAS THAT ARE
13 ASKED FOR, BUT THEY COULD BE DIFFERENT. FOR EXAMPLE,
14 YOU MIGHT HAVE A CERTAIN LEVEL OF CERTAINTY FOR THE
15 SAFETY AND EFFICACY OF THE ANGIOPLASTY, BUT YOU MIGHT
16 FEEL COMFORTABLE ABOUT WITH STENT THAN WITHOUT STENT,
17 AND I'M NOT SURE THAT'S CAPTURED BY HOW YOU'RE ASKING
18 THE QUESTIONS.
19 DR. GARBER: WHY DON'T WE START OUR
20 DISCUSSION AND SEE HOW THAT SHAKES OUT. THIS IS ALL
21 LEADING UP TO, SINCE WE'RE ANTICIPATING WHAT WE'RE
22 GOING TO SAY IN DISCUSSION, SO WHY DON'T WE GET RIGHT
23 TO IT? HAS EVERYBODY HAD A CHANCE TO READ QUESTION
24 1? I THINK CMS PUT THIS QUESTION IN FOR A REASON, SO
25 I THINK THE ANSWER WOULD BE NO DATA IF THAT'S WHAT

00189

1 YOU BELIEVE.
2 DR. COOPER: THERE ARE NONE UNDER
3 INVESTIGATION.
4 DR. GARBER: SO NO DATA NOW AND THERE
5 WON'T BE DATA, THAT'S WHAT WE'RE HEARING.
6 DR. PRESSMAN: IS IT INAPPROPRIATE TO ADD
7 MEDICAL THERAPY AS ONE OF THE QUESTIONS IN NUMBER 1?
8 DR. GARBER: WELL, THESE, I BELIEVE, ARE
9 ALL COMPARED TO MEDICAL THERAPY. NOW YOU COULD ADD A
10 QUESTION ABOUT MEDICAL THERAPY BETTER THAN PLACEBO,
11 BUT I THINK THE PRESUMPTION HERE WAS THAT AS A
12 BASELINE, PEOPLE WOULD BE RECEIVING MEDICAL THERAPY
13 FOR HYPERTENSION.
14 DR. PRESSMAN: BUT THE PRESUMPTION
15 SUGGESTS IT'S THE GOLD STANDARD, AND I DON'T THINK WE
16 HAVE THAT INFORMATION.
17 DR. GARBER: NO, IT JUST PRESUMES IT'S THE
18 STANDARD.
19 DR. PRESSMAN: BUT THAT'S MY CONCERN. I
20 DON'T THINK -- I MEAN, WHAT WE'VE HEARD TODAY AND
21 WHAT WE'VE READ, WE HAVE NO DATA TO INDICATE THAT.
22 DR. SCHWARTZ: IN THEORY, YOU KNOW, I WAS
23 THINKING A LOT ABOUT THAT SINCE I READ ALL THIS
24 MATERIAL IN PREPARATION. IF WE WEREN'T TALKING ABOUT
25 THIS SPECIFIC CONDITION, I'D HAVE THE SAME PROBLEM.

00190

1 THE ASSUMPTION IS THAT IF THERE ARE NO DATA THAT THE
2 MEDICAL PROCEDURE MUST BE THE STANDARD THAT WE'RE
3 COMPARING IT TO. I THINK IN THIS PARTICULAR CASE,
4 THOUGH, THERE IS A GOOD REASON FOR BELIEVING THAT,
5 AND THAT IS AS WAS STATED BY SEVERAL OF THE SPEAKERS,
6 ALL THESE PEOPLE HAVE INDICATIONS FOR AGGRESSIVE
7 CARDIOVASCULAR RISK PREVENTION ANYWAY, BECAUSE THEY
8 HAVE VASCULAR ATHEROSCLEROSIS. THEY SHOULD ALL BE ON
9 STATINS, AND OUTSIDE OF THE RENAL ARTERIES, THEY
10 SHOULD ALL BE TREATED FOR THEIR HYPERTENSION. SO IN
11 THIS PARTICULAR CASE, I THINK THERE IS, I FEEL
12 COMFORTABLE SAYING WHAT DOES THIS ADD TO SOMETHING
13 EVERYBODY SHOULD BE GETTING. ALTHOUGH I AGREE, WE
14 DON'T KNOW IF THAT IS DOING ANYTHING MORE FOR THE
15 RENAL ARTERY STENOSIS.
16 DR. GARBER: LINDA.
17 DR. BERGTHOLD: I DON'T LIKE ANSWERING
18 QUESTIONS WHERE THERE ARE TWO SORT OF ENDPOINTS.
19 YOU'RE TALKING ABOUT TWO THINGS. YOU'RE ASKING US TO
20 EVALUATE SAFETY AND CLINICAL EFFECTIVENESS. CAN WE
21 SEPARATE THEM OUT OR DO YOU THINK IT DOESN'T MATTER?
22 DR. CHARYTAN: I AGREE WITH THAT BECAUSE
23 THERE MIGHT BE GOOD DATA ON THE SAFETY OF THE
24 PROCEDURE, WHICH IS QUITE SEPARATE FROM WHETHER THE
25 PROCEDURE IS EFFECTIVE.

00191

1 DR. GARBER: WELL, STEVE IS NOT HERE, SO
2 LET ME TAKE A STAB AT TRYING TO ANSWER ON HIS BEHALF,
3 AND THEN MARCEL CAN CORRECT ME. BUT SOME OF THE
4 COMPLICATIONS OF THE PROCEDURE ARE ACTUALLY THE
5 THINGS THE PROCEDURE IS DESIGNED TO PREVENT, AND
6 GETTING TO AN ARGUMENT ABOUT WHETHER THAT'S A RISK OF
7 THE PROCEDURE OR FAILURE TO PREVENT IT OR SOMETHING
8 IS NOT VERY HELPFUL. SO I THINK THE CONCEPT HERE IS,
9 DOES IT PROVIDE A NET HEALTH BENEFIT? IRRESPECTIVE
10 OF WHETHER YOU CALL SOMETHING A SAFETY ISSUE OR NOT,
11 I MEAN, YOU CAN TALK ABOUT RELATIVELY NARROW
12 DEFINITIONS OF SAFETY ISSUES, BUT YOU THINK ABOUT
13 COMPLICATIONS AND THINGS LIKE EMBOLI, AND SOME OF
14 THOSE MAY ALSO BE REFLECTIONS OF THE UNDERLYING
15 DISEASE PROCESS. SO THE IDEA HERE IS REALLY ABOUT
16 NET HEALTH BENEFIT AND NOT AN ATTEMPT TO DISTINGUISH,
17 I DON'T THINK THEY CARE A LOT ABOUT DISTINGUISHING
18 WHAT THE SPECIFIC SAFETY CONCERNS ARE FROM THE
19 PROCEDURE. BARRY?
20 DR. PRESSMAN: SOMEONE WANTS TO SAY
21 SOMETHING.
22 DR. GARBER: YES, DR. SOS?
23 DR. SOS: WELL, CAN I COMMENT ON --
24 DR. SALIVE: WAIT. LET ME JUST ADDRESS
25 THIS. I THINK IF I UNDERSTOOD THE QUESTION, YOU'RE

00192

1 CONCERNED ABOUT NUMBER 1 BUT ALSO NUMBER 3, OR JUST
2 NUMBER 1, BECAUSE I THINK ALAN ADDRESSED NUMBER 3
3 PRETTY WELL. SO YOU KNOW, NUMBER 3 IS SORT OF A
4 COMBINATION OF THE TWO INTO NET HEALTH BENEFITS, I
5 THINK IMPROVED KEY HEALTH OUTCOMES IS HOW WE PHRASED
6 IT IN THIS VERSION.
7 BUT IF YOU FOCUS ON NUMBER 1, IT'S
8 ADEQUACY OF THE EVIDENCE, OKAY? I MEAN ANY EVIDENCE,
9 ALL THE EVIDENCE, THE TOTALITY OF EVIDENCE IS WHAT
10 WE'RE ASKING ABOUT. AND CERTAINLY, YOU KNOW, WITHIN
11 A TOTALITY OF EVIDENCE, IT HAS DIFFERENT AMOUNTS FOR
12 A RARE SAFETY ENDPOINT VIS-A-VIS, YOU KNOW, A
13 DIFFERENT LEVEL OF ADEQUACY PERHAPS FOR THE MAIN
14 EFFECTIVENESS OUTCOMES. WE'LL GRANT YOU THAT, BUT
15 WE'RE REALLY ASKING ABOUT THE ADEQUACY OF THE BODY OF
16 EVIDENCE TO ASSESS THESE SETS OF TREATMENTS.
17 DR. GARBER: DR. SOS.
18 DR. SOS: I'VE HEARD A LOT OF DISCUSSION
19 ON THE PANEL NOW ABOUT INDICATIONS, AND ONE WAS THE
20 RECURRENT FLASH PULMONARY EDEMA WITH BILATERAL
21 DISEASE AND WAS IT ASSOCIATED WITH RENAL DYSFUNCTION.
22 THE SECOND WAS RAPIDLY PROGRESSING RECENT ONSET
23 DYSFUNCTION, AND THE THIRD WAS HYPERTENSION.
24 UNFORTUNATELY, THERE IS A VERY IMPORTANT FOURTH ONE,
25 WHICH MAY ACCOUNT FOR THE VAST MAJORITY OF THE 30,

00193

1 40,000, HOWEVER MANY, AND THAT IS PATIENTS WHO MAY
2 HAVE HYPERTENSION AND MAY HAVE RENAL ARTERY DISEASE,
3 BUT THEY ARE NOT IN ANY WAY RELATED.
4 AND I THINK THAT THAT NEEDS TO BE
5 CONSIDERED VERY SIGNIFICANTLY BY YOU, BECAUSE I WILL
6 BET ANYTHING THAT THE VAST INCREASE IN THE NUMBER OF
7 PATIENTS BEING TREATED IS NOT FOR -- YOU CAN AGREE OR
8 DISAGREE WHETHER HYPERTENSION OR RENAL DYSFUNCTION IS
9 AN INDICATION IF IT IS RELATED TO THE STENOSIS. I'M
10 MUCH MORE CONCERNED ABOUT THE COINCIDENCE OF RENAL
11 ARTERY STENOSIS WHICH MAY BE A 20 OR 30 PERCENT
12 STENOSIS WHICH IS BEING TREATED IN SOMEBODY WHO MAY
13 OR MAY NOT BE HYPERTENSIVE, AND WHERE THERE'S NOT
14 EVEN AN ATTEMPT TO GET A GRADIENT ACROSS THIS. AND I
15 THINK THAT THAT OUGHT TO BE A VERY IMPORTANT PART OF
16 YOUR DISCUSSIONS.
17 DR. GARBER: OKAY, THANK YOU. SO WE'RE ON
18 VOTING QUESTION 1, YOU'VE HAD A CHANCE TO REVIEW THE
19 QUESTION, WE'VE HAD PRE-DISCUSSION, AND NOW WE CAN
20 HAVE DISCUSSION.
21 DR. SCHWARTZ: THE ONLY THING I WOULD SAY
22 BEFORE WE GET INTO IT, I WOULD FEEL MORE COMFORTABLE
23 IF WE SEPARATED SAFETY AND CLINICAL EFFECTIVENESS,
24 BECAUSE I THINK THERE ARE SOME SITUATIONS WHERE I
25 FEEL COMFORTABLE ABOUT THE DEGREE OF SAFETY

00194

1 INFORMATION A LOT MORE THAN I DO ABOUT ITS MEDICAL
2 EFFECTIVENESS. SO, I WONDER IF WE COULD JUST DRAW A
3 COLUMN DOWN AND VOTE ON THESE THINGS TWICE.
4 DR. GARBER: OKAY.
5 DR. MAISEL: I MAY BE STANDING ALONE ON
6 THE PANEL, BUT I THINK THEY NEED TO BE CONSIDERED
7 TOGETHER. I THINK THAT THERE ARE MEASURES OF
8 EFFECTIVENESS THAT ARE ALSO OR POTENTIALLY COULD BE
9 VIEWED AS SAFETY. I THINK IT'S HARD TO JUDGE SAFETY
10 WITHOUT KNOWING THE CLINICAL BENEFIT OR THE
11 EFFECTIVENESS, SO I THINK THE TWO ARE INEXTRICABLY
12 ENTWINED.
13 DR. GARBER: FIRST OF ALL, LET ME JUST
14 TAKE A STRAW POLL. HOW MANY PEOPLE WOULD PREFER TO
15 VOTE SEPARATELY ON SAFETY AND EFFECTIVENESS?
16 (SHOW OF HANDS.)
17 HOW MANY WOULD PREFER TO LINK THEM?
18 (SHOW OF HANDS.)
19 ESPECIALLY IF YOU COUNT VOTING MEMBERS,
20 THERE'S A CLEAR CONSENSUS.
21 SO LET ME JUST REPEAT, THIS WAS ONLY
22 EVIDENCE ADEQUACY, NOT -- BILL, DID YOU WANT TO MAKE
23 A STATEMENT?
24 DR. MAISEL: I JUST HAD ANOTHER
25 INTERESTING QUESTION FOR THE PANEL I'M STRUGGLING

00195

1 WITH A LITTLE BIT, WHICH IS THE ISSUE OF SURROGATE
2 ENDPOINTS AND WHAT EXACTLY WE WANT TO JUDGE THIS
3 QUESTION ON. CERTAINLY WE ALL RECOGNIZE HYPERTENSION
4 IS A PROBLEM, THAT LOWER IS GENERALLY BETTER WITH
5 REGARD TO THE GUIDELINES, BUT WE ALSO NEED TO
6 ACKNOWLEDGE THAT THERE ARE SOME MEDICATIONS THAT
7 LOWER BLOOD PRESSURE THAT HAVE A DIFFERENT MORTALITY
8 BENEFIT THAN ANOTHER MEDICATION, AND I'M NOT SO SURE
9 I'VE SEEN ANY DATA THAT A REDUCTION IN CREATININE OR
10 AN IMPROVEMENT IN GFR ACTUALLY TRANSLATES INTO A
11 CLINICAL BENEFIT FOR THE PATIENT. OBVIOUSLY THE
12 CORAL STUDY WILL HELP A LOT WITH CARDIOVASCULAR
13 OUTCOMES, BUT THESE ARE SICK PATIENTS WHO ARE GOING
14 TO HAVE CARDIOVASCULAR EVENTS AND WHETHER THEIR
15 CREATININE IS 1.8 OR 1.4, I'M STRUGGLING TO SEE IF
16 THAT'S REALLY A CLINICAL BENEFIT FOR THE PATIENT.
17 DR. GARBER: I'M GOING TO TAKE A CHANCE
18 SPEAKING FOR STEVE AND MARCEL HERE, BUT I THINK THE
19 QUESTION REFERS TO FINAL HEALTH OUTCOMES, NOT JUST
20 SURROGATE ENDPOINTS. IF YOU BELIEVE THERE IS GOOD
21 DATA SUPPORTING THAT THE INTERVENTION IN QUESTION
22 IMPROVES SURROGATE ENDPOINTS AND, FURTHERMORE, IF YOU
23 ARE ENTIRELY CONFIDENT THAT AN IMPROVEMENT IN
24 SURROGATE ENDPOINT TRANSLATES INTO AN IMPROVEMENT IN
25 FINAL ENDPOINT, THEN YOU WOULD VOTE THAT THERE IS

00196

1 ENOUGH EVIDENCE. IF YOU HAVE QUESTIONS ABOUT THAT
2 CONNECTION BETWEEN SURROGATE ENDPOINTS AND FINAL
3 ENDPOINTS AND YOU THINK THERE IS ONLY EVIDENCE ON
4 SURROGATE ENDPOINTS, THEN YOU WOULD PRESUMABLY NOT BE
5 CONFIDENT AT ALL IN YOUR RESPONSE TO THE QUESTIONS.
6 MARK?
7 DR. FENDRICK: THIS IS A QUESTION I ASK
8 EVERY TIME, AND I KNOW YOU ANSWER IT BEAUTIFULLY, BUT
9 THE DIFFERENCE BETWEEN UNCERTAIN AND NOT CONFIDENT IN
10 THE CONTEXT OF THIS QUESTION?
11 DR. SALIVE: UNCERTAIN IS NOT QUITE
12 BELIEVED.
13 DR. FENDRICK: THANK YOU, MARCEL.
14 DR. SCHWARTZ: SO THEN YOU WOULD BE
15 DEALING WITH BETWEEN A THREE OR A ONE.
16 DR. FENDRICK: NO, BECAUSE IN PREVIOUS
17 QUESTION, A THREE MEANT INJURIOUS -- I'M SORRY, ONE
18 MEANT INJURIOUS. I WILL, IF YOU DON'T MIND, TAKE THE
19 LIBERTY TO TALK ABOUT DRUG-ELUTING STENTS AND SINCE
20 THERE ARE NO DATA, I THINK UNCERTAIN IS A VERY FAIR
21 ANSWER. BUT WHEN THERE ARE DATA BUT YOU'RE NOT SURE,
22 IS THAT THREE OR ONE?
23 DR. GARBER: SO IF YOU ARE CONFIDENT ABOUT
24 THE DATA, YOU WOULD RANK THAT AS SOME HIGH NUMBER FOR
25 NUMBER 1. AND IF YOU'RE CONFIDENT THAT IT SHOWS

00197

1 HARM, THEN YOU WOULD GIVE IT A ONE ON QUESTION 3.
2 (INAUDIBLE COLLOQUY BETWEEN PANELISTS.)
3 DR. GARBER: LET ME JUST MAKE A QUICK
4 SUGGESTION. YOU'RE MAKING A PERFECTLY APPROPRIATE
5 AND PERFECTLY LOGICAL POINT. I THINK WE CAN HANDLE
6 THAT PART IN DISCUSSION RATHER THAN REVISING THE
7 DEFINITIONS. BUT LET'S DO THE VOTE AND THEN YOU CAN
8 EXPLAIN, IF YOU FEEL THAT WAY, THAT YOU'RE CONFIDENT
9 THAT IT'S NOT GOOD FOR YOU, OR HOWEVER YOU WANT TO
10 PUT IT, MARK. IT'S A VERY VALID POINT, THAT THERE IS
11 A WEAKNESS IN THIS SCORING SYSTEM.
12 DR. FENDRICK: YOU ANSWERED IT PERFECTLY.
13 THANK YOU.
14 DR. GARBER: SO, DOES EVERYBODY -- I JUST
15 REALIZED, IT'S POSSIBLE THAT NOT EVERYBODY WHO'S
16 VOTING HERE HAS GONE THROUGH THIS VOTING PROCEDURE
17 BEFORE, BUT WHEN YOU DECIDE WHAT SCORE YOU WANT TO
18 GIVE IT, ONE BEING NOT CONFIDENT AT ALL, FIVE BEING
19 HIGHLY CONFIDENT, JUST PUT OUT YOUR FLASH CARD WHEN I
20 CALL FOR THE VOTE, AND THEN SOMEBODY IS GOING TO
21 RECORD ALL THE SCORES, SO YOU NEED TO HOLD IT UP LONG
22 ENOUGH FOR THAT.
23 MS. ATKINSON: ALSO, YOU RECEIVED BALLOTS,
24 AND YOU WILL WRITE YOUR SCORE ON YOUR BALLOTS FOR
25 EACH QUESTION, AND THEN MARIA WILL COME AROUND AND

00198

1 PICK UP THE BALLOTS. SO YOU'RE DOING THE CARDS SO IT
2 SHOWS FOR THE PUBLIC AND FOR THE RECORD, AND THEN WE
3 USE THE BALLOTS TO PUT IT INTO THE SPREADSHEET.
4 DR. BERGTHOLD: SO IN OTHER WORDS, THEY
5 SHOULD BE THE SAME.
6 MS. ATKINSON: YES, PLEASE.
7 DR. GARBER: OKAY. ARE PEOPLE READY TO
8 VOTE ON 1.A?
9 DR. PRESSMAN: COULD I ASK ONE FURTHER
10 QUESTION? IF I'M CONFIDENT THAT THE DATA SHOWS
11 SOMETHING IS UNSAFE, IS THAT A FIVE OR A ONE?
12 DR. GARBER: THAT'S A FIVE, BUT THAT'S IF
13 YOU'RE HIGHLY CONFIDENT THAT THE DATA ARE ADEQUATE.
14 ONE OF THE REASONS FOR THIS QUESTION THAT'S DISTINCT
15 FROM GOOD OR BAD IS ARE FURTHER STUDIES LIKELY TO BE
16 NEEDED. SO IF YOU'RE HIGHLY CONFIDENT THAT IT IS
17 HARMFUL, FOR EXAMPLE, FOR THIS ONE YOU SHOULD ANSWER
18 FIVE. AGAIN, IN THE DISCUSSION, WE WANT YOU TO MAKE
19 THAT STATEMENT SO THAT IT'S NOT INTERPRETED THE
20 OPPOSITE OF WHAT IT MEANS.
21 DR. CHARYTAN: YEAH. THE QUESTIONS, SO
22 THE PEOPLE READING OR LOOKING AT THE FINAL VOTE
23 UNDERSTAND WHAT THE VOTE MEANT.
24 DR. GARBER: RIGHT, AND THAT REALLY SHOULD
25 GO INTO NUMBER 3, BUT OUR SCORING SYSTEM DOESN'T

00199

1 REALLY --
2 DR. SCHWARTZ: SO THE REASON FOR ONE ISN'T
3 HOW BAD (INAUDIBLE).
4 DR. GARBER: WELL, YEAH, THE REASON FOR
5 THAT IS THE PRINCIPAL ONE, DEFINITELY, THAT IS, IF
6 THE EVIDENCE IS ADEQUATE TO DRAW CONCLUSION, THEN IF
7 IT IS, WE DON'T NEED TO TALK ABOUT THIS INDICATION,
8 MEDICARE NEEDS TO FIGURE OUT A WAY TO DEVELOP MORE
9 EVIDENCE. IS THAT FAIR? OKAY.
10 LET ME ASK YOU TO VOTE THEN, 1.A, SURGICAL
11 RENAL ARTERY RECONSTRUCTION, HOW CONFIDENT ARE YOU
12 THAT THE EVIDENCE IS ADEQUATE?
13 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
14 WERE RECORDED BY STAFF.)
15 DR. GARBER: OKAY.
16 NOW I GUESS WE COULD ASK AT THIS POINT OR
17 IN NUMBER 3, BUT HOW MANY PEOPLE WHO ARE CONFIDENT
18 WERE CONFIDENT THAT IT DOESN'T WORK?
19 (SHOW OF HANDS.)
20 MR. LACEY: IT SEEMS TO HAVE A ROLE FOR A
21 VERY SMALL SUBSET OF PATIENTS, BUT A VERY HIGH RISK
22 OF COMPLICATIONS AND SIGNIFICANT MORBIDITY, SO FROM
23 THE DATA THAT I'VE SEEN --
24 DR. GARBER: FOR BOTH PEOPLE IT HARMS AND
25 PEOPLE IT HELPS.

00200

1 MR. LACEY: YEAH. SANDY?
2 DR. SCHWARTZ: I INTERPRET IT THE SAME
3 WAY. I DON'T SEE ANYBODY OUT THERE WHO WANTS TO DO
4 STUDIES OF SURGERY, YOU KNOW.
5 DR. GARBER: OKAY. LET'S DO B, THIS IS
6 ANGIOPLASTY WITHOUT STENT REPLACEMENT. AGAIN, WE'RE
7 VOTING ON CONFIDENCE IN THE AMOUNT OF EVIDENCE.
8 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
9 WERE RECORDED BY STAFF.)
10 DR. GARBER: DOES ANYBODY WANT TO EXPLAIN
11 THEIR VOTES, ESPECIALLY PEOPLE THAT GAVE IT FIVE, IN
12 THE SENSE THAT IT'S BENEFICIAL OR QUESTIONS ABOUT
13 THAT?
14 DR. EDWARDS: I'M A NONVOTING MEMBER, BUT
15 I WOULD SAY THAT I THINK THAT THE DATA FOR
16 ANGIOPLASTY ALONE IS STRONG AND THAT IT WOULD NOT BE
17 BENEFICIAL, AT LEAST FOR ATHEROSCLEROTIC DISEASE.
18 DR. GARBER: ANY OTHER COMMENTS?
19 DR. SLAUGHTER: I WOULD AGREE THAT THERE
20 IS A LACK OF EVIDENCE FOR CLINICAL EVIDENCE, BUT I
21 DON'T THINK THERE'S ENOUGH EVIDENCE TO TRULY SORT OF
22 DRAW A CONCLUSION. IT'S VERY LIMITED FOR SHORT-TERM
23 FOLLOW-UP, AND ANYTHING SIX MONTHS OR LESS REALLY
24 GIVES YOU NO IMPRESSION OF LONG-TERM REDUCTION IN
25 CARDIOVASCULAR RISKS AND WHETHER OR NOT THEY WOULD BE

00201

1 IMPACTED.
2 DR. GARBER: OKAY, THANK YOU.
3 DR. SCHWARTZ: AND I HAVE QUESTIONS ABOUT,
4 I'M NOT CONFIDENT, BECAUSE I'M PRETTY CONFIDENT IT'S
5 NOT AS EFFECTIVE AS DOING IT WITH STENTS, BUT
6 CLINICALLY I THINK IT IS IMPORTANT.
7 DR. GARBER: IS THAT A GENERAL CONSENSUS,
8 WHAT MARK AND SANDY JUST SAID? LET THE RECORD
9 REFLECT YES.
10 OKAY. NOW WITH BARE METAL STENTS, I.C.
11 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
12 WERE RECORDED BY STAFF.)
13 DR. GARBER: OKAY. THANK YOU. DOES
14 ANYBODY WANT TO EXPLAIN THEIR VOTES ON THIS ONE? I
15 THINK THEY WERE MOSTLY SELF-EXPLANATORY, BUT I
16 COULDN'T SEE IF ANYONE GAVE IT A FOUR OR FIVE.
17 OKAY. NOW, WE JUST HAD A DISCUSSION ABOUT
18 THE DRUG-ELUTING STENTS, SO THE QUESTION IS -- THIS
19 PARTICULAR ONE, FIRST WE'RE GOING TO VOTE ON
20 CONFIDENCE AND THE LEVEL OF EVIDENCE FOR
21 DRUG-ELUTING.
22 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
23 WERE RECORDED BY STAFF.)
24 DR. GARBER: WE MAY GET A UNANIMOUS VOTE
25 HERE.

00202

1 DR. CHARYTAN: THE PROBLEM WITH
2 DRUG-ELUTING STENTS, DOESN'T THAT DEPEND ON FIRST
3 DEMONSTRATING THAT STENTING HAS A BENEFIT AND THAT
4 DRUG-ELUTING STENT HAS AN ADDED, PRESUMED ADDED
5 BENEFIT OF MAINTAINING PATENCY? WHEREAS HERE, WE'RE
6 ARGUING WHETHER THERE'S ANY BENEFIT OF THE PROCEDURE
7 AT ALL, SO WORRYING ABOUT WHETHER THE DRUG-ELUTED
8 STENT ADDS TO THAT OR NOT IS REALLY A QUESTION THAT
9 FOLLOWS. THAT NEEDS AN ANSWER TO THE FIRST QUESTION,
10 DOES INTERVENTION GIVE ANY BENEFIT, AND THEN YOU CAN
11 WORRY ABOUT FINDING THE EXACT TECHNOLOGY TO MAXIMIZE
12 THAT BENEFIT.

13 DR. GARBER: I THINK THAT'S A VERY GOOD
14 RATIONALE FOR HOW THE VOTE ACTUALLY WENT, BECAUSE I
15 THINK EVERYBODY GAVE THAT A ONE. SO, DOES ANYBODY
16 DISAGREE, OR DOES EVERYONE PRETTY MUCH AGREE WITH
17 WHAT CHAIM SAID? OKAY.

18 DR. FENDRICK: AND CHAIM'S POINT GETS TO
19 QUESTION 3.

20 DR. GARBER: YES. OKAY. NOW, FIRST OF
21 ALL, CONGRATULATIONS. DOES EVERYBODY HAVE A GOOD
22 EXPLANATION AS WELL FOR VOTING THE WAY THEY DID? I
23 DON'T CARE HOW YOU VOTED, I JUST CARE THAT IT
24 ACCURATELY REFLECTED YOUR BELIEFS, AND SO FAR WE'RE
25 DOING PRETTY WELL.

00203

1 NUMBER 2, BASED ON THE EVIDENCE PRESENTED,
2 HOW CONFIDENT ARE YOU THAT PUBLISHED RESULTS APPLY TO
3 THREE DIFFERENT GROUPS? THE FIRST IS THE PATIENT
4 POPULATION, DOES IT APPLY TO MEDICARE PATIENTS WITH
5 TYPICAL COMORBIDITIES, PRESUMABLY MEANING TYPICAL
6 MEDICARE BENEFICIARIES WHO WOULD AT LEAST BE A
7 CANDIDATE FOR THE PROCEDURE.
8 DR. SCHWARTZ: HOW IS THAT DIFFERENT
9 FROM B?
10 DR. GARBER: QUESTION 1 IS INTENDED TO
11 ADDRESS JUST IN GENERAL IN ANY POPULATION, BUT
12 QUESTION 2 IS SPECIFICALLY, I'M NOT SAYING THAT'S THE
13 CASE HERE, BUT OFTENTIMES WE LOOK AT TECHNOLOGY
14 AND --
15 (INAUDIBLE COLLOQUY AMONG PANELISTS.)
16 DR. GARBER: OKAY. 2.B AND 2.C, I'M GOING
17 TO READ THE VOTING QUESTIONS, OKAY, AND THAT WHAT YOU
18 SHOULD VOTE ON, NOT WHAT'S TYPED ON THE BALLOT. SO
19 2.A SAYS, HOW CONFIDENT ARE YOU THAT THE PUBLISHED
20 RESULTS APPLY TO MEDICARE PATIENTS WITH DIFFICULT
21 COMORBIDITIES?
22 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
23 WERE RECORDED BY STAFF.)
24 DR. GARBER: SO DO THESE RESULTS APPLY
25 EITHER DIRECTLY OR GENERALIZED TO THE MEDICARE

00204

1 POPULATION. OKAY. DOES ANYBODY WANT TO MAKE ANY
2 COMMENTS ABOUT WHY THEY VOTED AS THEY DID, OR IS IT
3 SELF-EVIDENT? OKAY.
4 2.B. NOW THIS IS ABOUT PROVIDERS. IT
5 SAYS, HOW CONFIDENT ARE YOU THAT THE PUBLISHED
6 RESULTS APPLY TO PROVIDERS, I.E., FACILITIES OR
7 PHYSICIANS IN COMMUNITY PRACTICE? IN OTHER WORDS,
8 WERE THE TRIALS CONDUCTED BY A TOTALLY DIFFERENT TYPE
9 OF PROVIDERS, OR THE PUBLISHED STUDIES DONE BY
10 DIFFERENT PROVIDERS.
11 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
12 WERE RECORDED BY STAFF.)
13 DR. GARBER: OKAY. LINDA, DID YOU WANT TO
14 SAY SOMETHING?
15 DR. BERGTHOLD: YEAH. I JUST WANT TO MAKE
16 A COMMENT ABOUT WHY I VOTED ONE, AND AS SORT OF THE
17 PROTECTOR OF THE PATIENTS' RIGHTS, I WAS SURPRISED TO
18 HEAR THE TESTIMONY TODAY AND HOW COMPLICATED THESE
19 PROCEDURES ARE, AND TO THINK THAT THESE PROCEDURES
20 COULD BE DONE IN COMMUNITY HOSPITALS BY DOCTORS WHO
21 ARE NOT WELL TRAINED CONCERNED ME. SO I'M NOT
22 CONFIDENT THAT THE STUDY RESULTS SHOW THAT IF THIS
23 KIND OF PROCEDURE IS BEING DONE, IT SHOULD BE DONE AT
24 CENTERS OF EXCELLENCE, IT SHOULD BE DONE IN LOCALES
25 WHETHER THE PHYSICIANS ARE VERY WELL TRAINED AND

00205

1 SUPERVISED.
2 DR. CHARYTAN: I'D LIKE TO COMMENT ON THAT
3 COMMENT, IF I MAY. ALTHOUGH THE LAST INTERVENTION
4 WAS DONE AS EARLY AS IN THE '40S, I THINK THIS ISSUE
5 IS LESS, ALTHOUGH A QUESTION OF WELL TRAINED
6 INTERVENTIONS SO THAT'S ALWAYS A PROBLEM, THIS IS AN
7 ISSUE OF PHYSICIANS BEING APPROPRIATELY TRAINED,
8 WHETHER IT'S INTERNISTS, CARDIOLOGISTS OR
9 NEPHROLOGISTS IN THE PROPER SELECTION OF PATIENTS
10 GOING FOR THE PROCEDURE. SO THE PROBLEM HERE IS NOT
11 THE TRAINING OF THE INTERVENTIONALISTS BUT DEVELOPING
12 CLEAR EVIDENCE TO DEFINE WHICH PATIENTS AND BY WHAT
13 CRITERIA PATIENTS SHOULD BE SELECTED.
14 DR. GARBER: BILL.
15 DR. LEWIS: AND THE COROLLARY TO THAT IS,
16 THE TIGHTER THE SELECTION CRITERIA ARE, THE LOWER THE
17 NUMBER OF CASES, AND THEREFORE THE HIGHER THE
18 DIFFICULTY OF THE LEARNING CURVE. AND WHEN YOU LOOK
19 AT THE NUMBERS FROM CORAL, CORAL WILL PROBABLY, IF
20 YOU LOOK AT THE NUMBER OF CENTERS AND THE NUMBER OF
21 PATIENTS THEY'RE TRYING TO ENROLL, THE NUMBER OF
22 PATIENTS PER YEAR IS PROBABLY GOING TO BE ABOUT THREE
23 PER YEAR, AND IN DRASTIC THAT NUMBER WAS ACTUALLY ONE
24 PATIENT PER YEAR PER CENTER. SO WHEN WE LOOK AT THE
25 NUMBERS IT'S GOING TO BE IMPORTANT HOW THE STUDIES

00206

1 DEFINE THEIR CRITERIA. IF IT'S REQUIRED THAT YOU
2 HAVE A 20-MILLIMETER DROP IN A 70 PERCENT LESION, THE
3 NUMBERS OF PATIENTS ARE GOING TO BE MUCH SMALLER THAN
4 WHAT'S BEING CURRENTLY DONE, AND THE OPERATOR
5 CAPABILITY MAY BE VERY, VERY BROAD, THE RANGE OF
6 OPERATOR CAPABILITY MAY BE VERY, VERY BROAD.
7 DR. GARBER: OKAY, THANK YOU. ANYONE ELSE
8 WANT TO COMMENT ON THAT? OKAY.
9 NOW THIS ONE IS GOING TO BE POTENTIALLY
10 THE LARGEST OF THESE THREE SUBQUESTIONS. BASED ON
11 THE EVIDENCE PRESENTED, HOW CONFIDENT ARE YOU THAT
12 PUBLISHED RESULTS APPLY TO PATIENT SUBGROUPS NOT
13 REPRESENTED IN THE STUDY POPULATIONS? AND HERE I
14 THINK IT IS REALLY IMPORTANT FOR YOU TO MENTION, IF
15 YOU GIVE A LOW SCORE, WHICH SUBGROUPS YOU BELIEVE
16 WERE NOT WELL REPRESENTED, OKAY? DID YOU WANT TO
17 SAYING ANYTHING? OKAY.
18 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
19 WERE RECORDED BY STAFF.)
20 DR. TEXTOR: I'LL COMMENT ABOUT THAT. I
21 THINK THE ACHILLES HEEL OF THE PUBLISHED PROSPECTIVE
22 TRIALS IS THAT THEY ARE A VERY SMALL AND SELECTIVE
23 GROUP. THE NUMBER OF EXCLUSIONS, AND THAT'S BEEN A
24 PROBLEM, REALLY, IN ALL THE INTERVENTION TRIALS, IS
25 THE PRESUPPOSITION OF PEOPLE REALLY BEING TOO ILL OR

00207

1 NEEDING THE PROCEDURE TOO MUCH REALLY FORCED THE
2 SELECTION AND WE REALLY CAN'T GAUGE FROM THE
3 PUBLISHED LITERATURES, IT'S ALMOST IMPOSSIBLE TO KNOW
4 EXACTLY WHO THESE INDIVIDUALS WERE. SO I THINK IT'S
5 VERY LIKELY THAT THERE ARE LARGE GROUPS OF PEOPLE FOR
6 WHOM THOSE RESULTS DO NOT APPLY, AND I HAVE NO IDEA
7 WHO THEY ARE.
8 DR. SCHWARTZ: AND MY PROBLEM WITH THE
9 QUESTION THE WAY IT IS, EVEN FOR THOSE GROUPS WHO ARE
10 INCLUDED IN THE TRIALS, WE DON'T HAVE ADEQUATE POWER
11 AND WE NEVER WILL, BECAUSE THE FEW STUDIES BEING
12 DONE, LIKE CORAL, I ASSUME ARE BEING POWERED NOT FOR
13 SUBGROUP ANALYSIS BUT ARE BEING POWERED FOR A PRIMARY
14 ANALYSIS, AND UNFORTUNATELY WE'RE GOING TO HAVE TO
15 RELY IN THE FORESEEABLE FUTURE ON, YOU KNOW,
16 NONEXPERIMENTAL DATA ANALYSIS.
17 DR. GARBER: YEAH, I THINK SANDY HAS A
18 VERY IMPORTANT POINT. SO AS I HEAR YOUR POINT, EVEN
19 IF THE GROUP IS REPRESENTED IN TRIALS, THERE MAY BE
20 TOO FEW OF THEM TO BE ABLE TO DRAW CONCLUSIONS ABOUT
21 WHETHER IT WORKS OR HOW IT WORKS.
22 DR. SCHWARTZ: YEAH. WHAT ARE WE GOING TO
23 KNOW ABOUT PEOPLE WHO HAVE CORONARY DISEASE OR
24 DIABETES, OR, YOU KNOW, UNDERLYING OR INDEPENDENT
25 RENAL DISEASE. WE'RE NOT GOING TO HAVE ENOUGH OF

00208

1 THOSE PATIENTS IN ORDER TO BE ABLE TO SAY MUCH.
2 DR. CHARYTAN: BASED ON A LOT OF WHAT
3 WE'VE HEARD TODAY, IT SEEMS TO ME THAT THE CORAL
4 TRIAL IS ALMOST TOO INCLUSIVE, THAT THE PROBLEM IS
5 DOING PROCEDURES ON AN AWFUL LOT OF PATIENTS, AND THE
6 CONSENSUS THAT I TAKE FROM THE DISCUSSION HERE IS
7 THAT IT'S A VERY SELECT SUBGROUP OF PATIENTS WHO
8 PROBABLY MIGHT BENEFIT FROM THE PROCEDURE. AND IF
9 WE'RE GOING TO DO A STUDY THAT INCLUDES A LOT OF
10 PEOPLE, WE'RE ALMOST SETTING OURSELVES UP TO SHOW A
11 NEGATIVE OUTCOME, BECAUSE PERHAPS PEOPLE IMPROVE, BUT
12 BY DEFINITION MAY NOT BENEFIT FROM THE PROCEDURE.
13 DR. GARBER: WELL, THIS IS A GOOD POINT.
14 THAT MAY BE A STRONG ARGUMENT FOR FIGURING OUT HOW TO
15 GET A LOT MORE PATIENTS INTO CORAL SO THAT IT'S
16 POWERED TO ACTUALLY ANSWER QUESTIONS FOR SUBGROUPS.
17 DID YOU WANT TO SAY SOMETHING?
18 DR. DWORKIN: IF I CAN SAY SOMETHING ABOUT
19 THAT, IT'S AN OBVIOUS CONUNDRUM WHEN YOU'RE DESIGNING
20 CLINICAL TRIALS IS TO, YOU KNOW, SELECT A POPULATION
21 TO STUDY. I THINK CORAL WAS DESIGNED TO BE
22 INCLUSIVE, AGAIN, BECAUSE THE PERCEPTION OF MANY
23 PEOPLE IN THIS FIELD AND CERTAINLY PEOPLE THAT WROTE
24 THE PROTOCOL, MYSELF INCLUDED, WAS THAT WE WERE
25 UNABLE TO DEFINE A SUBSET OF PATIENTS WITH

00209

1 RENOVASCULAR DISEASE FOR WHOM IT WAS CLEAR THAT
2 REVASCULARIZATION PROVIDED BENEFIT. SO I KNOW YOU'VE
3 HEARD PEOPLE TELL YOU TODAY THAT PEOPLE WITH IMPAIRED
4 KIDNEY FUNCTION OR UNCONTROLLED HYPERTENSION OR
5 RECURRENT EPISODES OF PULMONARY EDEMA ARE SUBSETS OF
6 PATIENTS FOR WHOM OUTCOMES ARE BETTER WITH
7 REVASCULARIZATION, BUT WE DIDN'T FEEL THAT THAT WAS
8 ENOUGH, AND SO ALL OF THOSE PATIENTS ARE IN THE
9 TRIAL.
10 AND I THINK IN DESIGNING THE TRIAL, WE
11 DIDN'T WANT TO EXCLUDE ANY OF THOSE GROUPS BECAUSE
12 THEN WE WOULD STILL HAVE NO EVIDENCE ABOUT THOSE
13 GROUPS. NOW WHETHER WE WILL BE ABLE TO TEASE OUT ALL
14 THESE DIFFERENT SUBGROUPS AT THE END OF THE DAY, I
15 DON'T EXPECT THAT WE WILL BE ABLE TO. WE DO HAVE
16 SOME PREPLANNED SUBGROUP ANALYSES. WE WILL BE
17 LOOKING AT ISSUES LIKE UNILATERAL VERSUS BILATERAL
18 DISEASE, DIABETES, THE IMPACT OF GENDER AND RACE. SO
19 WE DO HAVE SOME PREPLANNED ANALYSES AND WE WILL BE
20 ABLE TO LOOK AT SOME OF THE COMPONENTS OF THE
21 COMPOSITE ENDPOINT INDIVIDUALLY, SO WE WILL PROBABLY
22 HAVE DECENT POWER TO LOOK AT SOMETHING LIKE
23 MORTALITY. BUT YOU KNOW, THERE WILL BE UNANSWERED
24 QUESTIONS CLEARLY.
25 DR. GARBER: OKAY. DID ANYBODY ELSE WANT

00210

1 TO RAISE OR BRING UP ANY OTHER POINTS? THEN WE WILL
2 MOVE ON TO QUESTION 3.
3 DR. TEXTOR: BEFORE WE LEAVE THAT, COULD I
4 JUST ASK THE QUESTION? I MEAN, PART OF THE PROBLEM
5 THAT STRIKES ME WITH A TRIAL THAT IS HAVING SLOW
6 ENROLLMENT IS THAT YOU REALLY RUN THE RISK OF A
7 MOVING TARGET AND NEVER ACCRUING THE CRITICAL NUMBER
8 OF PEOPLE YOU NEED TO ANSWER THIS QUESTION IN SOME
9 REASONABLE PERIOD OF TIME. WHAT WOULD BE THE
10 ARGUMENT AGAINST REQUIRING ALL PATIENTS TO BE IN A
11 TRIAL SETTING IF THEY'RE GOING TO BE TREATED.
12 DR. GARBER: STEVE, I THINK THAT'S THE
13 HEART OF OUR DISCUSSION TODAY, AND IF I COULD JUST
14 ASK YOU TO BRING THAT UP AGAIN WHEN WE GET TO
15 QUESTION 4, AND IN FACT WITH 4, WE CAN BRING UP
16 ISSUES OF POWER, WHETHER WE WANT TO KNOW ABOUT SOME
17 SUBGROUPS, AND IS A REGISTRY ADEQUATE, DO WE WANT
18 MORE PEOPLE ENROLLED IN RANDOMIZED TRIALS, SO ON AND
19 SO FORTH. THAT'S GOING TO BE THE HEART OF THE
20 DISCUSSION FOR QUESTION 4, SO WE WILL GET INTO IT
21 VERY SOON HOPEFULLY.
22 QUESTION 3 -- AND BY THE WAY, I HOPE THAT
23 ALL THE PEOPLE REPRESENTING CORAL WILL REMAIN FOR
24 THAT DISCUSSION, BECAUSE THAT'S GOING TO BE VERY
25 IMPORTANT THERE.

00211

1 ALL RIGHT. QUESTION 3. BASED ON THE
2 EVIDENCE PRESENTED FOR PATIENTS WITH ATHEROSCLEROTIC
3 RENAL ARTERY STENOSIS, HOW CONFIDENT ARE YOU THAT
4 COMPARED TO AGGRESSIVE MEDICAL TREATMENT ALONE THERE
5 ARE IMPROVED KEY HEALTH OUTCOMES ATTRIBUTABLE TO THE
6 FOLLOWING CO-INTERVENTIONS? SO THE VOTING IS GOING
7 TO, LET ME JUST SUGGEST WHEN YOU VOTE, IT'S GOING TO
8 BE ONE TO FIVE THAT ONE, YOU'RE NOT CONFIDENT, FIVE,
9 YOU'RE HIGHLY CONFIDENT. AND THEN WE WILL STEP TO A
10 SEPARATE QUESTION IF YOU'RE PRETTY CONFIDENT THAT IT
11 IS HARMFUL, OKAY?
12 DR. SCHWARTZ: I KNOW I SHOULD HAVE SAID
13 THIS IN THE CONFERENCE CALL A COUPLE WEEKS AGO, BUT I
14 HADN'T READ THROUGH ALL THE MATERIALS AT THAT TIME
15 YET. BUT I DON'T THINK WE SHOULD CHANGE, WE CAN'T
16 CHANGE THE WORDS ON EVERY QUESTION, BUT THE WAY I'M
17 GOING TO BE VOTING ON THIS, IT RELATES TO WHAT YOU
18 WERE SAYING BEFORE. THERE'S A PRESUMPTION IN HERE
19 THAT AGGRESSIVE MEDICAL TREATMENT IS THE BEST
20 TREATMENT. WE DON'T EVEN KNOW IF THAT'S EFFECTIVE
21 FOR RENAL ARTERY STENOSIS PER SE. I FEEL THE WAY WE
22 SHOULD THINK ABOUT THIS IS WHAT'S THE INCREMENTAL
23 BENEFIT OR CLINICAL BENEFIT OF THESE APPROACHES OVER
24 AND ABOVE THE AGGRESSIVE MEDICAL THERAPY THAT PEOPLE
25 ARE GOING TO BE GETTING FOR HYPERTENSION AND

00212

1 CARDIOVASCULAR RISK REDUCTION, BUT WITHOUT A
2 PRESUMPTION THAT THESE ARE PARTICULARLY EFFECTIVE IN
3 PEOPLE WITH RENAL ARTERY STENOSIS, BECAUSE I DON'T
4 THINK WE KNOW THAT.
5 DR. GARBER: I THINK THAT THAT'S A GOOD
6 STATEMENT OF WHAT I UNDERSTAND TO BE THE INTENT OF
7 THE QUESTION. I THINK WHAT SANDY IS SAYING IS, THIS
8 IS AN ISSUE THAT COMES UP NOT INFREQUENTLY, THAT THE
9 COMPARATOR IS SOMETHING ABOUT WHICH WE HAVE VERY
10 LITTLE EVIDENCE. AND WHAT WE'RE BEING ASKED TO VOTE
11 ABOUT IS HOW CONFIDENT ARE WE THAT THIS IS BETTER
12 THAN A COMPARATOR REGARDLESS OF OUR LEVEL OF
13 IGNORANCE ABOUT THE COMPARATOR, THAT THE COMPARATOR
14 IN THIS CASE IS AGGRESSIVE MEDICAL MANAGEMENT OR
15 WHATEVER, IS BETTER THAN PLACEBO.
16 DR. SCHWARTZ: YEAH. AND I'M NOT THINKING
17 ABOUT THIS AS A COMPARATOR SINCE ALL THESE PEOPLE
18 CLINICALLY SHOULD BE ON THIS OTHER REGIMEN ANYHOW FOR
19 REASONS OTHER THAN KIDNEY FUNCTION OR RENAL ARTERY
20 STENOSIS, JUST BECAUSE THEY HAD ATHEROSCLEROTIC
21 DISEASE. SO I DON'T SEE IT AS A COMPARATOR, I SEE IT
22 AS SORT OF A BASELINE TREATMENT THAT EVERYBODY OUGHT
23 TO BE GETTING.
24 IT'S SORT OF LIKE IF YOU WANTED TO LOOK
25 AT, WHAT'S THE IMPACT IN A GROUP OF PEOPLE WHO ARE

00213

1 GETTING THEIR HYPERTENSION TREATED ARE GETTING SOME
2 SMOKING CESSATION, BEING ON BABY ASPIRIN, BEING ON A
3 BETA BLOCKER, YOU KNOW, WHATEVER THE BASELINE
4 TREATMENT IS.
5 DR. GARBER: WELL, SANDY, I DON'T WANT TO
6 GET INTO A LENGTHY DISCUSSION WITH YOU, BUT WHEN YOU
7 SAY IMPROVED HEALTH OUTCOMES IT MEANS RELATIVE TO
8 SOMETHING, AND THAT'S THE REASON I USED THE TERM
9 COMPARATOR, WHAT IT'S RELATIVE TO. MARK?
10 DR. FENDRICK: I WAS FINE UNTIL YOU
11 CONFUSED ME. BECAUSE THE WORD IMPROVED IS IN THE
12 QUESTION, YOU COULD VOTE FOR IT AND SAY IT'S HARMFUL?
13 I DON'T THINK THAT'S CORRECT.
14 DR. GARBER: NO, NO, NO. THAT WAS ON
15 QUESTION 1 WHERE I --
16 DR. FENDRICK: I KNOW, BUT YOU JUST
17 SAID --
18 DR. GARBER: THEN I MISSPOKE. I'M SORRY.
19 I SAID IF IT WAS POSITIVE, YOU COULD VOTE FOR IT. IF
20 IT'S NEGATIVE IN YOUR DISCUSSION. I DIDN'T SAY --
21 DR. FENDRICK: I MISSED A COMMA THEN. YOU
22 COULD VOTE FOR, AND SAY WHY IT'S NEGATIVE?
23 DR. GARBER: NO, NO, NO. THIS SAYS
24 IMPROVED. YOU CAN'T VOTE FOR IT.
25 DR. FENDRICK: OKAY, WE'RE IN AGREEMENT.

00214

1 DR. GARBER: SO IF YOU'RE NOT CONFIDENT,
2 IF YOU THINK IT'S HARMFUL, I WOULD GIVE IT A ONE.
3 AND THEN IN EXPLANATION, THAT ACTUALLY IT'S NOT THAT
4 YOU'RE NOT CONFIDENT THAT IT'S BENEFICIAL, BUT IF
5 YOU'RE SURE THAT IT'S NOT, THAT SHOULD COME IN
6 COMMENT, OKAY?
7 DR. CHARYTAN: JUST AS A QUESTION, AND
8 IT'S A REPETITION, BUT HOW CLEAR WILL IT BE TO THE
9 PEOPLE WHO READ THIS THAT WE'RE VOTING FOR A GROUP AS
10 A WHOLE, BUT THAT MANY OF US MAY FEEL THAT THERE ARE
11 SUBGROUPS IN WHICH THESE THERAPIES MAY BE BENEFICIAL
12 AND IT NEEDS TO BE VIEWED FROM THAT PERSPECTIVE?
13 DR. GARBER: YOU SHOULD ABSOLUTELY MAKE
14 COMMENTS TO THAT EFFECT IN EXPLAINING YOUR VOTE. AND
15 IT WILL BE A MISUSE OF THE RESULTS OF OUR PROCEEDINGS
16 TODAY IF PEOPLE IGNORE THE COMMENTS. THOSE ARE
17 ABSOLUTELY CRITICAL.
18 DR. SLAUGHTER: THIS MAY MAKE IT A BIT
19 MORE CONFUSED, BUT I THINK YOU DO HAVE TO COMPARE IT
20 TO MEDICAL THERAPY BECAUSE THE ASSUMPTION HERE IN ALL
21 THE PRESENTATIONS IS THAT RENAL ARTERY STENOSIS,
22 WHETHER DIRECTLY OR THROUGH SOME COMPLEX SYSTEM THAT
23 MAY NOT BE WELL DESCRIBED, IS RESPONSIBLE FOR THE
24 ADVERSE OUTCOMES. SO THEREFORE WHAT WE'RE SAYING IS
25 MEDICAL TREATMENT, YOU KNOW, OF THIS COMPLEX WHICH

00215

1 MAY OR MAY NOT BE EXACERBATED BY, OR IS SOLELY
2 RESPONSIBLE FOR THE RENAL ARTERY STENOSIS, EXTENDING
3 THAT IS GOING TO GIVE YOU A BETTER OUTCOME THAN
4 MEDICAL THERAPY, NOT JUST NO TREATMENT.
5 BECAUSE CERTAINLY THERE ARE ADVANTAGES TO
6 ANTIHYPERTENSIVE THERAPY, STATINS, LIPIDS FOR THIS
7 COMPLEX. AND THE ISSUE IS, IS USING A STENT BETTER
8 THAN ORALLY INDUCED MEDICAL THERAPY FOR THIS DISEASE
9 PROCESS THAT RESULTS IN STROKE, KIDNEY FAILURE, HEART
10 ATTACKS AND DEATH.
11 DR. GARBER: RIGHT, BUT THE ONLY POINT I
12 WANT TO MAKE ABOUT HOW YOU SHOULD VOTE ON THIS IS THE
13 FOLLOWING. YOU ARE ASSUMING THAT THIS IS A
14 COMPARISON OF RAR, STENTING, WHATEVER, TO MEDICAL
15 THERAPY. I DON'T CARE HOW CONFIDENT YOU ARE ABOUT
16 WHETHER MEDICAL THERAPY WORKS. THAT'S NOT THE
17 QUESTION. THE QUESTION IS, IS THIS, ARE YOU
18 CONFIDENT THAT THIS IS BETTER, OR HOW MUCH BETTER
19 THIS IS THAN MEDICAL THERAPY, REGARDLESS OF THE LEVEL
20 OF EVIDENCE, ET CETERA, FOR MEDICAL THERAPY.
21 THAT'S HOW YOU'RE VOTING. IS THIS BETTER?
22 AND IF YOU THINK YOU KNOW IT'S WORSE, GIVE THIS A
23 ONE, AND THEN IN THE COMMENTS EXPLAIN WHY YOU THINK
24 IT'S NOT JUST THIS BETTER BENEFIT, BUT WHY YOU THINK
25 IT'S WORSE. IS EVERYBODY CLEAR WITH THAT? MARK,

00216

1 SANDY? OKAY.
2 SO FIRST WE ARE VOTING ON -- AND I WANT TO
3 MAKE SURE YOUR BALLOTS CORRESPOND TO WHAT WE HAVE
4 HERE. THE FIRST ONE IS SURGICAL RENAL ARTERY
5 RECONSTRUCTION.
6 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
7 WERE RECORDED BY STAFF.)
8 DR. GARBER: DOES ANYBODY WANT TO DISCUSS
9 REASONS FOR THEIR VOTE? THIS ONE I THINK WE HAVE
10 SORT OF ALREADY IMPLIED WHY YOU VOTED THE WAY YOU
11 DID.
12 DR. KRIST: I'LL PUT A CAVEAT IN MINE. I
13 SAID ONE, BUT AN EXCEPTION MIGHT BE SOMEBODY WHO'S
14 UNDERGOING SURGERY FOR ANOTHER REASON AS WE TALKED
15 ABOUT.
16 DR. FLAMM: THAT'S WHY I VOTED TWO.
17 DR. GARBER: OKAY, GREAT.
18 DR. EDWARDS: I HELD UP TWO CARDS, NOT
19 JUST BECAUSE I'M CRYING FOR ATTENTION, BUT AS TO
20 SURGERY, I WOULD VIEW IT AS A TWO IN REFERENCE TO
21 BEST MEDICAL SECONDARY PREVENTION AT THIS TIME FOR
22 CARDIOVASCULAR EVENTS, BUT I'M UNCERTAIN FOR RENAL
23 FUNCTION.
24 DR. GARBER: RIGHT. OKAY. PTRR WITHOUT
25 STENT PLACEMENT.

00217

1 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
2 WERE RECORDED BY STAFF.)
3 DR. GARBER: SO THIS IS NOT REALLY WHAT
4 THE QUESTION ASKS EXACTLY BUT IT'S PART OF THE REASON
5 FOR YOUR VOTE. IS EVERYBODY CONVINCED THAT STENTS
6 ARE BETTER THAN PTRS WITHOUT STENTS?
7 (CHORUS OF AYES.)
8 DR. GARBER: SO MAYBE THAT'S A MESSAGE
9 THAT CMS NEEDS TO TAKE AWAY FROM THAT. OKAY.
10 C IS STENTING WITH BARE METAL STENTS.
11 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
12 WERE RECORDED BY STAFF.)
13 DR. GARBER: AND NOW IS THE TIME TO LET US
14 KNOW ABOUT ANY SUBGROUPS FOR WHICH YOU WANT TO MAKE A
15 DISTINCT CASE OR DISTINCT REASON FOR VOTING THE WAY
16 YOU DID.
17 DR. CHARYTAN: WELL, I THINK THIS REALLY
18 NEEDS TO BE EMPHASIZED, PARTICULARLY IF MEDICARE IS
19 GOING TO LOOK AT THIS IN A SUBSEQUENT COVERAGE
20 DECISION THAT THERE IS CLEARLY CLINICAL EVIDENCE OF
21 STANDARD OF PRACTICE, WHICH IS JUST THAT THERE ARE
22 SUBGROUPS OF PATIENTS THAT PROBABLY BENEFIT IF
23 CAREFULLY SELECTED. AND PERHAPS THE OUTCOME THAT WAS
24 GIVEN BY, I DON'T REMEMBER THE NAME OF THE GENTLEMAN
25 WHO IS AT THE BACK OF THE ROOM, MIGHT BE ENOUGH ON

00218

1 THOSE SITUATIONS WITH BILATERAL RENAL ARTERY
2 STENOSIS, UNILATERAL RENAL ARTERY STENOSIS, AND
3 PATIENTS WITH DEMONSTRATED RECURRENT PULMONARY EDEMA
4 IN A SETTING OF RENAL ARTERY STENOSIS AND REDUCED
5 KIDNEY FUNCTION. AND PERHAPS VERY WELL TREATED
6 PATIENTS WHO DESPITE WELL PROVEN THERAPY DO NOT
7 RESPOND AND HAVE EVIDENCE OF RENAL ARTERY DISEASE,
8 AGAIN, VERY WELL SELECTED. BUT THERE ARE SUBGROUPS
9 WHO WILL BENEFIT AND THOSE NEED TO BE IDENTIFIED.
10 DR. GARBER: ANY OTHER COMMENTS?
11 DR. LEWIS: DR. DWORKIN'S COMMENTS ASIDE,
12 THE ISSUE IS GOING TO BE THAT THERE ARE CERTAIN
13 PATIENTS THAT ARE REALLY NOT GOING TO QUALIFY, AND
14 I'M THINKING IF FLASH PULMONARY EDEMA OR
15 CARDIOVASCULAR HEART DISEASE CANNOT BE CONTROLLED,
16 AND IT'S CLEAR THAT THIS IS RELATED. AND I THINK
17 IT'S DIFFICULT TO GO AGAINST, YOU KNOW, THE LIMITED
18 DATA THAT'S OUT THERE SAYING WE REALLY SHOULD EXCLUDE
19 THOSE PATIENTS FROM THIS THERAPY.
20 DR. GARBER: SANDY?
21 DR. SCHWARTZ: I'M SURE THAT AT LEAST HALF
22 THE PEOPLE, OR PERHAPS EVERYBODY IS THINKING THE SAME
23 THING, BUT JUST TO GET IT ON THE RECORD, I THINK THAT
24 EVEN IF THERE IS A LEVEL OF UNCERTAINTY, THE
25 ALTERNATIVE TO USING THE INTERVENTION FOR THE

00219

1 UNDERLYING RISK IS WITHOUT USING THE INTERVENTION.
2 SO IF SOMEBODY, THERE MAY NOT BE REAL GOOD DATA ON
3 UNCONTROLLED HYPERTENSION, BUT IF EVERYTHING YOU'RE
4 DOING IS NOT WORKING AND WE KNOW WHAT'S THERE IS BAD,
5 SO I THINK WHATEVER MEDICARE DOES, I THINK WE NEED TO
6 INFORM THAT EVEN IF THERE IS A GENERAL CONSENSUS,
7 THERE STILL ALWAYS NEEDS TO BE A STRONG EXCEPTION
8 POLICY FOR PATIENTS WHO WE KNOW ARE GOING TO DO
9 POORLY IN THE ABSENCE OF IT. IN OTHER WORDS, TAKING
10 ON THE RISK IS WORTH IT IN THOSE SITUATIONS.
11 DR. GARBER: MIKE.
12 MR. LACEY: I JUST WANTED TO REEMPHASIZE
13 WHAT I THOUGHT WAS A VERY POWERFUL (INAUDIBLE)
14 TOTALITY OF THE EVIDENCE TO DATE. IT SEEMS THERE WAS
15 A VERY STRONG SYSTEM TREND IN THESE OUTCOMES THAT ARE
16 BEING MEASURED. AND I DIDN'T VOTE FIVE, BUT I VOTED
17 FOUR BECAUSE I DEFINITELY THINK THAT, BASED ON THIS
18 DISCUSSION, ADDITIONAL DATA NEEDS TO BE COLLECTED IN
19 ALL THE AREAS.
20 AND I JUST HOPED TO BRING UP ONE OTHER
21 POINT, THAT IN THE CASE OF THREE OR FOUR-DRUG
22 THERAPY, WE ALSO HAVE TO THINK ABOUT COMPLIANCE. AND
23 I THINK THERE WAS A MENTION OF IT, BUT NOT REALLY ANY
24 DISCUSSION ABOUT IT, AS WELL AS THE BURDEN OF COST TO
25 THE PATIENT AND THE COST EFFECTIVENESS AS IT RELATES

00220

1 TO MEDICARE. SO I THINK IT HAS A ROLE THERE AND WHEN
2 WE THINK ABOUT THE OVERALL COVERAGE AND THE ABILITY
3 FOR THE AVERAGE POPULATION TO ACHIEVE THE AGGRESSIVE
4 MEDICAL MANAGEMENT, THAT IS ALSO A BIG CHALLENGE IN
5 TERMS OF COMPLIANCE.
6 DR. GARBER: LET THE RECORD REFLECT THAT
7 ONLY THE INDUSTRY REPRESENTATIVE REFERRED TO COST.
8 MR. LACEY: I'M AN ECONOMIST.
9 DR. SCHWARTZ: THE OTHER THING THAT WAS
10 REALLY DRIVEN HOME BY THE FIRST PRESENTATION TODAY,
11 AND THIS IS NOT A CRITICISM OF THE PRESENTATION, BUT
12 IT'S AN UNDERSCORING OF THE NEED TO GET PEOPLE INTO
13 TRIALS QUICKLY AND TO GET THESE ANSWERS QUICKLY. ONE
14 OF THE CRITICISMS THAT'S OFTEN MADE, AND AS YOU KNOW,
15 WHEN WE SIT ON TECS, WHAT WE OFTEN HEAR IS COMPARED
16 TO THIS TRIAL THING OR THAT, BUT THE RANDOMIZED
17 TRIALS THAT WERE TALKED ABOUT TODAY WERE PUBLISHED IN
18 1998, WHICH MEANS THEY WERE COMPLETED IN '96 OR '97,
19 WHICH MEANT THEY WERE DESIGNED IN '90 OR '92, AND
20 THERE WAS NO EVIDENCE AT THAT TIME THAT STATINS --
21 STATINS WERE JUST BEING TESTED AT THAT POINT. AND
22 YOU KNOW, FOR ACE INHIBITORS, THE EVIDENCE WAS STILL
23 ACCUMULATING.
24 SO IN THIS PARTICULAR SITUATION IT DOESN'T
25 BOTHER ME AS MUCH AS IT WOULD IN GENERAL AND I THINK

00221

1 IT WILL IN THE FUTURE, BECAUSE THE ORIGINAL STUDIES,
2 ESPECIALLY CLINICAL TRIALS, WERE MORE CONVINCING IN
3 TERMS OF THE EFFECTIVENESS OF THE INTERVENTION. BUT
4 IT DOES RAISE THE ISSUE, PARTICULARLY WITH DEVICES,
5 OR WITH ANYTHING, IT GETS BACK TO THE BASELINE,
6 WHAT'S THE COMPARATOR TREATMENT? AND WE'RE ALWAYS
7 GOING TO BE, BY THE TIME CORAL COMES OUT, WE'RE GOING
8 TO BE EXPECTING IT TO, WE'RE GOING TO SAY WELL, IT
9 DIDN'T COMPARE IT TO SOMETHING THAT JUST COMES OUT IN
10 A JOURNAL IN THE NEXT TWO WEEKS.
11 SO WE'RE ALWAYS GOING TO SORT OF BE BEHIND
12 THE EIGHT BALL AND I THINK WE NEED TO FIGURE OUT, AND
13 I DON'T HAVE A GOOD ANSWER, BUT I THINK WE NEED TO
14 FIGURE OUT HOW TO BUILD THAT IN TO MAKE SURE WE'RE
15 PRACTICING STATE OF THE ART MEDICINE AND OUR POLICIES
16 REFLECT THAT, BUT ALSO RECOGNIZING THE REALITY THAT
17 WE'RE ALWAYS LAGGING.
18 DR. GARBER: YEAH, BARRY.
19 DR. PRESSMAN: I THINK MOST OF US VOTED
20 THREE, AND I DON'T KNOW WHAT THE OTHER PEOPLE'S
21 INDICATIONS FOR THAT WERE, BUT MY VOTE WASN'T TO SAY
22 THAT I DON'T BELIEVE STENTS ARE VALUABLE. MY VOTE
23 SHOULDN'T BE USED BY CMS TO DENY STENTS IN PATIENTS
24 WHO FAIL MEDICAL THERAPY FOR THE MOMENT. IT'S ONLY
25 TO SAY THAT I THINK WE NEED MORE DATA TO FIND OUT,

00222

1 BUT IN THE MEANTIME IT'S UNCERTAIN, AND BEING
2 UNCERTAIN, I THINK CMS HAS TO ACT AS THOUGH THEY
3 DON'T KNOW AND BE VERY, VERY CAREFUL ABOUT WHAT THEY
4 DO AND DON'T PAY FOR GOING FORWARD UNTIL WE HAVE THE
5 ANSWERS. BECAUSE IF THEY DON'T PAY FOR IT, THEY'VE
6 ALREADY DECIDED IT'S CERTAIN.
7 DR. GARBER: THAT'S ACTUALLY NOT MY
8 UNDERSTANDING. IF THEY DON'T PAY FOR IT, THEY MAY DO
9 THAT BECAUSE IT'S UNCERTAIN, BUT THIS AGAIN IS
10 SOMETHING THAT SHOULD BE TALKED ABOUT IN THE CONTEXT
11 OF QUESTION 4.
12 DR. EDWARDS: I WOULD JUST LIKE TO VERIFY
13 THAT I VOTED AGAIN WITH TWO, THREE FOR CARDIOVASCULAR
14 AND FOUR FOR RENAL FUNCTION. BUT I WANT TO BE
15 CERTAIN THAT, A, WE ALL THANK THE PEOPLE WHO SET UP
16 CORAL, BECAUSE EVEN THOUGH I WOULD SAY IT'S FOUR FOR
17 RENAL FUNCTION, THAT'S BASED ON MY DIGEST OF THE
18 LITERATURE AND MY RELATIVE KNOWLEDGE OF THE PRACTICE
19 IN RENAL DISEASE. BUT I CERTAINLY FEEL THAT THERE
20 IS -- I MEAN, I WOULD CERTAINLY HAVE CLINICAL
21 EQUIPOISE IN PUTTING PATIENTS INTO TRIALS SUCH AS
22 CORAL, AND IT IS CRITICALLY IMPORTANT THAT IF THERE
23 ARE ANY MEASURES WE CAN TAKE TO MAKE THEIR ENROLLMENT
24 MORE ROBUST TO ALLOW FOR THE SECONDARY ANALYSIS OF
25 ALL THESE GROUPS THAT WE HAVE MENTIONED, AND I THINK

00223

1 THAT HAS TREMENDOUS MERIT.

2 (DR. GARBER AND DR. SALIVE CONFERRED OFF
3 THE RECORD.)

4 DR. GARBER: OKAY, THANK YOU. I JUST
5 WANTED TO ASK THE PANEL THIS, WHAT I WAS ASKING
6 MARCEL ABOUT. FOR 3.B, IT'S ABOUT THE DRUG-ELUTING
7 STENTS AND THE PANEL UNANIMOUSLY GAVE THAT A ONE.
8 YOU DON'T HAVE TO VOTE ON HOW EFFECTIVE YOU THINK IT
9 IS IF ALL OF YOU THINK THERE IS NO EVIDENCE AT ALL.
10 SO WOULD YOU BE COMFORTABLE JUST SAYING THERE'S NO
11 EVIDENCE ON WHICH TO MAKE A DETERMINATION?

12 (CHORUS OF AYES.)

13 DR. GARBER: DOES ANYBODY DISAGREE THEN?

14 (NO RESPONSE.)

15 DR. GARBER: OKAY. SO QUESTION 4, YOU
16 HAVE ALL BEEN CHOMPING AT THE BIT FOR THIS ONE. AND
17 LET ME ADD, I THINK MARK ALLUDED TO THIS, THIS IS
18 CALLED THE MEDICARE EVIDENCE DEVELOPMENT AND COVERAGE
19 ADVISORY COMMITTEE. THE REASON FOR THE CHANGE IN ITS
20 NAME, THE ADDING OF EVIDENCE DEVELOPMENT IS NOT JUST
21 SAYING THE EVIDENCE ISN'T ADEQUATE AND NOT ONLY
22 SAYING THERE HAVE TO BE MORE STUDIES, BUT TO ACTUALLY
23 BE ABLE TO DO SOMETHING MORE ACTIVE IN TERMS OF
24 MAKING SURE EVIDENCE GETS COLLECTED, SO WE CAN ASK
25 QUESTIONS LIKE THE FIRST THREE QUESTIONS TODAY WITH A

00224

1 BETTER EVIDENCE BASE.
2 SO THIS IS YOUR CHANCE TO TALK ABOUT, ARE
3 THERE SOME CIRCUMSTANCES OR ARE THERE WAYS THAT WE
4 MIGHT THINK ABOUT USING MEDICARE COVERAGE POLICY TO
5 ENCOURAGE THE DEVELOPMENT OF MORE EVIDENCE, WHETHER
6 IT'S RANDOMIZED TRIALS, REGISTRIES, OR SOME OTHER
7 MECHANISM ALTOGETHER. BARRY, DID YOU WANT TO MAKE A
8 COMMENT?
9 DR. PRESSMAN: NOT SPECIFICALLY TO THIS
10 QUESTION, NOT THE ONE YOU JUST RAISED.
11 DR. GARBER: WELL, THAT WAS A LEAD-IN TO
12 THIS QUESTION, WHICH IS, SHOULD MEDICARE NATIONAL
13 COVERAGE OF ANY NON-MEDICAL TREATMENTS FOR
14 ATHEROSCLEROTIC RENAL ARTERY STENOSIS BE LIMITED ONLY
15 TO PATIENTS ENROLLED IN QUALIFIED CLINICAL RESEARCH
16 STUDIES? BUT THAT PART OF IT IS GOING TO BE, WHAT DO
17 YOU MEAN BY A QUALIFIED CLINICAL RESEARCH STUDY. SO
18 YOU MIGHT SAY I DON'T THINK THEY HAVE TO BE ENROLLED
19 IN A RANDOMIZED TRIAL BUT THEY HAVE TO BE IN SOME
20 KIND OF REGISTRY, SOME KIND OF NATIONAL REGISTRY.
21 YOU MIGHT SAY IT SHOULD BE PROVIDED FOR
22 EVERYBODY WHO WANTS IT BUT YOU'D LIKE, OF COURSE,
23 CORAL TO GO FORWARD. OR YOU MIGHT SAY THERE SHOULD
24 BE INCENTIVES TO GET MORE PATIENTS INVOLVED IN CORAL
25 AND THESE RANDOMIZED TRIALS.

00225

1 SO THERE'S A WHOLE SERIES OF OPTIONS YOU
2 MIGHT COME UP WITH TO ANSWER THIS QUESTION, BUT PART
3 OF IT IS YES-NO, SHOULD THERE BE SOME RESTRICTIONS ON
4 PEOPLE ENROLLED IN STUDIES. BUT IF YOU THINK THERE
5 SHOULD BE SOME INCENTIVE TO ENROLLMENT IN STUDIES,
6 THEN YOU SHOULD SAY SOMETHING ABOUT WHAT KIND OF
7 STUDY YOU HAVE IN MIND, WHAT THE SPECIFIC DETAILS
8 ARE, OKAY? GO AHEAD, BARRY.
9 DR. PRESSMAN: I WOULD LIKE TO REFER BACK
10 TO A QUESTION THAT I ASKED DR. MURPHY EARLIER, AND I
11 THINK HE RESPONDED TO IT. I ASKED HIM FOR THIS
12 SPECIFIC PURPOSE, BECAUSE I DO BELIEVE IT'S VERY
13 IMPORTANT THAT WE MAKE THIS AVAILABLE TO PATIENTS
14 WITH SOME CRITERIA, AND THOSE CRITERIA OUGHT TO BE AT
15 LEAST SOME OF THE ONES HE MENTIONED, INCLUDING TWO OR
16 THREE MONTHS OF FAILED MEDICAL THERAPY, SO IT'S NOT
17 JUST THAT EVERY PATIENT WHO COMES IN WITH RENAL
18 ARTERY STENOSIS, WHETHER OR NOT THEY HAVE
19 HYPERTENSION, IS TREATED. AND NONE OF THESE WILL BE
20 WHAT WE CALL AT MY HOSPITAL DRIVE-BYS, THEY HAPPEN TO
21 BE THERE FOR ANOTHER PROCEDURE, YOU NOTICE RENAL
22 ARTERY STENOSIS IS THERE, AND YOU FIX IT ON THE WAY.
23 WE WANT TO PREVENT THOSE KIND OF
24 TREATMENTS BUT WHAT WE WANT TO DO, I THINK, IS MAKE
25 IT AVAILABLE TO PATIENTS WHO AT LEAST IN SOME OF THE

00226

1 CATEGORIES HAVE SEVERAL MONTHS OF FAILED ADEQUATE
2 THERAPY, THEY HAVE TO HAVE A CERTAIN DEGREE OF
3 STENOSIS, THEY SHOULD HAVE A GRADIENT. AND THERE ARE
4 OTHER CRITERIA THAT THE CLINICIANS MAY COME UP WITH
5 THAT I'M MISSING HERE, BUT I WOULD LIKE TO BE SURE
6 THAT WE MAKE IT AVAILABLE. AND FOR THE REGISTRY, I
7 WOULD LIKE TO MAKE SURE WE ARE GETTING SOMETHING FOR
8 IT, THAT WE'RE LEARNING SOMETHING AT THE SAME TIME.
9 DR. GARBER: SO BARRY, YOU'RE SAYING
10 EVERYBODY SHOULD HAVE TO ENROLL IN THE REGISTRY EVEN
11 IF THEY HAVE THOSE CHARACTERISTICS, OR JUST PEOPLE
12 WHO DON'T FIT IN THOSE CATEGORIES?
13 DR. PRESSMAN: I'M SAYING IT SHOULDN'T BE
14 DONE AT ALL IF YOU DON'T HAVE THE CHARACTERISTICS AND
15 EVERYBODY WHO'S DONE SHOULD BE IN THE REGISTRY.
16 DR. GARBER: OKAY, GOT IT. THANKS. YEAH,
17 MARK?
18 DR. SLAUGHTER: WHAT CONCERNED ME A LOT IS
19 AS THEY SHOWED OVER THE YEARS, A FAIRLY BRIEF TIME
20 PERIOD, IT HAS GONE FROM 7,000 TO 18,000, THEN UP TO
21 35 TO 40,000 PROCEDURES. AND THE FACT OF THE MATTER
22 IS, THE CORAL STUDY IS AT A HUNDRED WONDERFUL
23 INSTITUTIONS THAT I'M CERTAIN ARE BUSY. SO THE
24 QUESTION IS, IF THERE'S 30,000 A YEAR BEING DONE NOW,
25 THE QUESTION IS WHY CAN'T THEY GET A THOUSAND

00227

1 PATIENTS WITHIN A YEAR. AND THE ISSUE IS, MOST OF
2 THESE PATIENTS ARE BEING DONE MOST LIKELY IN
3 INSTITUTIONS WITHOUT A LOT OF RIGOR AND OVERSIGHT.
4 AND THIS ALL GREW WHEN THERE WAS LITTLE OR
5 AT LEAST EQUIVOCAL DATA. I DO THINK IT IS VERY
6 DIFFICULT TO ENROLL PATIENTS IN RANDOMIZED TRIALS,
7 AND I'VE PARTICIPATED IN NUMEROUS ONES, FOR VARIOUS
8 REASONS, FINANCIAL BEING ONE, WHICH IS UNFORTUNATELY
9 TRUE. SO I DO THINK THERE'S A LOT OF VALUE IN A
10 MANDATED REGISTRY AND I DO NOT THINK IT'S
11 UNREASONABLE IF YOU HAVE A MANDATED REGISTRY WITH SET
12 DATA POINTS THAT SAY, YOU KNOW, A FIVE-PAGE CASE
13 REPORT HAS TO BE FILLED OUT PRIOR TO DOING THE
14 PROCEDURE. SO WITHIN TWO YEARS, YOU WOULD HAVE
15 60,000 PATIENTS AND YOU WOULD BE ABLE TO ANSWER A LOT
16 OF THESE SUBSETS, AND YOU WOULD AT LEAST HAVE A HUGE
17 START.
18 SO I AGREE, PATIENTS SHOULD STILL HAVE
19 ACCESS TO IT. I THINK THE CURRENT DATA IS CERTAINLY
20 EQUIVOCAL, BUT IT'S CERTAINLY PROMISING. AND I THINK
21 A REGISTRY WOULD BE ONE APPROACH, AS WELL AS ONGOING
22 INDIVIDUAL RANDOMIZED TRIALS FOR SPECIFIC SUBSETS.
23 DR. GARBER: BILL MAISEL, I THINK YOU WERE
24 NEXT.
25 DR. MAISEL: I WAS JUST LOOKING FOR A

00228

1 LITTLE BIT OF CLARIFICATION ON THE QUESTION AND WHAT
2 THE MEANING OF ANY WAS, BECAUSE I COULD READ THE
3 QUESTION AS, SHOULD MEDICARE NATIONAL COVERAGE OF
4 SOME NON-MEDICAL TREATMENTS FOR ATHEROSCLEROSIS BE
5 LIMITED, OR IT COULD BE COVERAGE OF ALL NON-MEDICAL
6 TREATMENTS. SO I'M WITH THE PANEL, MEANING I FIND
7 SOME GROUPS THAT I DEFINITELY FEEL SHOULD BE
8 ENROLLED, AND SOME THAT I DEFINITELY FEEL DO NOT NEED
9 TO BE ENROLLED, BUT I'M JUST HAVING TROUBLE
10 INTERPRETING THE ACTUAL QUESTION.
11 DR. GARBER: I THINK IT'S ANY OF THE FOUR
12 NON-MEDICAL TREATMENTS THAT WE DISCUSSED TODAY IS
13 WHAT'S MEANT BY THE QUESTION.
14 (INAUDIBLE COLLOQUY BY PANELISTS.)
15 DR. SCHWARTZ: AS PART OF THE DISCUSSION,
16 I MEAN, I THINK EVERY SPEAKER TODAY SAID THERE'S NO
17 REASON FOR DOING THIS, WE'RE LOOKING AT A PREVENTIVE
18 OR PRESUMPTIVE BASIS, BUT JUST BECAUSE SOMEBODY IS
19 FOUND TO HAVE SOME RENAL ARTERY STENOSIS, THAT
20 DOESN'T MEAN THEY WILL GET THE INTERVENTION, AND I
21 THINK THAT'S THE QUESTION. I THINK EVEN WITHIN THE
22 CONSTRAINT OF SORT OF A TAINTED RETURN FOR DATA
23 COLLECTION, I THINK THERE STILL NEEDS TO BE, OR THERE
24 IS THE OPPORTUNITY FOR INDICATIONS OF NONINDICATIONS.
25 AND THAT MAY SOUND SO OBVIOUS, BUT THE

00229

1 FACT IS THERE IS THIS VERY LARGE INCREASE IN THE RATE
2 OF PROCEDURES IN THE TOTAL ABSENCE OF ANY SUPPORTIVE
3 DATA. YOU KNOW, IT ISN'T LIKE THERE WAS A NEW STUDY
4 THAT CAME OUT OR ANYTHING LIKE THAT. AND WHILE WE'RE
5 COLLECTING THE DATA, I THINK WE REALLY NEED TO BE
6 CONCERNED ABOUT GROSSLY INAPPROPRIATE USE OF THIS
7 PROCEDURE, INAPPROPRIATE USE, OR WHATEVER ADJECTIVE
8 YOU WANT TO PUT THERE.
9 DR. GARBER: LET ME JUST ASK SOMETHING.
10 BARRY HAD SAID EVERYBODY THAT GETS PROCEDURES SHOULD
11 BE IN THE REGISTRY AND THE PROCEDURES SHOULD BE
12 LIMITED TO CERTAIN INDICATIONS. YOU MAY SAY INSTEAD,
13 PEOPLE WITH CERTAIN INDICATIONS NEED TO BE IN A
14 REGISTRY, PEOPLE WITH OTHER INDICATIONS DON'T NEED TO
15 BE IN A REGISTRY AT ALL, THERE NEEDS TO BE NO DATA
16 COLLECTION. AND THE FIRST QUESTION IS, ARE THERE
17 SOME GROUPS FOR WHOM YOU FEEL CONFIDENT THERE NEEDS
18 TO BE NO DATA COLLECTION WHATSOEVER. THAT SORT OF
19 CONTRADICTS THE VOTES ON QUESTION 1.
20 AND THEN YOU MAY SAY THAT THERE ARE
21 DIFFERENT DATA COLLECTION EFFORTS FOR DIFFERENT TYPES
22 OF PATIENTS WITH DIFFERENT INDICATIONS. SO MAYBE
23 WE'LL SWITCH THE VOTING QUESTION IF IT EMERGES THAT
24 THERE IS SOME CONSENSUS THAT YOU NEED DIFFERENT
25 REQUIREMENTS FOR DIFFERENT POPULATIONS.

00230

1 CHAIM, OR MARCEL?
2 DR. SALIVE: I WANTED TO RESPOND TO THE
3 QUESTION ABOUT THE WORD ANY. I WOULD READ THE WORD
4 ANY TO MEAN NOT ALL, BUT TO MEAN SELECTIVELY ANY OF
5 THESE. SO IF YOU THOUGHT ONLY ONE OF THEM SHOULD BE
6 LIMITED TO A STUDY, SPECIFICALLY STENTING WITH A BARE
7 METAL STENT, THAT WOULD BE IN THIS REALM. IT DOES
8 NOT MEAN ALL.
9 DR. SCHWARTZ: SHOULD WE JUST GET RID OF
10 THE WORD ANY?
11 DR. SALIVE: PROBABLY.
12 DR. GARBER: I THINK IT'S IMMATERIAL
13 BECAUSE IF YOU THINK THERE IS AN ISSUE FOR A
14 PARTICULAR APPROACH, YOU NEED TO SAY WHAT THAT IS AND
15 NOT WORRY ABOUT WHETHER IT'S SOME OR ALL OR WHAT. WE
16 NEED TO KNOW WHAT IT IS.
17 DR. SALIVE: AND THE DISCUSSION IS THE
18 IMPORTANT PART.
19 DR. GARBER: CHAIM.
20 DR. CHARYTAN: FIRST OF ALL, THE QUESTION
21 ABOUT THE REGISTRY, IT SAYS WHETHER COVERAGE SHOULD
22 BE EXTENDED ONLY TO PATIENTS IN A STUDY. NOW IF
23 WE'RE GOING TO CHANGE THE QUESTION THEN, THAT'S A
24 DIFFERENT ISSUE, BUT IF THE QUESTION STANDS, THEN I
25 HAVE SEVERAL COMMENTS THAT I WOULD LIKE TO MAKE.

00231

1 FIRST OF ALL, THE WORD WAS USED BEFORE
2 THAT THIS IS AN UNPROVEN THERAPY, AND I THINK THAT
3 MAY BE A MISAPPLICATION OF THE WORD. THE LUNG
4 REDUCTION THERAPY WHEN IT WAS DEALT WITH BY CMS ON A
5 PANEL, A SIMILAR PANEL, WAS AN UNPROVEN THERAPY.
6 THIS IS A THERAPY THAT HAS BEEN USED FOR MANY YEARS
7 BY MANY DISCIPLINES, AND PERHAPS IT HAS BEEN
8 OVERUSED, BUT THERE'S A CLEAR RECOGNITION STATED
9 TODAY AND OVER THE YEARS THAT IT HAS BENEFITS. AND
10 WHAT'S NEEDED IS SOME KIND OF GUIDELINES OR A BETTER
11 CRITERIA FOR DEFINING IT, RATHER THAN FOR PROVING THE
12 THERAPY AS A WHOLE.
13 SO I DON'T THINK IT SHOULD QUALIFY AS
14 UNPROVEN, YOU KNOW, BE DEFINED AS UNPROVEN THERAPY;
15 RATHER ONE THAT NEEDS TO HAVE A BETTER DEFINITION OF
16 WHEN IT SHOULD BE USED. AND IF WE'RE GOING TO VOTE
17 ON MEDICARE RESTRICTING COVERAGE, IT SHOULD NOT BE
18 RESTRICTING COVERAGE TO STUDIES, BUT RESTRICTING
19 COVERAGE TO CERTAIN CRITERIA THAT PERHAPS CAN BE SET
20 UP BY AN APPROPRIATE PANEL OR GROUP.
21 SECONDLY, BE VERY CAREFUL. YOU KNOW, WHEN
22 YOU WISH FOR SOMETHING YOU MAY GET IT AND THEN THAT'S
23 NOT WHAT YOU WANT. WE ARE TALKING ABOUT SETTING A
24 POTENTIALLY VERY SERIOUS PRECEDENT OVER HERE.
25 MEDICARE COVERS PROCEDURES THAT HAVE BEEN ACCEPTED

00232

1 AND FOLLOW A CERTAIN STANDARD OF PRACTICE. IN RARE
2 EXCEPTIONS FOR UNPROVEN THERAPIES AND NEW THERAPIES
3 IT MAY REQUIRE A STUDY FIRST. BUT THIS IS NOT THE
4 SAME SITUATION, AND I THINK WE SHOULD BE VERY CAREFUL
5 ABOUT SETTING A PRECEDENT THAT MAY BE INAPPROPRIATE
6 AND MIGHT CREATE ISSUES, AND MIGHT CARRY OVER TO
7 OTHER AREAS.
8 SETTING GUIDELINES AND SETTING
9 RESTRICTIONS UNDER WHICH CIRCUMSTANCES A THERAPY IS
10 COVERED IS ONE ISSUE. SAYING THAT A THERAPY SHOULD
11 BE COVERED ONLY AS PART OF A STUDY OR USING MEDICARE
12 AS A WAY TO PUSH PEOPLE INTO A STUDY MAY NOT BE THE
13 APPROPRIATE WAY TO GO, AND I WOULD ARGUE VERY
14 STRONGLY IT IS NOT THE APPROPRIATE WAY TO GO AND THAT
15 THE QUESTION AS RAISED SHOULD NOT BE SUPPORTED BY US,
16 BECAUSE OF THE RISKS OF SETTING A PRECEDENT THAT
17 POTENTIALLY MAY HAVE MANY, MANY BAD CONSEQUENCES.
18 DR. GARBER: CAROLE, THEN SANDY, THEN
19 MIKE, THEN STEVE.
20 DR. FLAMM: I JUST WANTED TO ADD COMMENTS
21 TO THE OTHER COMMENTS ABOUT THE SUPPORT OF BOTH
22 PROMOTING ENROLLMENT IN THE ONGOING CLINICAL TRIAL,
23 CORAL, BUT ALSO OFFERING OTHER INFRASTRUCTURE TO
24 GATHER EVIDENCE.
25 ALONG THE LINES OF THE REGISTRY, I THINK

00233

1 WE NEED TO ASK OURSELVES WHETHER THIS REGISTRY WILL
2 BE MULTIPLE PROCEDURES IN ONE REGISTRY, OR A SINGLE
3 PROCEDURE, AND THINK ABOUT THOSE KINDS OF
4 OPPORTUNITIES OF COMPARISONS.
5 I WOULD LIKE TO RAISE A QUESTION ALSO
6 ABOUT WHETHER THERE ARE, WHEN THEY'RE IN A NARROWLY
7 DEFINED CLINICAL SUBSET WHERE THERE MIGHT BE ACUTE
8 CLINICAL INDICATIONS THAT ARE COMPELLING REASONS FOR
9 WANTING TO DO THIS, IF WE SET UP AN INFRASTRUCTURE
10 THAT REQUIRES PARTICIPATION IN A REGISTRY IN ORDER TO
11 BE ABLE TO DO IT AND GET PAID BY MEDICARE, THERE
12 COULD BE BARRIERS FOR PATIENTS WHO MIGHT, AND I WOULD
13 REALLY ASK THE CLINICIANS TO ANSWER THAT QUESTION,
14 WHETHER THAT'S A NARROWLY DEFINED PATIENT POPULATION,
15 THAT MIGHT RECEIVE THE PROCEDURE IN AN ACUTE SETTING
16 EVEN OUTSIDE THE REGISTRY.
17 DR. GARBER: SANDY.
18 DR. SCHWARTZ: A COUPLE THINGS. FIRST A
19 QUESTION FOR YOU OR MARCEL OR SOMEBODY FROM CMS.
20 WHAT'S A QUALIFIED CLINICAL RESEARCH STUDY? ARE
21 THERE METHODS FOR DETERMINING WHAT QUALIFIED MEANS?
22 WHO DOES THAT? CAN I DO THAT, OR WAS THIS SOMETHING
23 THAT MEDICARE, CMS WOULD HAVE TO DO, SET UP A
24 MECHANISM TO DO?
25 DR. SALIVE: WELL, I THINK THE REFERENCE

00234

1 HERE IS TO OUR CLINICAL TRIALS POLICY, AND THERE IS
2 IN THAT POLICY A PROCEDURE FOR QUALIFYING CLINICAL
3 TRIALS.

4 DR. SCHWARTZ: SO CMS HAS A PROCEDURE
5 WHEREBY SOMEBODY COULD SUBMIT A CLINICAL TRIAL AND
6 HAVE SOMEBODY EVALUATE IT AND DETERMINE WHETHER THEY
7 WERE QUALIFIED?

8 DR. SALIVE: RIGHT. AND I WILL ALSO SAY
9 THAT IN OUR GUIDANCE ON COVERAGE AND EVIDENCE
10 DEVELOPMENT, THAT DISCUSSES BOTH CLINICAL TRIALS AND
11 THE USE OF REGISTRIES IN THAT ARENA. SO I THINK
12 WE'RE TRYING TO GET AT THAT IN THIS QUESTION, IT'S
13 NOT NARROWLY FOCUSED. I MEAN, WE DON'T DISTINGUISH
14 AT CMS BETWEEN A STUDY AND REGISTRY, THOSE ARE BOTH,
15 I THINK, TOGETHER IN THIS QUESTION.

16 DR. GARBER: ONE POINT ABOUT THAT, THOUGH,
17 ALTHOUGH IT'S NOT INCORRECT, HHS HAS NOT ISSUED ITS
18 NEW CLINICAL TRIAL POLICY, HAS IT, AS OF YET? SO WE
19 DON'T KNOW EXACTLY WHAT IT MEANS TO BE QUALIFIED AT
20 THIS POINT IN TIME.

21 DR. SALIVE: NO, IT EXISTS, AND THE 2000
22 POLICY WAS UPDATED LAST WEEK WITH SOME LANGUAGE, AND
23 THERE IS A POSSIBILITY IT WILL CHANGE IN THE FUTURE
24 THROUGH A NATIONAL COVERAGE DECISION. I THINK THAT'S
25 UNDER DISCUSSION.

00235

1 DR. SCHWARTZ: SECOND, I WOULD LIKE TO PUT
2 A LITTLE BIT MORE IN TO SUPPORT WHAT HAS ALREADY BEEN
3 SAID. MARK FENDRICK AND I WERE BOTH PRINCIPALS IN
4 THE LUNG VOLUME REDUCTION SURGERY, AND IN FACT WE
5 FACED THE EXACT SAME SITUATION. THE SURGEONS AT THE
6 TIME FELT THAT IT WAS FRUITFUL. WE HAD A HELL OF A
7 TIME ENROLLING PATIENTS IN THAT TRIAL, IT TOOK
8 FOREVER, AND CERTAIN SITES I THINK EVEN HAD TO BE
9 DROPPED, BECAUSE SO FEW OF THEIR SURGICAL PATIENTS
10 WOULD BE ENROLLED.
11 SO I THINK A LOT OF THIS SORT OF DEPENDS
12 ON SORT OF WHERE YOU SIT. BUT THE MOST IMPORTANT
13 THINGS SAID ABOUT CORAL TODAY, I AGREE WITH IT. BUT
14 THE PRECEDENCE OF THIS IS VERY, VERY IMPORTANT, AND I
15 WISH BERNIE WERE HERE, BUT I THINK THIS IS A LITTLE
16 MORE COMPLICATED ETHICALLY FOR A PROCEDURE THAT'S
17 BEEN OUT THERE AND BEING USED, AND, YOU KNOW, I'VE
18 JUST EXHAUSTED MY KNOWLEDGE OF BIOMEDICAL ETHICS
19 HERE, ALTHOUGH I DID WATCH THE TAPE. BUT I THINK
20 DEPENDING ON HOW IT'S STRUCTURED, PARTICULARLY FOR
21 PROCEDURES OR SERVICES THAT ARE ALREADY IN SERVICE,
22 IN SOME ASPECTS SOME ETHICIST MAY TAKE ISSUE WITH THE
23 COERCIVE ASPECT OF THIS.
24 WHICH LEADS ME TO THE THIRD QUESTION WHICH
25 IS FOR THE CORAL INVESTIGATORS, AND I MEAN, ALL OF US

00236

1 HAVE BEEN INVOLVED IN CLINICAL TRIALS WHERE
2 EVERYTHING'S A STRUGGLE AND WE ALL HAVE THE SAME
3 ISSUES. I JUST WONDER IF YOU HAVE ANY SENSE OF WHY
4 IT'S SO DIFFICULT. I MEAN, YOU COULD ASK ME ABOUT
5 TRIALS I'VE BEEN INVOLVED IN ON DIFFERENT OCCASIONS,
6 BUT WHY HAS THIS BEEN SO DIFFICULT, WHAT HAVE THE
7 BARRIERS BEEN? BECAUSE IF THE BARRIER IS PRIMARILY
8 FINANCIAL, WHICH IS ALMOST A PRESUMPTION ON PART OF
9 THIS QUESTION, THEN A REGISTRY ISN'T GOING TO
10 SOLVE -- AND I'M NOT A BIG -- I'M A BELIEVER IN
11 MYSELF AND I'M A BIG BELIEVER IN OBSERVATIONAL DATA
12 WHEN IT'S ANALYZED PROPERLY FROM
13 QUASI-NON-EXPERIMENTAL DATA.
14 BUT I THINK IT'S IMPORTANT FOR US TO
15 UNDERSTAND IN THE CONTEXT OF THIS QUESTION WHERE THE
16 BARRIERS TO ENROLLMENT HAVE BEEN. IS IT THAT
17 PRACTITIONERS JUST BELIEVE THERE IS GOOD, IS THERE A
18 HUGE FINANCIAL INCENTIVE FOR PEOPLE DOING THIS? DO
19 THE PATIENTS REALLY HAVE, ONCE THEY HEAR ABOUT THEY
20 HAVE AN OPTION, DO THEY WANT THIS OPTION? DO YOU
21 HAVE A SENSE OF THAT?
22 DR. GARBER: MAYBE YOU COULD ALSO ADD,
23 WHAT COULD CMS DO TO HELP INCREASE ENROLLMENT.
24 DR. COOPER: THIS IS CHRIS COOPER, THE PI
25 OF THE CORAL TRIAL. TO SOME EXTENT, MY PREFERENCE

00237

1 WOULD BE TO DEFER TO STEVE TEXTOR AND DR. ROSENFELD
2 AND A FEW OTHERS IN THE AUDIENCE, CHRIS WHITE, WHO
3 ARE ACTIVE PARTICIPANTS IN THE TRIAL, BECAUSE THEY
4 ACTUALLY HAVE THE EXPERIENCE OF ENROLLING PATIENTS IN
5 THE TRIAL. BUT I'LL TRY TO GIVE YOU SOME GENERAL
6 COMMENTS ABOUT WHY IT'S DIFFICULT TO ENROLL IN
7 RANDOMIZED TRIALS, THIS ONE IN SPECIFIC, AND THEN
8 ALSO TRY TO ADDRESS WHAT CMS MIGHT BE ABLE TO DO.
9 I THINK ONE OF THE THINGS THAT I ALLUDED
10 TO THIS MORNING IS YOU HAVE THIS BROAD DIVERGENCE IN
11 THE PRACTITIONERS WHO TAKE CARE OF PATIENTS WITH
12 ISCHEMIC RENAL DISEASE. WE'VE HEARD NOW SOME OF THAT
13 SENSE IN THE DISCUSSION THIS MORNING WHERE FOLKS WITH
14 AN INTERNAL MEDICINE BACKGROUND AND NEPHROLOGY VIEW
15 IT AS THERAPY WITH SOME HEALTHY DEGREE OF SKEPTICISM.
16 AND SO TYPICALLY, THE PATIENTS THAT THEY'RE EVEN
17 SCREENING ARE THE ONES WITH RAPIDLY PROGRESSIVE RENAL
18 DYSFUNCTION, OR UNCONTROLLABLE HYPERTENSION ON SIX
19 DRUGS.
20 IN CONTRAST, FOR THE BELIEVERS, AND I PUT
21 MYSELF IN THAT CAMP, WE THINK THAT THIS IS AN
22 EFFECTIVE THERAPY THAT NEEDS TO BE PROVEN WITH
23 BENEFITS. OFTENTIMES THERE'S ISSUES, LIKE SHOULD I
24 REALLY PUT THIS PATIENT IN THE TRIAL BECAUSE MAYBE
25 I'LL PREVENT THEM FROM GOING INTO KIDNEY FAILURE FIVE

00238

1 YEARS FROM NOW, OR I'LL HELP CONTROL THEIR BLOOD
2 PRESSURE TO PREVENT CARDIOVASCULAR EVENTS. SO I
3 THINK ONE OF THE FUNDAMENTAL ISSUES AT MANY OF OUR
4 SITES THAT WE'VE VISITED IS THAT YOU HAVE THIS GREAT
5 DICHOTOMY BETWEEN THE HYPERTENSION AND NEPHROLOGY
6 GUYS WHO WON'T SCREEN, LET ALONE REFER FOR INCLUSION
7 IN A TRIAL, AND THE INTERVENTIONAL GUYS WHO FEEL
8 COMPELLED TO TREAT EVERYTHING. AND OBVIOUSLY EACH
9 SIDE HAS ITS OWN DYNAMICS.
10 DR. SCHWARTZ: AND ALSO THEY HAVE A
11 FINANCIAL DISINCENTIVE.
12 DR. COOPER: EXACTLY. AND YOU KNOW, THE
13 FINAL ISSUE IS THAT I DON'T THINK WE IGNORE THE
14 FINANCIAL DISINCENTIVE OF PARTICIPATING IN A TRIAL
15 LIKE THIS. YOU KNOW, IF I ENROLLED ONE OF MY
16 PATIENTS INTO CORAL, CMS PAYS ME NOTHING FOR THE TIME
17 THAT I'VE SPENT IN DISCUSSION WITH THE PATIENT,
18 WHEREAS IF I SHORTCHANGE THE DISCUSSION AND SAY SURE,
19 I CAN FIX YOU, AND I PUT IN A STENT, I GET THIS BILL
20 FOR THE ANGIOGRAPHY, I GET THE BILL FOR THE STENT
21 PROCEDURE, AND THE PATIENT THINKS I'M THE GREATEST
22 DOCTOR. AND SO THERE IS A REAL FINANCIAL INCENTIVE
23 FOR A PERSON LIKE MYSELF TO SKIP THE TRIAL AND GO
24 AHEAD AND TREAT THE PATIENT.
25 WHAT COULD CMS DO IN SPECIFIC? I WOULD

00239

1 LOVE TO SEE CMS VIEW THIS AS INSTRUMENTAL TO MAKING
2 GOOD DECISIONS. AND AS SOMEBODY WHISPERED IN MY EAR
3 A FEW MINUTES AGO, IF YOU GAVE US A MILLION DOLLARS,
4 NOT A BIG AMOUNT OF MONEY COMPARED TO HOW MUCH YOU'RE
5 SPENDING ON STENTS, WE COULD GIVE THE SITES AN
6 ADDITIONAL \$10,000 PER ENROLLED PATIENT AND MAYBE
7 INCENT ENROLLMENT.
8 YOU KNOW, IN THIS PROCESS YOU HAVE THREE
9 ARMS OF THE FEDERAL GOVERNMENT, THE FDA, CMS AND THE
10 NIH, ALL APPARENTLY WORKING AT CROSS-PURPOSES FOR AN
11 AREA WHERE OVERT ALIGNMENT WOULD BE BENEFICIAL. SO
12 ANYWAYS, I'LL STOP AT THIS JUNCTURE. AND AGAIN, I
13 WOULD LOVE TO HEAR FROM STEVE TEXTOR OR KEN
14 ROSENFELD OR CHRIS WHITE ABOUT WHAT INVESTIGATORS
15 WHO ARE PARTICIPATING IN THIS TRIAL THINK WE OUGHT TO
16 DO, OR WHAT THE BARRIERS ARE.
17 DR. TEXTOR: I GUESS I'LL MAKE A COMMENT
18 ON THAT. I THINK ONE WAY OF LOOKING AT THIS -- LET
19 ME JUST COME BACK TO WHAT MIGHT SEEM REPETITIVE, BUT
20 I THINK YOU COULD ARGUE THAT WE'RE COMING FROM A
21 DIFFERENT BACKGROUND THAN THE INTRODUCTION OF OTHER
22 NEW DEVICES. WE'RE COMING FROM A DISEASE WHERE THE
23 STANDARD OF THERAPY HAS BEEN AS LONG AS (INAUDIBLE),
24 WE (INAUDIBLE), YOU COULD ARGUE THAT THE STANDARD OF
25 CARE IS TO REVASCULARIZE PATIENTS WHICH ARE

00240

1 THREATENED BY IMPAIRED CIRCULATION. AND REALLY IT'S
2 INTUITIVE AND IT'S NOT INVASIVE, AND THERE MAY BE A
3 MAJOR HAZARD TO LEAVE IT UNTREATED. AND UP UNTIL
4 PROBABLY 10 YEARS AGO OR 15, IT REALLY WAS
5 UNTREATABLE WITH MEDICAL THERAPY.
6 SO ONE DIFFERENT WAY OF CASTING THIS
7 QUESTION IS REALLY, WHAT'S THE ROLE OF THE CURRENT
8 MEDICAL THERAPY? WE'VE HAD LOTS OF EVIDENCE AND
9 HEARD LOTS OF DATA CONCERNING STATINS AND OTHER
10 AGENTS AND YOU COULD ARGUE, WE REALLY NEED TO SORT
11 THIS OUT IN A HURRY. IF YOU ASK ME WHAT A RATIONAL
12 STEP MIGHT BE, IT WOULD BE TO TAKE THE APPROACH OF
13 THE CANCER INSTITUTE, THAT THE ONCOLOGY GROUP
14 PRACTICING AROUND THE COUNTRY HAS DONE WITH NEW
15 PROMISING THERAPIES. WE'RE NOT SURE WHAT THE
16 OUTCOMES ARE GOING TO BE, WE'RE NOT QUITE SURE IN
17 THIS DISEASE, BUT THERE CERTAINLY IS AGREEMENT AMONG
18 OURSELVES TO ENROLL ALL PATIENTS WITH THIS DISEASE
19 FOR X PERIOD OF TIME. EVEN IF YOU'RE NOT SURE OF THE
20 OUTCOME, WHICH HAS BEEN CLEAR, YOU TAKE THE NEXT 500
21 OR THOUSAND INDIVIDUALS WITH SMALL CELL CANCER OF THE
22 LUNG TO GET IN THIS TRIAL, BECAUSE WE NEED TO KNOW.
23 I THINK WE'RE ALMOST IN THIS POSITION WITH
24 THIS DISEASE, NOT SO MUCH BECAUSE OF STENTS PER SE,
25 BUT BECAUSE OF A SHIFT WHERE WE'RE SORT OF SAYING

00241

1 INTENSIVE MEDICAL THERAPY WILL PROBABLY DO AS WELL OR
2 MAYBE BETTER, WE'RE NOT SURE WE WILL GAIN MUCH WITH
3 THE ISSUE OF REVASCULARIZING KIDNEYS.
4 BUT THE STIMULATING AND UNIQUE PROBLEM IS
5 WHY WE'RE HAVING THIS DISCUSSION TODAY. WE TAKE THE
6 TACK, YOU KNOW, IN THE PATIENTS I'M SEEING, BASICALLY
7 WE TELL THEM WE'RE NOT SURE OF THE BEST ROUTE. WE
8 WOULD LIKE TO PREVENT THEM FROM RUNNING INTO TROUBLE
9 AND TREAT THEM THE BEST WE CAN. I'M NOT SURE WHETHER
10 STENTS ARE THE WAY TO GO OR NOT, AND THEY ACCEPT
11 THAT, AND BASICALLY WE HAVE NOT HAD THE DIFFICULTY.
12 AND I THINK THE OBVIOUS FEELING HERE IN THE ROOM IS
13 THAT IT TAKES TIME, IT'S A LOT OF WORK, THERE'S A LOT
14 OF MONEY INVOLVED.
15 FRANKLY, I THINK WHAT CMS CAN DO IS REALLY
16 REQUIRE COMPLETING THE ENROLLMENT PHASE OF THIS TRIAL
17 BEFORE WE PAY FOR MORE STENTS.
18 DR. GARBER: CHAIM.
19 DR. CHARYTAN: COULD THIS QUESTION
20 NUMBER 4 PERHAPS BE BROKEN DOWN INTO TWO OR THREE
21 PARTS?
22 ONE IS THAT WE WOULD RECOMMEND, OR BOTH IF
23 WE DO SO, FOR A REGISTRY OF ALL PATIENTS WHO UNDERGO
24 THIS PROCEDURE. WE MAY STILL HAVE TO VOTE ON THIS
25 QUESTIONS AS PHRASED, BUT I SUSPECT THE VOTE MIGHT BE

00242

1 DIFFERENT THAN WHETHER ALL PATIENTS SHOULD BE COVERED
2 ONLY DURING A TRIAL, BUT A SEPARATE QUESTION WHETHER
3 ALL PATIENTS WHO ARE COVERED SHOULD BE PART OF A
4 REGISTRY. AND PERSONALLY, I DON'T KNOW IF THIS IS IN
5 ORDER, BUT IT IS CERTAINLY A RECOMMENDATION THAT SOME
6 SORT OF GROUP BE SET UP TO DEFINE CRITERIA FOR
7 COVERAGE OF THIS PROCEDURE BASED ON CURRENTLY
8 AVAILABLE KNOWLEDGE AND PENDING NEW DATA.
9 DR. GARBER: WELL, I THINK EXCEPT FOR THE
10 LAST PART, THAT'S APPROPRIATE FOR THIS GROUP. WE
11 HAVE NOT BEEN ASKED TO DEFINE CONDITIONS FOR
12 COVERAGE, WE HAVE BEEN ASKED TO DEFINE WHETHER YOU
13 NEED TO BE ENROLLED IN A QUALIFIED STUDY, AND WE
14 COULD SAY A LITTLE BIT ABOUT IT.
15 I DON'T KNOW ABOUT THE REST OF YOU, BUT
16 I'VE SAT IN ON MEETINGS ABOUT HOW CMS CAN DECIDE
17 WHAT'S A QUALIFIED STUDY, AND I HAVE NO IDEA.
18 DR. SALIVE: LET ME CLARIFY WHAT I SAID
19 EARLIER. I THINK THAT, YOU KNOW, WE HAVE IN THE PAST
20 DEFINED WHAT'S A QUALIFIED STUDY, BUT IN AN NCD SUCH
21 AS THIS WE COULD DEFINE WHAT'S A QUALIFIED STUDY. SO
22 WE'RE ASKING YOU, YOU KNOW, IF YOU TOOK THE WORD
23 QUALIFIED OUT AND ANSWERED YES TO THIS QUESTION, THEN
24 WE CAN DISCUSS WHAT ARE THOSE QUALIFICATIONS. SO I'M
25 NOT SAYING WE NEED TO CHANGE THE QUESTION, I'M JUST

00243

1 SAYING THAT AS PART OF THE QUESTION, WHAT WOULD BE A
2 QUALIFIED STUDY IN YOUR MINDS, WHAT WOULD THAT BE.
3 SO IF YOU SAY IT SHOULD BE A REGISTRY WITH THE
4 FOLLOWING CHARACTERISTICS, IT SHOULD BE BASED ON
5 CERTAIN PATIENT CHARACTERISTICS, IT SHOULD BE BASED
6 ON CERTAIN FACILITY CRITERIA, THOSE ARE SOME OF THE
7 THINGS WE'RE SEEKING.
8 DR. SCHWARTZ: THAT GOES TO THE
9 FUNDAMENTAL QUESTION, BECAUSE WHAT I WAS TRYING TO
10 SAY BEFORE IS, MY CONCERN ABOUT A REGISTRY IS THAT A
11 REGISTRY WOULD UNDERMINE THE ABILITY TO, COMPLETELY
12 UNDERMINE THE ABILITY TO HOLD A RANDOMIZED TRIAL.
13 BECAUSE IF IT'S SO MUCH EASIER, I'M GOING TO GET
14 PAID, THE PATIENT IS GOING TO GET THE SERVICE, AND
15 ALL I HAVE TO DO IS FILL OUT A PAGE OR TWO FORM THAT
16 I'LL HAVE MY FELLOW OR SECRETARY OR PATIENT FILL OUT.
17 SO YOU KNOW, I DON'T KNOW THE ANSWER HERE,
18 BUT WE HAVE TO BE REAL CAREFUL ABOUT HOW WE TAKE THIS
19 THROUGH. AND SO IN A GENERAL SENSE, I GENERALLY
20 SUPPORT THIS, BUT THE DEVIL'S IN THE DETAILS HERE AND
21 I DON'T KNOW IF THIS IS SOMETHING CMS HAS BEEN
22 STRUGGLING WITH OR PLAYING AROUND WITH WITH THE
23 BACKDROP OF PULMONARY TRANSPLANTS, LUNG REDUCTION
24 SURGERY, OXYGEN, AND A COUPLE OF OTHER THINGS THEY
25 HAVE TRIED TO PUSH THE ENVELOPE IN TERMS OF GETTING

00244

1 IT DONE, BUT THIS ONE WILL STILL BE A TOUGH ONE.
2 DR. GARBER: MIKE, THERE ARE A COUPLE
3 OTHER PEOPLE WAITING TO TALK. YOU'VE HAD YOUR HAND
4 UP FOR A LONG TIME; DO YOU WANT TO GO FIRST?
5 MR. LACEY: THAT'S FINE.
6 DR. GARBER: OKAY. DR. DWORKIN, DO YOU
7 WANT TO MAKE A COMMENT?
8 DR. DWORKIN: WELL, I REALLY JUST WANTED
9 TO AGREE WITH WHAT WAS JUST SAID ABOUT THE POTENTIAL
10 DOWNSIDE OF A REGISTRY. SO, A REGISTRY WILL BE A
11 COLLECTION OF PATIENTS WHO HAVE ALL HAD THE
12 INTERVENTION. IT WON'T REALLY ADDRESS THE
13 FUNDAMENTAL QUESTION OF WHETHER MEDICAL THERAPY, OR
14 WHAT THE COMPARATOR IS BETWEEN THE MEDICAL APPROACH
15 AND THE INTERVENTION.
16 AND IT COULD BE A HUGE DISINCENTIVE, I
17 THINK, TO ENROLL THEM IN A RANDOMIZED TRIAL, BECAUSE
18 OBVIOUSLY IF YOU PUT A PATIENT INTO A REGISTRY, IT'S
19 A LOT LESS WORK AND EVERY PATIENT GETS STENTED, SO I
20 DON'T THINK THAT WILL HELP THE CORAL TRIAL, INSISTING
21 THAT PATIENTS BE IN A REGISTRY. NOW THAT MAY BE
22 SOMETHING THAT, YOU KNOW, THE GROUP FEELS IS
23 IMPORTANT TO DO, BUT IT'S NOT GOING TO HELP US AND
24 I'M AFRAID IT COULD SERIOUSLY HURT ENROLLMENT
25 INSTEAD.

00245

1 DR. GARBER: ACTUALLY I WANTED TO FOLLOW
2 UP ON THAT WITH BOTH YOU AND DR. COOPER, BECAUSE
3 DR. COOPER, I WAS KIND OF SOMEWHAT UNDERSTANDING BUT
4 SOMEWHAT PERPLEXED BY YOUR ANSWER BEFORE ABOUT THE
5 BARRIERS TO ENROLLMENT. UNDOUBTEDLY IT'S VERY
6 DIFFICULT WHEN THE PROVIDER COMMUNITY IS POLARIZED
7 AND YOU HAVE A SET OF PEOPLE WHO ABSOLUTELY BELIEVE
8 THE INTERVENTION WORKS AND A SET OF PEOPLE WHO DON'T,
9 AND SO THEY DON'T WANT THEIR PATIENTS RANDOMIZED.
10 BUT THAT IS NOT AN UNUSUAL SITUATION. IN
11 FACT, MY IMPRESSION OF THE STUFF THAT WE STUDY IN
12 VARIOUS CONTEXTS, THAT'S THE RULE, NOT THE EXCEPTION.
13 USUALLY PEOPLE WHO ARE PASSIONATE ABOUT STUDYING
14 SOMETHING BELIEVE IN IT. I MEAN, THEY MAY BELIEVE IN
15 THE INTERVENTION, THEY MAY BELIEVE IN THE
16 ALTERNATIVE, ONE OR THE OTHER. AND AS SOMEBODY WAS
17 SAYING, THE INTERSECTION OF THOSE MAY BE CLOSE TO
18 EMPATHY.
19 BUT WHEN YOU LOOK AT SOMETHING LIKE
20 AUTOLOGOUS MARROW TRANSPLANTATIONS FOR BREAST CANCER,
21 IN THAT CASE I WOULD SAY THE OBSERVATIONAL DATA WAS
22 INFINITELY MORE COMPELLING ABOUT THE EFFICACY OF THE
23 PROCEDURE THAN WHAT WE'VE SEEN TODAY. THAT IS TO
24 SAY, THERE WERE HUGE MORTALITY BENEFITS IN THE
25 OBSERVATIONAL STUDIES OF AUTOLOGOUS MARROW

00246

1 TRANSPLANTATION PATIENTS. AND AS YOU KNOW, THE
2 RANDOMIZED TRIALS, WHEN THEY WERE EVENTUALLY
3 COMPLETED, SHOWED NO BENEFIT OVER CONVENTIONAL
4 CHEMOTHERAPY.
5 BUT THE ONE THING THAT CAUSED A HUGE
6 SLOWDOWN IN RECRUITMENT IN RANDOMIZED TRIALS WAS WHEN
7 PAYERS STARTED PAYING FOR THE TRANSPLANTATION. IT
8 WAS A HUGE EFFECT AND PROBABLY, I WOULD GUESS, THERE
9 ARE OTHER PEOPLE WHO KNOW A LOT ABOUT THIS, BUT I
10 WOULD GUESS THAT WAS THE SINGLE MOST IMPORTANT FACTOR
11 BEYOND EVERYTHING ELSE.
12 SO I'M A LITTLE PERPLEXED TO HEAR YOU SAY
13 WELL, IF CMS WOULD JUST GIVE US A MILLION MORE
14 DOLLARS. I DON'T KNOW THAT MUCH ABOUT RENAL ARTERY
15 STENOSIS AND ITS TREATMENTS, BUT BASED ON THE HISTORY
16 OF OTHER INTERVENTIONS, THE FIRST THING A PAYER COULD
17 DO IS SAY WE WILL ONLY PAY IF YOU ENROLL IN A TRIAL,
18 AND THAT WOULD PRESUMABLY HAVE AN IMMEDIATE AND HUGE
19 EFFECT ON ENROLLMENT.
20 NOW I'M NOT PROPOSING THAT THAT BE DONE,
21 BUT I THINK IT'S IMPORTANT FOR US TO HAVE A CLEAR
22 IDEA ABOUT HOW ALL THE TOOLS THAT CMS HAS AVAILABLE
23 MIGHT WORK. DR. ROSENFELD, DID YOU WANT TO SAY
24 SOMETHING ON THAT POINT?
25 DR. ROSENFELD: JUST A COUPLE OF THINGS

00247

1 TO ANSWER THE QUESTION ABOUT ENROLLMENT, BUT ACTUALLY
2 I WAS INTERESTED IN STEVE TEXTOR'S COMMENT BECAUSE
3 WHAT HE'S SAYING IS MEDICAL THERAPY IS THE THING
4 THAT'S CHANGED, SO MAYBE WE SHOULD ACTUALLY START
5 FROM AN INTERVENTION AT THE BASELINE AND ADD MEDICAL
6 THERAPY AS THE EXPERIMENTAL VARIABLE. JUST KIDDING.
7 BUT HONESTLY, I THINK IT'S IMPORTANT TO
8 UNDERSTAND THAT THIS IS DIFFERENT THAN MANY OF THE
9 OTHER THERAPIES THAT HAVE BEEN PRESENTED AS NEW AND
10 NOVEL TREATMENTS. WE'RE TALKING ABOUT RESCINDING
11 SOMETHING THAT HAS BEEN OUT THERE AND MANY, MANY
12 PEOPLE BELIEVE IN ALREADY, AND THAT MAY BE PART OF
13 THE ISSUE -- THAT IS THE ISSUE WITH ENROLLMENT IN
14 THIS TRIAL. IT'S NOT JUST THAT THE INTERVENTIONIST
15 BELIEVES IN THIS, BECAUSE QUITE HONESTLY, I FEEL THAT
16 WE NEED TO GET THE ANSWERS TO THIS QUESTION AS WELL.
17 BUT AS AN INTERVENTIONALIST AT THE END OF
18 THE REFERRAL LINE, I HAVE A SERIES OF GENERAL
19 INTERNISTS, CARDIOLOGISTS AND OTHERS, NONINVASIVE
20 FOLKS WHO REFER IN TO ME, AND PATIENTS THAT EXPECT
21 THAT AT THE END OF THE LINE THEY'RE GOING TO GET
22 REVASCULARIZED BECAUSE THEY'VE BEEN TOLD THAT. SO
23 THERE IS A WHOLE HUGE EDUCATIONAL PROCESS THAT
24 REQUIRES SORT OF UNDOING 15 YEARS OF WHAT WE, MANY OF
25 US BELIEVE WE'VE LEARNED IS AN EFFECTIVE THERAPY.

00248

1 AND I THINK YOUR POINT IS A GOOD ONE, THAT
2 THIS IS KIND OF A LITTLE BIT, NOT UNPRECEDENTED
3 PERHAPS, I'M NOT SURE OF THE HISTORY WITH CMS AND
4 WHAT THEY'VE DONE IN TERMS OF WITHDRAWING AND
5 RESCINDING COVERAGE, BUT IT CERTAINLY IS GOING
6 TOWARDS THAT DIRECTION AND THAT'S WHY ALL THE
7 DISCUSSION ABOUT MEDICAL ETHICS.
8 SO, I WOULD ALSO MAKE A COUPLE OF OTHER
9 POINTS. ONE IS THAT THERE HAS BEEN A LOT OF
10 DISCUSSION ABOUT THE NUMBERS RAMPING WAY UP. IF YOU
11 LOOK AT THE NUMBERS OVER THE LAST THREE YEARS,
12 THERE'S ACTUALLY BEEN A SIGNIFICANT PLATEAU EFFECT.
13 IN FACT, OVER THE PAST THREE YEARS, THERE HAS NOT
14 BEEN A SIGNIFICANT CHANGE, SUBSTANTIVE CHANGE IN THE
15 PERCENTAGE OF PATIENTS, THE NUMBER OF PATIENTS
16 UNDERGOING RENAL STENTING. SO, I THINK THAT WAS AN
17 EFFECT OF HAVING A NEW TREATMENT THAT BECAME
18 AVAILABLE IN THE MID '90S, LATE '90S, THAT WAS A MUCH
19 LESS INVASIVE TREATMENT COMPARED TO WHAT WAS
20 AVAILABLE, AND SUDDENLY, YOU KNOW, HAVING IT
21 AVAILABLE, PEOPLE TAKING ADVANTAGE OF IT AND THEN
22 RAMPING UP.
23 I JUST WANT TO SAY ONE OTHER COMMENT, OR
24 TWO OTHER COMMENTS. ONE WAS, THE COMMENT THAT TIM
25 MURPHY MADE ABOUT WHAT MIGHT BE THE SPECIFIC

00249

1 INDICATIONS WERE ACTUALLY THE SAME AS THE AHA/ACC
2 GUIDELINES THAT WERE DESCRIBED EARLIER BY DR. HIRSCH,
3 AND I THINK THAT'S -- WE HAVE -- IT'S INTERESTING
4 THAT DR. MURPHY SAID THE SAME CRITERIA THAT WERE
5 ESSENTIALLY DEFINED BY THESE EXPERTS IN AHA/ACC.
6 DR. SCHWARTZ: BUT MY GUESS IS THAT 80
7 PERCENT OF THE PEOPLE GETTING THE PROCEDURE DON'T
8 MEET THAT CRITERIA.
9 DR. ROSENFELD: I'M NOT SURE ABOUT THAT,
10 BUT I THINK THAT NONE OF US THAT STOOD UP HERE ON THE
11 INTERVENTIONAL SIDE OR PROMOTING THIS TECHNIQUE
12 SUGGESTED THAT PEOPLE SHOULD BE TREATED
13 PROPHYLACTICALLY. NONE OF US BELIEVES THAT, AND NO
14 DOUBT THERE ARE PEOPLE WHO ARE BEING TREATED
15 PROPHYLACTICALLY AND THEY SHOULD NOT BE TREATED. AND
16 SO IF WE CLEANED UP THAT LITTLE MESS, THAT MIGHT
17 ACTUALLY BE A SIGNIFICANT IMPROVEMENT. BUT I DON'T
18 THINK IT'S 80 PERCENT, AND FOR ANYBODY TO SUGGEST
19 THAT, THERE ARE VERY GOOD -- I WOULD SAY THAT 85
20 PERCENT OF THE GOOD CLINICIANS OUT THERE ARE MAKING
21 VERY GOOD JUDGMENTS AND IT'S THE 10 OR 15 PERCENT --
22 DR. SCHWARTZ: I WITHDRAW 80 PERCENT. I
23 WAS JUST MAKING THE POINT THAT IT'S LIKE ANYTHING
24 ELSE, YOU KNOW.
25 DR. ROSENFELD: YEAH. AND THE LAST THING

00250

1 IS ABOUT REGISTRIES. I THINK REGISTRIES ARE A VERY
2 GOOD THING AND YOU CAN GET A LOT OF INFORMATION FROM
3 THEM. IN THE PCI WORLD AS AN NCDR PERSON, YOU KNOW,
4 THEY ARE ENHANCING OUR KNOWLEDGE BASE GREATLY. I
5 DON'T THINK ACTUALLY -- YOU KNOW, COMPARED TO WHERE
6 WE ARE NOW, I DISAGREE WITH DR. DWORKIN THAT IT WOULD
7 ACTUALLY COMPROMISE OUR ENROLLMENT IN CORAL. I THINK
8 IT WOULD ENHANCE IT, PARTICULARLY COMPARED TO WHERE
9 WE ARE NOW.
10 NOW IF YOU SAID THE ALTERNATIVE IS TO SAY
11 WE'LL WITHDRAW COVERAGE COMPLETELY UNLESS YOU ENROLL
12 IN CORAL, THEN SURE, THAT'S GOING TO BE THE BEST FOR
13 ENHANCING ENROLLMENT. I DON'T THINK THAT'S A
14 REALISTIC OR PRACTICAL, OR PERHAPS NOT ETHICAL
15 STANCE. HOWEVER, TO SAY LET'S PUT ONE MORE BARRIER,
16 YOU HAVE TO PARTICIPATE IN A REGISTRY, AND THERE ARE
17 MANY OF US IN THE ROOM HERE FROM SVS, ACR AND ACC WHO
18 COULD HELP CONSTRUCT SUCH REGISTRY. THERE ARE SOME
19 ISSUES HERE. YOU WOULD HAVE TO FIGURE OUT WHO IS
20 GOING TO PAY FOR IT. BUT IF YOU SAY YOU CANNOT GET
21 REIMBURSED FOR RENAL STENTING UNLESS YOU PARTICIPATE
22 IN A REGISTRY THAT IS CERTIFIED BY CMS, AND WE'VE
23 GONE THIS ROUTE, DR. SALIVE, WITH OTHER REGISTRIES,
24 IT IS A BARRIER THAT MIGHT ACTUALLY HELP ENROLLMENT
25 IN CORAL. SO I KIND OF DISAGREE ON THAT POINT.

00251

1 DR. GARBER: BILL MAISEL, THEN MIKE.
2 DR. MAISEL: I JUST WANTED TO MAKE THE
3 OBSERVATION THAT A LOT OF THE DISCUSSION HAS FOCUSED
4 ON GETTING THIS RANDOMIZED TRIAL COMPLETED.
5 COMPLETED THIS TRIAL MAY BE FANTASTIC, BUT WE MAY NOT
6 GET ALL THE ANSWERS WE THINK WE'RE GOING TO GET FROM
7 THE RANDOMIZED TRIAL. SO I THINK TO PUT ALL OUR EGGS
8 IN ONE BASKET AND HOPE THAT IN 2009 OR 2010 WE'LL
9 HAVE A DEFINITIVE ANSWER, I THINK IS A LITTLE BIT
10 RISKY, AND I THINK WE HAVE SEVERAL YEARS OF DATA
11 COLLECTION THAT WE COULD GET IN THE MEANTIME.
12 I AM A PROPONENT OF THE REGISTRY. I THINK
13 THE COMPONENT FACTORS FOR ME WOULD BE THAT IT CANNOT
14 IMPAIR PATIENT ACCESS TO NEEDED PROCEDURES. I THINK
15 WE'VE HEARD FROM A LOT OF THE WELL RESPECTED
16 CLINICIANS AND THE AHA AND ALL THE OTHER PROFESSIONAL
17 SOCIETIES THAT THERE ARE MANY PHYSICIANS WHO ARE WELL
18 RESPECTED WHO STRONGLY BELIEVE THAT THIS IS AN
19 INDICATED PROCEDURE FOR CERTAIN PATIENTS, AT LEAST
20 CERTAIN SUBSETS OF PATIENTS, AND I THINK WE NEED TO
21 BE VERY CAREFUL ABOUT LIMITING ACCESS TO THAT GROUP
22 OF PATIENTS. FOR ME IT WOULD BE THE BILATERAL RENAL
23 ARTERY STENOSIS OR RECURRING PULMONARY EDEMA PATIENT
24 OR WHAT HAVE YOU, I THINK WE COULD CARVE OUT CERTAIN
25 GROUPS.

00252

1 BUT IF A REGISTRY WAS UBIQUITOUS LIKE AN
2 NCDR REGISTRY, THAT PATIENTS HAD ADEQUATE ACCESS, WE
3 DIDN'T HAVE TO WORRY ABOUT ACCESS TO THE PROCEDURE,
4 THEN I WOULD BE COMFORTABLE WITH THAT.
5 THE FINAL POINT I WOULD LIKE TO MAKE IS
6 THAT THERE IS PRECEDENT FOR HAVING A REGISTRY TO A
7 PROCEDURE THAT'S ALREADY OUT THERE. IF YOU LOOK AT
8 IMPLANTABLE DEFIBRILLATORS. PRIMARY INTERVENTION OF
9 IMPLANTABLE DEFIBRILLATORS WERE IMPLANTED IN MORE
10 PATIENTS THAN THIS PROCEDURE HAS BEEN DONE IN, AND A
11 REGISTRY WAS REQUIRED THERE, WHICH WAS PAINFUL, BUT
12 IT WAS DONE.
13 DR. GARBER: MIKE.
14 MR. LACEY: I JUST WANT TO COMMENT ON THE
15 PERCENT IN SLOWDOWN OR TOTAL NUMBER PERCENTAGE
16 INCREASE. THAT SEEMS TO BE, BOTH FROM COMMENTS THAT
17 WERE WRITTEN BY (INAUDIBLE) AND ALSO BOSTON
18 SCIENTIFIC TODAY THAT SUGGESTED THAT THE INCREASE IS
19 TOPPING OFF. AND IN SOME OF MY CONVERSATIONS, IT
20 SEEMED AS IF PART OF THAT IS THAT AT A LOCAL COVERAGE
21 POLICY LEVEL, MANY OF THE GUIDELINES ARE (INAUDIBLE)
22 AND THE SO-CALLED DRIVE-BY ANGIOGRAPHY IS BECOMING
23 LESS OF AN ISSUE. I'M VERY CONCERNED THAT WHEN YOU
24 START RESTRICTING ACCESS TO 50 OR 60,000 PEOPLE FROM
25 THIS PROCEDURE WITH A VERY CRUDE MEASUREMENT, IT

00253

1 SHOULD BE MANAGED BY SUGGESTING COMPLIANCE WITH
2 GUIDELINES OR SOME OTHER MORE SUBTLE INCENTIVES THAT
3 DON'T STOP ACCESS TO THIS TECHNOLOGY, BUT RATHER
4 ENCOURAGE BETTER DATA COLLECTION.
5 DR. GARBER: LINDA.
6 DR. BERGTHOLD: I WANT TO MAKE A STRONG
7 AND RINGING ENDORSEMENT FOR WHAT CMS HAS BEEN TRYING
8 TO DO, AND I HAVE BEEN ON THE PANEL SINCE THE
9 BEGINNING. THE WHOLE IDEA OF THIS ENTITY WAS TO TRY
10 TO KEEP PATIENTS SAFE AND BE SURE THAT WE DID THE
11 BEST WE COULD TO ASSURE PEOPLE THAT WE WERE PROVIDING
12 TREATMENT FOR WHICH THERE WAS SOME GOOD EVIDENCE OF
13 EFFECTIVENESS. SO THE PRECEDENT THAT I'M HAPPY TO
14 SET IS THE PRECEDENT WHERE WE DO NOT SUPPORT
15 TREATMENTS FOR WHICH THE EVIDENCE IS NOT GOOD FOR
16 EFFECTIVENESS. AND IT DOESN'T BOTHER ME AS A
17 POTENTIAL PATIENT OR CONSUMER AT ALL THAT WE WOULD DO
18 THAT, AND I WOULD HOPE THAT WE WOULD SAVE FOLKS FROM
19 HAVING TREATMENTS THAT WERE OF NOT PROVEN
20 EFFECTIVENESS.
21 SO I WOULD LEAVE IT UP TO CMS ON THIS
22 QUESTION NUMBER 4 TO DEFINE QUALIFIED CLINICAL
23 RESEARCH STUDIES, BUT I DO REALLY STRONGLY BELIEVE
24 THAT UNTIL WE HAVE BETTER -- I MEAN, I'M HEARING ALL
25 OF YOU ALL SORT OF ARGUING ABOUT WHAT IS EFFECTIVE

00254

1 AND NOT, AND AS A CONSUMER I'M SAYING, YOU KNOW, IF I
2 NEED THIS, I WANT TO BE SURE THAT THE DATA IS BETTER
3 THAN IT IS TODAY. SO HOWEVER WE GET PATIENTS INTO
4 STUDIES AND WHAT KIND OF STUDIES THEY ARE, I HOPE WE
5 DO GET THEM INTO THOSE STUDIES SO THAT WE CAN MAKE
6 THE DECISIONS BETTER.
7 DR. GARBER: GO AHEAD, ALAN.
8 DR. HIRSCH: JUST A QUICK COMMENT TO
9 REITERATE SOME OF THE STATEMENTS I'VE HEARD SAID.
10 YOU KNOW, THE GUIDELINE WRITING COMMITTEE HAD EXACTLY
11 THE SAME CHALLENGE YOU ALL FACE, AND I PITY YOU LIKE
12 I PITIED US. WE SPENT YEARS LOOKING AT THE EVIDENCE,
13 REALIZED IT WASN'T EXCELLENT, WE HAD A SUBTLETY TO
14 MANAGE, WHICH IS TO MEASURE INDIVIDUAL PATIENTS THAT
15 DIDN'T HAVE ACCESS, INDIVIDUAL CONSUMERS, INDIVIDUAL
16 MEDICARE RECIPIENTS IN AREAS WHERE THERE WAS CLASS I
17 AND CLASS IIA, OCCASIONALLY CLASS IIB AREAS WHERE WE
18 THOUGHT THERE REALLY WAS EFFICACY.
19 NOW (INAUDIBLE) ENTHUSIASM FOR DRIVE-BY
20 ANGIOGRAPHY OR ANGIOPLASTY, PERHAPS THAT WAS BECAUSE
21 THE VASCULAR PROFESSIONAL SOCIETIES DID GET TOGETHER,
22 REVIEW THE EVIDENCE, AND HAVE BEEN UTTERLY UNIFIED IN
23 USING CLINICAL CARE GUIDELINES WITH A LOT OF UNDUE
24 ENTHUSIASM. THAT'S A GOOD PROCESS. SO IT'S NOT
25 ENOUGH TO BE AWARE OF IT. CMS HAS TO ALIGN ITS

00255

1 PRIORITIES AND ITS SORT OF POLICY WITH CLINICAL CARE
2 STANDARDS THAT PROFESSIONAL SOCIETIES HELPED
3 CO-CREATE. IF WE DIVERGE THERE, I THINK THERE IS A
4 DANGEROUS PRECEDENT THAT MIGHT BE SET.
5 SO FROM THE AMERICAN HEART ASSOCIATION
6 VIEWPOINT, WE HAVE TO GO DOWN TO INDIVIDUAL CONSUMER
7 ENTITIES AND CONVINCED THEM OF THE NEED FOR MORE
8 RESEARCH. I ALMOST ALWAYS AGREE WITH STEVE TEXTOR,
9 WE OFTEN END UP AT THE SAME POINT. BUT I AM
10 CONCERNED, STEVE, THAT RESTRICTING ACCESS TO THESE
11 PROCEDURES MERELY TO CLINICAL TRIALS REALLY WILL SET
12 A CHALLENGING PRECEDENT. SO I SIMPLY MAKE THAT
13 STATEMENT AND AGAIN, FROM A POLICY PERSPECTIVE,
14 THAT'S NOT SOMETHING THAT WE SUPPORT.
15 AND THE THIRD ONE IS, THIS IS A VERY LARGE
16 ONE TO THREE MILLION POPULATION, SO TAKING ONE OF
17 DR. COOPER'S POINTS, IT'S ONE THING TO HAVE A
18 REGISTRY TO LOOK AT ONE OUTCOME OF STENTING, BUT WE
19 DON'T KNOW SOME FUNDAMENTAL THINGS. SO THE NEED FOR
20 BOTH REGISTRIES AND FOR CLINICAL TRIALS IS SUCH THAT
21 WE NEED TO KNOW THE POINT ESTIMATES, THE SAMPLE SIZE
22 REQUIRED, THE RELATIVE RISK REDUCTION IN THE TOTAL
23 POPULATION THAT WE CAN ONLY GET THROUGH A CLINICAL
24 TRIAL. THE RELATIVE BENEFITS AND RISKS BETWEEN THE
25 TWO GROUPS, THE REGISTRY CAN'T GIVE THAT, AND THE

00256

1 TARGETS WILL CONTINUE TO MOVE.
2 SO THE PRECEDENT WE SET WITH CMS IS AN
3 ONGOING ONE. I URGE GREAT CAUTION IN YOUR POLICY
4 DECISION.
5 DR. GARBER: OKAY. LET ME JUST REMIND
6 YOU, PUBLIC SPEAKERS ACTUALLY ARE ONLY RECOGNIZED TO
7 ANSWER QUESTIONS BY THE PANEL, AND WE REALLY WANT TO
8 HEAR FACTUAL ANSWERS. SO I APPRECIATE WHAT YOU SAID,
9 BUT YOU HAD YOUR CHANCE TO SAY YOUR PIECE ABOUT
10 ADVOCATING, AND RIGHT NOW WE REALLY WANT TO JUST GET
11 ANSWERS SPECIFIC TO THE QUESTIONS THE PANEL IS
12 FACING. BILL.
13 DR. MAISEL: IF WE REALLY WANT TO GET
14 CREATIVE, WE COULD MAKE THE REGISTRY NOT JUST FOR
15 THESE INTERVENTIONS BUT FOR ANYONE UNDERGOING RENAL
16 ANGIOGRAPHY, AND THEN YOU'D HAVE A NICE CONTROL GROUP
17 BUILT IN.
18 DR. GARBER: I'M GLAD YOU MADE THAT
19 STATEMENT, BECAUSE I HAD A QUESTION FOR THE PANELISTS
20 IN SUPPORT OF A REGISTRY. WHEN I HEARD ABOUT THE
21 REASONS CORAL IS BEING DONE AND THE KINDS OF
22 ENDPOINTS THAT PEOPLE LOOK AT, I WAS WONDERING WHAT
23 YOU WOULD POSSIBLY LEARN ABOUT, FOR EXAMPLE,
24 PROGRESSION TO RENAL FAILURE, FROM A REGISTRY THAT
25 HAD NO CONTROLS. OR WHAT WOULD YOU LEARN ABOUT

00257

1 CHANGE IN CARDIOVASCULAR RISK. SO I THINK THAT'S A
2 VERY IMPORTANT POINT THAT YOU MADE, BILL, AND I THINK
3 IT'S SOMETHING THAT WE NEED TO FIGURE OUT, WHETHER A
4 REGISTRY IS ACTUALLY GOING TO PROVIDE US WITH GOOD
5 INFORMATION.
6 IN THE CASE OF THE ICD REGISTRY, THE
7 STRONGEST ARGUMENT MADE IN ITS FAVOR WAS THAT WE
8 DON'T KNOW COMPLICATION RATES IN THE COMMUNITY. BUT
9 THE IDEA THAT YOU COULD ANSWER A QUESTION LIKE
10 WHETHER SOMEONE WITH AN EJECTION FRACTION OF 33
11 PERCENT BENEFITS FROM ICD, THAT COULD BE ANSWERED BY
12 A REGISTRY, AND NO ONE ARGUED THAT IT WOULD BE
13 HELPFUL. SO THAT KIND OF QUESTION, I THINK THAT SOME
14 OF THE QUESTIONS THAT HAVE BEEN RAISED BY THE
15 PRESENTERS TODAY, IT'S HARD TO IMAGINE ANSWERING IN
16 THE CONTEXT OF A REGISTRY WITHOUT SOME SORT OF
17 CLINICAL TRIAL. BILL.
18 DR. MAISEL: I THINK THERE ARE SOME
19 IMPORTANT QUESTIONS WHICH COULD BE ANSWERED WITH A
20 REGISTRY, A "SINGLE ARM," PATIENT DOES THEIR OWN
21 CONTROL. CERTAINLY WE'D GET AN IDEA WITH A LARGE
22 NUMBER OF PATIENTS WHAT THE RISK OF ENDING UP WITH
23 END-STAGE RENAL DISEASE OR THEIR CREATININES, WE
24 WOULD BE ABLE TO GET SOME INFORMATION REGARDING RENAL
25 FUNCTION. WITH PHARMACY RECORDS WE MIGHT GLEAN SOME

00258

1 INFORMATION ABOUT TREATMENT, I'M NOT SAYING THAT IS
2 GOING TO BE HIGH QUALITY DATA, BUT IT WILL BE MORE
3 THAN WE HAVE.
4 I THINK IT WOULD BE AMAZING IF WE COULD
5 GET RENAL ANGIOGRAPHY REGISTRY DATA, BUT I DON'T KNOW
6 THE NUMBERS OF PATIENTS THAT ARE UNDERGOING RENAL
7 ANGIOGRAPH, AND I DON'T KNOW THAT I WOULD USE THE
8 WORD ETHICAL, BUT I DON'T KNOW IF IT MAKES MONETARY
9 SENSE TO ENROLL ALL THOSE PATIENTS IN A REGISTRY TO
10 LOOK AT THEM.
11 DR. GARBER: WELL, YOU COULD CHANGE THE
12 RECOMMENDATION TO SAY THAT CMS DEVELOPS AN
13 APPROPRIATE CONTROL GROUP FOR REGISTRY, WHETHER IT'S
14 BASED ON RENAL ANGIOGRAPHY OR SOME OTHER KIND OF
15 INDICATOR. CAROLE.
16 DR. FLAMM: JUST TO EXTEND ON THAT IDEA,
17 THE NOTION OF PUTTING THIS INTO A CLINICALLY DEFINED
18 POPULATION, PERHAPS THOSE WITH RENAL ARTERY STENOSIS,
19 THOSE THAT MEET THIS CLINICAL POPULATION OF INTEREST,
20 AND FIND SOME WAY TO PROVIDE SOME SORT OF
21 LONGITUDINAL GATHERING OF INFORMATION TO LEARN MORE
22 THAN WE KNOW TODAY. I DON'T KNOW THAT IT WILL BE
23 THAT EFFECTIVE.
24 DR. GARBER: OR TO MODIFY THE QUESTION TO
25 SOMETHING THAT'S MORE AMENABLE.

00259

1 DR. CHARYTAN: COULD WE MODIFY IT INTO THE
2 TWO CATEGORIES, THE FIRST ONE BEING VOTING FOR THE
3 REGISTRY AND THE SECOND ONE BEING WHETHER PATIENTS
4 SHOULD BE COVERED ONLY AS FAR AS THE TRIAL? I FEEL
5 MUCH MORE COMFORTABLE VOTING ON THOSE TWO SEPARATELY.
6 DR. GARBER: WHAT'S THE SENSE OF THE
7 PANEL? THERE'S A SPECIFIC THING THAT BARRY SAID
8 BEFORE, AND I WANT TO MAKE SURE THAT YOUR PROPOSAL IS
9 THE SAME. BARRY SAID THAT FOR THE INDICATIONS FOR
10 WHICH IT IS COVERED, EVERY MEDICARE ENROLLEE MUST BE
11 ENROLLED IN A REGISTRY TO BE ELIGIBLE FOR
12 REIMBURSEMENT. IS THAT WHAT YOUR PART A IS?
13 DR. CHARYTAN: WELL, THAT'S A DETAIL. I
14 CERTAINLY WOULD HAVE NO PROBLEM WITH THAT. BUT IF WE
15 DEFINE OR WE RECOMMEND THAT A REGISTRY BE SET UP,
16 SOMEONE WOULD OBVIOUSLY HAVE TO SET UP AND DEVELOP
17 THE DETAILS THAT GO INTO THAT IF WE WANT TO DO THAT.
18 I WOULD HAVE NO PROBLEM WITH WHAT YOU JUST SAID, BUT
19 I THINK A REGISTRY OUGHT TO BE SET UP AND I WOULD
20 CERTAINLY BE IN FAVOR OF THAT.
21 DR. GARBER: SO THE QUESTION ON THE TABLE
22 NOW IS WHETHER THIS SHOULD BE THE VOTING QUESTION.
23 MARK?
24 DR. FENDRICK: KNOWING THAT YOU WILL TAKE
25 A STRAW POLL EVENTUALLY, I WOULD KEEP IT THE WAY IT

00260

1 IS. I THINK FOR SOMEONE WHO HAS BEEN AROUND A GOOD
2 BIT OF TIME, THE FACT THAT WE ACTUALLY HAVE AN
3 EXPLOSIVE QUESTION ABOUT PROVISIONAL COVERAGE WITH
4 EVIDENCE DEVELOPMENT IS A HUGE STEP FORWARD. JUST
5 THAT QUESTION, WHETHER WE BELIEVE IT'S -- GOING TO
6 DR. COOPER'S POINT -- NOT ONLY DO QUALIFIED CLINICAL
7 RESEARCH STUDIES, WHILE THEY DIFFER BY RIGOR, THEY
8 ALSO DIFFER SUBSTANTIALLY BY HOW MUCH THEY COST, AND
9 I THINK WE WOULD DECIDE HOW MUCH, WHICH TRIALS TO DO
10 IF WE KNEW HOW MUCH MONEY WE HAD, WHICH WE CLEARLY
11 DON'T. SO I WOULD ARGUE TO KEEP THE QUESTION THE WAY
12 IT IS.

13 DR. CHARYTAN: BUT MY, AGAIN, MY STRONG
14 CONCERN IS THAT IF WE LEAVE IT AS IS, SOMEONE MAY
15 INTERPRET THIS AS SUPPORT FOR COVERAGE ONLY AS PART
16 OF THE STUDY AND I THINK THAT, AGAIN, IS SETTING A
17 VERY, VERY DANGEROUS PRECEDENT. AND I APPRECIATE
18 WHAT YOU SAID, THAT A REGISTRY IS INCLUDED AS A
19 STUDY, BUT I FELT AND I SUSPECT MANY OF US HAVE FELT
20 WITH CMS IS THAT WHAT WE INTEND TO RECOMMEND IS NOT
21 ALWAYS THE WAY THINGS ARE IMPLEMENTED. AND THAT'S
22 WHY WE MUST BE VERY CLEAR THAT WE SUPPORT A REGISTRY,
23 BUT NOT NECESSARILY RESTRICTING COVERAGE TO ONLY
24 THOSE PATIENTS WHO ARE PART OF A STUDY.
25 DR. GARBER: SANDY.

00261

1 DR. SCHWARTZ: I THINK THE UNEASE HERE IS
2 TWOFOLD. ONE IS ON THE ONE HAND, I'M A LITTLE LOATH
3 TO SPECIFY SPECIFIC RESEARCH DESIGN TO CMS AT THIS
4 POINT. BUT I THINK THAT THERE IS A DIFFERENCE
5 BETWEEN SOMETHING THAT HAS BEEN OUT THERE AND USED IN
6 THE ABSENCE OF WHAT I WOULD CONSIDER GOOD EVIDENCE ON
7 IT, THERE'S STRONG ACCESS TO IT WITH CLEAR
8 INDICATIONS, AS OPPOSED TO SOMETHING WHICH IS DE NOVO
9 AND JUST COMING ON THE MARKET.
10 SO I AGREE WITH MARK, I WOULD SORT OF LIKE
11 TO KEEP IT THE WAY IT IS WITH THE SENSE OF THE GROUP
12 BEING, OR THE COMMENTS BEING MAYBE SOMETHING SPECIFIC
13 THAT THIS DOESN'T, THAT THIS SHOULDN'T BE IMPLEMENTED
14 IF IT MEANS WITHDRAWING ACCESS FOR PEOPLE WHO MEET
15 CLEARCUT INDICATIONS AS PER THE PROFESSIONAL SIDE,
16 WHICH I THOUGHT DID A VERY GOOD JOB. AND I WAS
17 SURPRISED, HAVING DONE GUIDELINES FOR 30 YEARS, WITH
18 THE LEVEL OF CONSENSUS.
19 DR. GARBER: YEAH, THE LEVEL OF CONSENSUS
20 GIVEN THE LEVEL OF EVIDENCE. BILL.
21 DR. LEWIS: I THINK THERE ARE TWO ISSUES
22 HERE. ONE IS, I DON'T THINK WE SHOULD REALLY WORRY
23 TOO MUCH ABOUT WITHDRAWING SUPPORT FOR UNINDICATED
24 PROCEDURES. SO THAT IF YOU MEET CLASS I OR CLASS IIB
25 INDICATIONS, AS THE AHA'S ARGUED, YOU KNOW, MAYBE

00262

1 THOSE PEOPLE GO ON REGISTRIES, AND THE OTHER ONES, I
2 DON'T THINK THAT THEY SHOULD -- I MEAN, WE'RE TALKING
3 ABOUT DRIVE-BY SHOOTINGS AGAIN, AND THAT'S PROBABLY
4 NOT THE GREATEST THING IN THE WORLD, SO I DON'T HAVE
5 ANY PROBLEM WITH TRYING THAT.
6 THE SECOND POINT TO MAKE ABOUT THIS IS AS
7 ONE WHO FILLS OUT A SHEET EVERY TIME HE PUTS IN AN
8 IMPLANTABLE DEFIBRILLATOR, I DON'T THINK IT'S TOO
9 MUCH OF A -- IT DOESN'T RESTRICT MY ABILITY TO
10 ACTUALLY ENROLL PATIENTS BY PUTTING THEM IN THAT
11 REGISTRY. I THINK THAT THERE IS SOME LIMITED AMOUNTS
12 OF DATA THAT COULD BE GAINED FROM THAT BASED ON AN
13 IDEA OF WHAT THE ABILITY AND THE NUMBERS OF
14 PROCEDURES ARE FOR A CERTAIN INDIVIDUAL PERFORMING
15 THEM, AND WHATEVER COMPLICATION RATES ARE, I THINK
16 THERE IS VALUABLE INFORMATION WITH A REGISTRY.
17 DR. GARBER: BARRY.
18 DR. PRESSMAN: FIRST I WANT TO CLARIFY.
19 IF WE VOTE ON THE QUESTION AS IT IS, AND MOST IF NOT
20 ALL OF US ARE SAYING, I THINK, THAT WE REALLY DON'T
21 BELIEVE THAT ALL PATIENTS SHOULD BE IN CLINICAL
22 TRIALS INSTEAD OF A REGISTRY, THEN I THINK YOU WOULD
23 FIND THAT WE STRONGLY DISAGREE. THEN WE WOULDN'T
24 HAVE THE PROBLEM. AS WAS SUGGESTED, EITHER YOU COULD
25 HAVE A STRAW POLL ON ADDITIONAL CRITERIA AND/OR A

00263

1 REGISTRY, SO YOU COULD BREAK IT UP IN TWO, OR WE
2 COULD ADD TWO OTHER QUESTIONS HERE.
3 I THINK WE'RE CLEAR ON WHAT MOST OF US IS
4 SAYING IS A FIVE, THEN I DON'T THINK WE'RE GETTING TO
5 THE NATURE OF IT IF CMS WILL KEEP IT AS QUALIFIED
6 TRIALS.
7 DR. GARBER: SO, JUST FOR POINT OF
8 CLARIFICATION HERE, AGAIN, I DON'T KNOW IF THEY'RE
9 USING QUALIFIED WITH A CAPITAL Q, MEANING SUBJECT TO
10 THE HHS POLICY, WHATEVER IT IS. THAT DOES NOT
11 REQUIRE THAT IT BE A RANDOMIZED CLINICAL TRIAL. A
12 REGISTRY COULD QUALIFY. SO IF YOU THINK EVERYBODY
13 SHOULD BE IN A REGISTRY AT A MINIMUM, THEN YOU
14 WOULDN'T VOTE FIVE ON THIS.
15 (INAUDIBLE COLLOQUY AMONG PANELISTS.)
16 DR. GARBER: ACCORDING TO AT LEAST THE
17 EXISTING POLICY, FOR EXAMPLE, THERE'S SOMETHING
18 CALLED DEEMING, AND IT INCLUDES PHASE ONE STUDIES OF
19 DRUGS BEING CONDUCTED AT NCI-DESIGNATED CANCER
20 CENTERS. SO THAT IS NOT RANDOMIZED, IT'S NOT EVEN
21 REALLY CONTROLLED, PLUS THE DOSE-RESPONSE STUDIES.
22 SO A REGISTRY ACTUALLY COMES CLOSER TO A CONTROLLED
23 STUDY THAN THAT. SO THE EXISTING CLINICAL TRIALS
24 DEFINITION, AGAIN, I DON'T REALLY KNOW WHAT IT IS AT
25 THIS MOMENT, BUT IT INCLUDES STUFF THAT'S PURELY

00264

1 OBSERVATIONAL AND STUFF THAT MOST OF US WOULD THINK
2 BARELY QUALIFIES AS A STUDY, PERIOD. SO I THINK,
3 MARCEL, MAYBE YOU WANT TO COMMENT MORE ABOUT THIS.
4 DR. SALIVE: YES, CMS DEFINITELY INCLUDES
5 REGISTRIES UNDER THIS QUESTION, IF I WAS UNCLEAR
6 BEFORE. MOST OF OUR POLICIES DEALING WITH COVERAGE
7 AND EVIDENCE DEVELOPMENT HAVE ARTICULATED THOSE AS
8 SOME OF THE OPTIONS, A REGISTRY, A PROSPECTIVE STUDY,
9 A RANDOMIZED TRIAL. THERE ARE SOME THINGS NOT
10 INCLUDED, AND I THINK THOSE ARE MORE IN THE REALM OF
11 RETROSPECTIVE STUDIES GOING BACK, BUT IT'S HARD TO
12 ENVISION HOW THAT WOULD BE IMPORTANT, SINCE COVERAGE
13 IS DONE PROSPECTIVELY.
14 DR. GARBER: SO, ARE WE CLEAR ABOUT THAT?
15 THIS DOESN'T MEAN RANDOMIZED, IT'S A PRETTY BROAD
16 DEFINITION.
17 DR. TEXTOR: LET ME JUST ASK SOMETHING.
18 HOW DOES CMS, HOW SHOULD ONE APPROACH THE ISSUE OF
19 IDENTIFYING AND DECLINING COVERAGE ON OBSOLETE
20 PROCEDURES?
21 DR. SALIVE: THAT'S A GOOD QUESTION. I
22 THINK IN GENERAL WE HAVE NOT GONE BACK TO OBSOLETE
23 PROCEDURES TO NONCOVER THEM, SO YOU KNOW, WE HAVEN'T
24 DEALT WITH THAT VERY MUCH FRANKLY.
25 DR. GARBER: MIKE.

00265

1 MR. LACEY: DOES THIS QUESTION ALSO APPLY
2 TO SURGERY AS WELL?

3 DR. GARBER: YES.

4 MR. LACEY: (INAUDIBLE.)

5 DR. SALIVE: I THINK YOU HAVE TO SPECIFY.

6 THIS CASTS A WIDE NET IN THE QUESTION. WE ARE ASKING
7 THE PANEL TO WEIGH IN BEYOND JUST VOTING ON HOW WOULD
8 YOU DEFINE A STUDY THAT YOU WANT TO SEE. IF THE VOTE
9 IS ON THE AGREEMENT SIDE OF THIS QUESTION, WHAT KIND
10 OF STUDY WOULD YOU WANT TO SEE? SO WE'VE HAD A GOOD
11 DISCUSSION SO FAR, AND IF YOU DON'T WANT TO SEE
12 STUDIES OF SURGERY, PLEASE SAY THAT. IF YOU DO WANT
13 TO SEE THEM, PLEASE SAY THAT.

14 MR. LACEY: I'M JUST TRYING TO GET A SENSE
15 OF ACCESS TO CARE AND HOW THIS MIGHT IMPACT THAT.
16 AND MY CONCERN IS, AGAIN, THAT BY REQUIRING THAT AS A
17 CONDITION FOR COVERAGE, THAT YOU WOULD LIMIT ACCESS
18 TO CARE FOR PEOPLE, AND IF THERE WERE OTHER WAYS FOR
19 YOU TO ENCOURAGE DATA COLLECTION. AND THEN LASTLY,
20 IT REALLY DOES SEEM, THE FUNDAMENTAL QUESTION HAS TO
21 HAVE A CONTROL OR CONTROLLED STUDY. A REGISTRY COULD
22 ANSWER SOME QUESTIONS THAT ARE RELEVANT, BUT WE CAN
23 ALWAYS ASK FOR MORE DATA TO GET TO THE KEY POINT THAT
24 YOU REALLY WANT, WHICH IS A COMPARISON BETWEEN
25 MEDICAL AND SURGICAL.

00266

1 DR. SCHWARTZ: BUT THE WAY I'M THINKING
2 ABOUT IT IS THAT THE PURPOSE FOR REQUIRING THEM TO
3 ENROLL IN A CLINICAL TRIAL IS NOT TO CONTROL ACCESS.
4 THE ACCESS, I THINK, IN THIS SITUATION IS CONTROLLED
5 BY THE INDICATIONS OF APPROPRIATENESS. THE REASON
6 FOR (INAUDIBLE) FAVOR OF A REQUIREMENT TO REQUIRE
7 SOME INVOLVEMENT IN SOME SORT OF CLINICAL STUDY IS TO
8 FACILITATE AND EXPEDITE COLLECTION OF DATA THAT
9 EVERYONE AGREES NEEDS TO BE DONE SO THAT IT DOESN'T
10 TAKE 20 YEARS, WE MIGHT SEE IT IN THREE TO FIVE
11 YEARS. BUT FOR ME IT'S A MATTER OF, YOU KNOW, WITHIN
12 THIS CONTEXT, NOT BEING RESTRICTIVE, BUT THE GOAL
13 BEING TO GENERATE EVIDENCE IN AN EXPEDITIOUS FASHION.
14 MR. LACEY: THAT'S FAIR, BUT AS SAID
15 BEFORE, WITH A REGISTRY, IT DEPENDS ON WHAT YOU'RE
16 REGISTERING. YOU KNOW, (INAUDIBLE) FOCUSED ON A
17 PROCEDURE, BUT FOCUSED ON A PATIENT POPULATION. YOU
18 COULD TAKE A REGISTRY AND WE COULD CREATE CONTROL
19 GROUPS BUT (INAUDIBLE).
20 DR. GARBER: BILL.
21 DR. MAISEL: I AM NOT IN FAVOR OF HAVING
22 SURGICAL PATIENTS IN A REGISTRY. I THINK THE
23 FRAMEWORK FOR INTERVENTIONAL PATIENTS SUCH AS
24 CORONARY OR CAROTID REGISTRIES ARE ALREADY THERE. I
25 DON'T THINK IT'S A HUGE LEAP TO ADD RENAL STENTING

00267

1 AND BALLOON ANGIOPLASTY TO THAT. I'M ALSO NOT SURE
2 HOW MANY PATIENTS ARE ACTUALLY UNDERGOING THE
3 SURGERY, IF IT'S 20,000 A YEAR GETTING STENTS, YOU
4 KNOW, MAYBE SOMEONE HAS AN IDEA, BUT I DON'T THINK
5 IT'S THAT LARGE. SO I DON'T THINK THAT'S NECESSARY.
6 DR. CHARYTAN: COULD I ASK A QUESTION? IF
7 THE CONSENSUS SEEMS TO BE THAT WE ALL SUPPORT A
8 REGISTRY, IS THERE ANY REASON WHY THIS QUESTION
9 COULDN'T BE REWORDED IN A POSITIVE WAY, THAT IS, THAT
10 THE PANEL VOTES TO SUPPORT A REGISTRY AND --
11 DR. GARBER: THAT IS A VERY DIFFERENT
12 QUESTION. I MEAN, YOU CAN REDUCE THE ANSWER, BUT I
13 WOULD SUGGEST THAT YOU CAN, WE CAN HAVE A FOLLOW-ON
14 QUESTION AFTER WE VOTE ON THIS ONE, BUT THAT'S A
15 COMPLETELY DIFFERENT QUESTION FROM THIS.
16 SO THE POINT IS, FIRST OF ALL, I JUST WANT
17 TO MAKE SURE, ARE PEOPLE COMFORTABLE VOTING ON THE
18 QUESTION AS STATED AT THIS POINT IN THE DISCUSSION?
19 I SEE A LOT OF NODS. SO WHY DON'T WE FIRST VOTE AND
20 THEN EXPLAIN YOUR ANSWER. FOR EXAMPLE, BILL JUST
21 SAID HE WOULD NOT INCLUDE SURGICAL CASES IN A
22 REGISTRY, SO HE WOULD EXEMPT THAT. BUT HE MIGHT SAY
23 BUT I WOULD IN OTHER CASES. SO IN ANY CASE, THE MOST
24 IMPORTANT THING IS TO EXPLAIN HOW YOU VOTED.
25 OKAY. YOU WANT TO PUT UP THE NUMBERS?

00268

1 (MEMBERS OF THE PANEL VOTED, RESULTS WHICH
2 WERE RECORDED BY STAFF.
3 DR. GARBER: THIS MUST BE OUR HIGHEST
4 VARIANCE VOTE OF THE DAY. WHO WANTS TO START
5 EXPLAINING YOUR VOTES?
6 DR. TEXTOR: I DON'T MIND. MY VIEW IS
7 THAT THIS IS A PRESSING AREA WITH TREMENDOUS
8 AMBIGUITY, WE'VE HEARD ABOUT IT TODAY. I THINK WE
9 REALLY NEED TO DEFINE FOR THE MEDICARE POPULATION THE
10 NET GAINS AND BENEFITS OF MEDICAL THERAPY WHICH WE
11 NOW ALL ACCEPT, ALBEIT INTENSIVE AS DISCUSSED BEFORE,
12 WITH INTERVENTIONAL THERAPIES, ALSO WHICH ARE BEING
13 WIDELY PRACTICED. AND I THINK THE ONLY WAY WE COULD
14 ANSWER THAT IS REALLY TO LIMIT COVERAGE TO THOSE
15 PEOPLE WHO ARE ENROLLED IN TRIALS THAT WILL GIVE US
16 MORE INFORMATION.
17 DR. EDWARDS: I WOULD LIKE TO ECHO PARTS
18 OF WHAT DR. TEXTOR SAID. I CERTAINLY THINK THAT THIS
19 IS AN ISSUE BASED JUST ON THE SHEER NUMBERS OF
20 INDIVIDUALS AFFECTED AND THE POTENTIAL RAMIFICATIONS
21 FOR THOSE INDIVIDUALS, THAT THIS IS A MATTER OF GREAT
22 PUBLIC HEALTH SIGNIFICANCE. AND ALTHOUGH I TIP MY
23 HAT TO THE INDIVIDUALS WHO SLAVED IN THE ROOMS IN THE
24 HOTELS TO COME UP WITH CONSENSUS GUIDELINES, I
25 PERSONALLY FEEL THE CONSENSUS IN PRACTICE GUIDELINES

00269

1 SHOULD APPLY TO SITUATIONS TOO RARE TO STUDY OR IN
2 SITUATIONS WHERE WE POSSIBLY HAVE AN OUTDATED
3 INTERVENTION, A NEW INTERVENTION COMING ON, WHERE IT
4 MAY NOT BE ETHICAL OR FEASIBLE OR PRACTICAL TO STUDY
5 IT DIRECTLY.

6 THIS IS NOT ONE OF THOSE CONDITIONS. TENS
7 OF THOUSANDS OF THESE PROCEDURES ARE DONE EACH YEAR
8 AND WE OUGHT TO BE ABLE TO GET SOME MEANINGFUL
9 INFORMATION RATHER EXPEDITIOUSLY AND ANSWER A LOT OF
10 THE QUESTIONS THAT REMAIN, AND NOT TO DO SO I THINK
11 WOULD BE A PRETTY POOR STATEMENT.

12 DR. GARBER: ANY OTHER COMMENTS? BILL.

13 DR. MAISEL: I HAVE THE UNIQUE DISTINCTION
14 OF BEING THE ONLY ONE WHO HELD UP THE NUMBER THREE,
15 AND I VOTED THREE BECAUSE DR. COOPER'S A BIMODAL
16 PERSON. I FELT THAT I WANTED TO VOTE A ONE AND A
17 FIVE. I FELT STRONGLY THAT SOME PATIENTS SHOULD NOT
18 NEED TO HAVE DATA COLLECTED ON THEM, I THINK THE
19 CONSENSUS OF THE CLINICAL COMMUNITY IS THAT THERE ARE
20 CERTAIN PATIENTS WHO NEED THIS PROCEDURE AND I THINK
21 THEY SHOULD HAVE ACCESS TO IT. BUT ON THE OTHER
22 HAND, I THINK THE VAST MAJORITY OF PATIENTS
23 UNDERGOING THIS PROCEDURE SHOULD HAVE THE DATA
24 COLLECTED ON THEM.

25 DR. GARBER: LET ME JUST ASK FOR THE

00270

1 PEOPLE WHO VOTED FIVE, DOES EVERYBODY AGREE THAT
2 THERE IS A SUBSET OF PATIENTS FOR WHOM DATA NEED TO
3 BE COLLECTED, WHETHER IT'S A REGISTRY OR NOT?

4 MR. LACEY: I DO, I FEEL THAT HAVING
5 COVERAGE CONDITIONED UPON PARTICIPATION WILL
6 INHERENTLY RESTRICT ACCESS.

7 DR. GARBER: BUT YOU ARE SAYING THAT
8 THERE'S SOME SUBGROUPS FOR WHOM YOU THINK THAT'S
9 APPROPRIATE, OR NOT?

10 MR. LACEY: YES, IT DOES SEEM THAT.

11 DR. CHARYTAN: I ABSOLUTELY AGREE. MY
12 CONCERN WAS A DIFFERENT ONE, NOT TO RESTRICT THE
13 PROCEDURE IN SOME PATIENTS WHO ARE NEEDED, AND I
14 POINTED OUT THAT WE OUGHT TO HAVE STRICT CRITERIA.
15 SO MY FIVE WAS PROCEDURAL, IF YOU WILL, AND BASED ON
16 THE EXPERIENCE OF DEALING WITH CMS, AND FORGIVE ME,
17 AND OUTCOMES THAT MAY BE OTHER THAN WHAT'S INTENDED.
18 AND I THINK WE HAVE TO BE CAREFUL IN CONFUSING GOALS
19 AND THE WAY THE BUREAUCRATIC SYSTEM WORKS.

20 DR. GARBER: SO I WANT TO MAKE SURE THAT
21 WE GET ON THE RECORD HOW THE ENTIRE PANEL FELT. I
22 THINK THERE IS A CONSENSUS AMONGST EVERYONE THAT
23 THERE IS A SUBSET OF PATIENTS FOR WHOM ABSOLUTELY
24 DATA NEEDS TO BE COLLECTED AS A CONDITION OF
25 COVERAGE, WHETHER IT'S REGISTRY OR TRIAL. WE DIDN'T

00271

1 GET INTO TOO MUCH DETAIL ABOUT WHAT THAT MIGHT BE.
2 THERE ARE SOME PEOPLE WHO THINK DATA NEEDS
3 TO BE COLLECTED FOR EVERY PATIENT WHO GETS THE
4 PROCEDURE, AND I THAT'S THE PEOPLE WHO VOTED ONE ON
5 THIS QUESTION.
6 AND DOES THAT ENCOMPASS EVERYONE SOMEWHERE
7 ALONG THAT SPECTRUM? BARRY?
8 DR. PRESSMAN: I VOTED TWO, EVEN THOUGH I
9 RAISED THE IDEA OF A REGISTRY. I FELT LIKE CHAIM
10 DID, THERE ARE SOME PATIENTS WHO OUGHT TO BE ABLE TO
11 GET IN EVEN IF YOU CAN'T GET INTO A REGISTRY, BUT
12 THEY MUST FULFILL CERTAIN CRITERIA, WHATEVER THOSE
13 CRITERIA ARE. I DON'T THINK IT SHOULD BE THE WILD
14 WILD WEST, WHERE A DOCTOR JUST CHOOSES ON HIS OWN AND
15 EXPECTS TO GET REIMBURSED, THERE HAS TO BE SOME
16 CLINICAL LOGIC TO IT, SO THAT'S WHY I VOTED TWO.
17 DR. GARBER: OKAY. ANY OTHER COMMENTS?
18 NOW YOU GET YOUR CHANCE TO HAVE SOME
19 DISCUSSIONS OF THE STRENGTHS OF THE TRIALS. I DON'T
20 KNOW HOW MUCH PEOPLE WANT TO DISCUSS THESE PARTICULAR
21 TRIALS. IT WAS JUST SOMETHING TO SORT OF EXPAND ON
22 ANY DEFICIENCIES YOU MIGHT THINK OF AND ANY GAPS IN
23 WHAT KIND OF INFORMATION IS AVAILABLE. BILL.
24 DR. MAISEL: I WAS JUST CURIOUS, AND MAYBE
25 ONE OF THE CORAL INVESTIGATORS CAN COMMENT. THIS IS

00272

1 AN UNBLINDED STUDY, AT LEAST ACCORDING TO THE
2 PROTOCOL THAT I READ. OBVIOUSLY SOMEONE COULD ARGUE
3 IS DOES MATTER IN MORTALITY, WHAT HAVE YOU, BUT
4 CARDIOVASCULAR ENDPOINTS YOU COULD ARGUE COULD BE
5 AFFECTED BY BIAS OR LACK OF BLINDING. WHY AREN'T THE
6 PATIENTS BLINDED?
7 DR. DWORKIN: I MEAN, IT'S A PRACTICAL
8 ISSUE. HOW CAN YOU BLIND SOMEBODY TO WHETHER THEY'VE
9 HAD A RENAL ARTERY INTERVENTION? IT'S NOT EASY TO
10 DO.
11 DR. MAISEL: HOW ABOUT PATIENTS UNDERGOING
12 ANGIOGRAPHY?
13 DR. DWORKIN: NOT ANYMORE. WE HAVE
14 NONINVASIVE PATHWAYS NOW BY ULTRASOUND, BY MR, SO
15 FROM A PRACTICAL POINT OF VIEW IT WOULD REALLY BE
16 IMPOSSIBLE TO BLIND PATIENTS AS TO WHETHER THEY WERE
17 GETTING INTERVENED OR NOT.
18 THAT BEING SAID, THE MEDICAL INTERVENTION
19 IS EXACTLY THE SAME FOR BOTH ARMS OF THE STUDY, AND
20 WE HAVE SPECIFIC TARGETS FOR BLOOD PRESSURE,
21 CHOLESTEROL, HEMOGLOBIN A1C, ET CETERA, ET CETERA,
22 ET CETERA, AS WELL AS A REPORT CARD SYSTEM AND A
23 COMMITTEE THAT'S MONITORING SITE PERFORMANCE IN TERMS
24 OF MEETING THESE THREE TARGETS. THAT APPLIES TO BOTH
25 ARMS OF THE STUDY. SO THE MEDICAL INTERVENTION IS

00273

1 IDENTICAL, THE TARGETS ARE IDENTICAL, AND IF THE
2 PROTOCOL FUNCTIONS AS IT'S DESIGNED, THERE WON'T BE
3 DIFFERENCES IN BLOOD PRESSURE, LDL CHOLESTEROL AND
4 ALL OF THESE OTHER CARDIOVASCULAR RISK FACTORS THAT
5 WE'RE TRYING TO CONTROL BETWEEN THE TWO GROUPS.
6 WHAT THE STUDY WILL REALLY ANSWER IS
7 WHETHER RENAL ISCHEMIA PER SE, EVEN INDEPENDENT OF
8 SOME OF THESE CONSEQUENCES LIKE HYPERTENSION ACTUALLY
9 DRIVES ADVERSE OUTCOMES. AND THAT COULD OCCUR
10 BECAUSE OF DIFFERENCES IN KIDNEY FUNCTION,
11 DIFFERENCES IN THIS NEUROHUMORAL ACTIVATION AND
12 WHETHER OR NOT YOU CAN REALLY ADEQUATELY INTERRUPT IT
13 OR AS EFFECTIVELY INTERRUPT IT AS YOU CAN BY
14 REVASCULARIZATION.
15 ONE OF THE REVIEWERS OF THE STUDY
16 SUGGESTED THAT THE ADVANTAGE OF INTERVENING IN RENAL
17 ARTERIES MIGHT BE THAT IT WILL ALLOW MORE PATIENTS TO
18 GET RENAL ANGIOTENSIN BLOCKING, AND THAT MIGHT BE THE
19 WHOLE BENEFIT, WHICH IN TERMS OF THE CLINICAL TRIAL
20 WOULD BE FINE, BECAUSE IT STILL SHOWS A DIFFERENCE
21 BETWEEN THE TWO APPROACHES, ALTHOUGH MAYBE NOT THE
22 ONE THAT PEOPLE ARE ACCEPTING OR EXPECTING.
23 BUT I THINK WE ARE TRYING TO ADDRESS THIS
24 ISSUE OF BIAS IN TERMS OF THOSE OTHER RISK FACTORS
25 VERY AGGRESSIVELY IN THE TRIAL.

00274

1 DR. TEXTOR: ALAN, COULD I COMMENT? I
2 THINK IT'S VERY HELPFUL, AND I APPRECIATE THE EFFORT
3 PEOPLE HAVE GONE THROUGH TO LOOK AT THE TRIALS IN
4 PROGRESS, BECAUSE WE NEED TO KNOW ABOUT WHAT'S OUT
5 THERE. I AM IMPRESSED WITH HOW WEAK THOSE TRIALS
6 ARE. I THINK IF ONE LOOKS AT THEM, MANY OF THEM SORT
7 OF BUY INTO THIS VERY DIFFERENT FRAMEWORK OF WHAT
8 THEY EXPECT THE OUTCOMES TO BE.
9 STAR, IF YOU LOOK AT IT, ASSUME THAT WITH
10 120 PATIENTS, THEY'RE ASSUMING THAT 50 PERCENT OF
11 THESE ARE GOING TO PROGRESS TO END-STAGE RENAL
12 DISEASE. ALTHOUGH THEY HAVE EXCLUDED OR STRATIFIED
13 FOR BOTH BILATERAL AND UNILATERAL DISEASE, THEY
14 INCLUDE PEOPLE WITH MALIGNANT HYPERTENSION, AND I
15 THINK IT'S ALMOST CERTAINLY GOING TO BE A NEGATIVE
16 PROBLEM. RENAL ARTERY STENOSIS IS DEFINED BY MRA OR
17 CTA ONLY.
18 YOU KNOW, WE HAVE A LONG EXPERIENCE THAT
19 IT'S VERY LIKELY THAT THESE TRIALS ARE NOT GOING TO
20 SEE THE RATES OF PROGRESSION THAT THEY EXPECT. WE
21 DON'T THINK IT'S GOING TO HAPPEN AND WE HAVEN'T HEARD
22 OF AN OUTCOME FROM THE STUDIES STARTED AND FINISHED.
23 THE SAME IS TRUE FOR RAVE. THEY ARGUE
24 THAT THEIR PRIMARY OUTCOME IS LOSS OF KIDNEY
25 FUNCTION, BUT IN THAT TRIAL THEY HAD EXCLUDED PEOPLE

00275

1 WITH (INAUDIBLE) VERY ENLIGHTENING FIVE YEARS FROM
2 NOW TO ANSWER THIS QUESTION, AND THAT'S PART OF MY
3 RATIONALE, THAT IF WE ANTICIPATE RAMPING UP
4 PARTICIPATION IN TREATMENT TO 35,000 OR MORE A YEAR,
5 WE REALLY OUGHT TO ANSWER THIS QUESTION WITH STUDIES
6 THAT ARE WELL DESIGNED, DONE IN THE UNITED STATES,
7 THAT WE CAN HANG OUR HATS ON.
8 DR. GARBER: MARK.
9 DR. FENDRICK: AND QUICKLY FOR THE RECORD,
10 AS ONE WHO HAS DURING MY TENURE SPENT AN AWFUL LOT OF
11 TIME RANTING AND RAVING ABOUT BIASES THAT ARE ALREADY
12 IMPLEMENTED INTO THE DESIGN OF CLINICAL TRIALS, I
13 WANT TO COMMEND THE CORAL INVESTIGATORS FOR ACTUALLY
14 DOING ALMOST EVERYTHING YOU CAN TO SHOW EXPLICITLY
15 THAT THE INTERVENTION ON THE RENAL ARTERY IS GOING TO
16 BE THE INTERVENTION THAT SHOWS THE DIFFERENCE. THIS
17 LAST POINT THAT YOU MADE ABOUT THAT THE MEDICAL
18 THERAPY IS THE BEST THAT WE KNOW AND IS IN BOTH ARMS
19 OF THE TRIAL IS A GREAT CONTRIBUTION TO THAT, BECAUSE
20 WE HAVE SEEN IN RESPONSE TO OUR REQUESTS FOR TRIALS
21 TO LET DOCTORS DO WHAT THEY WOULD TYPICALLY DO, AND
22 THE FACT THAT YOU'RE STACKING THE DECK IN A WAY
23 AGAINST THE POSITIVE OUTCOME, YOU SHOULD BE
24 COMMENDED.
25 DR. GARBER: I SECOND THAT. ETHAN.

00276

1 DR. BALK: I WANT TO ECHO SOMETHING
2 SOMEBODY SAID A WHILE BACK. IF YOU THINK ABOUT THE
3 STUDIES THAT ARE OUT THERE AND THE POINTS THAT WERE
4 JUST MADE, MOST OF THEM ARE VERY SMALL, THEY'RE NOT
5 GOING TO GIVE, OR ARE UNLIKELY TO GIVE CLINICAL
6 RESULTS. SO IT'S ESSENTIALLY GOING TO BE THE CORAL
7 STUDY IN SEVERAL YEARS TIME. WITH THAT ONE TRIAL,
8 EVEN IF IT'S INCREDIBLE, A GREAT TRIAL, HIGHLY
9 APPLICABLE, ET CETERA, ET CETERA, WE WOULD STILL NOT
10 HAVE SAID THAT THERE WAS ROBUST EVIDENCE FOR ANYTHING
11 BECAUSE IT'S ONE TRIAL.

12 DR. SCHWARTZ: WHAT ABOUT ASTRAL?

13 DR. BALK: WELL, THAT'S POSSIBLE, BUT IF
14 YOU THINK THAT -- YOU KNOW, MOST OF THE CONVERSATION
15 HAS BEEN FOCUSED ON CORAL. YOU KNOW, IT WILL BE
16 INTERESTING TO SEE WHAT ASTRAL IS ABOUT ALSO, EVEN
17 WITH ALL THE OTHERS. SO IF THEY BOTH COME OUT AND
18 THEY SAY EXACTLY THE SAME THING IN BOTH OF THOSE
19 STUDIES, THAT'S REALLY THE ONLY OPPORTUNITY FOR THERE
20 TO BE ROBUST EVIDENCE, WHICH IS SOMEWHAT SIMILAR TO
21 THE AHA/ACC GUIDELINES AT LEVEL 1, YOU STILL NEED A
22 NUMBER OF TRIALS THAT ARE CONSISTENT. I JUST WANTED
23 TO POINT THAT OUT.

24 DR. TEXTOR: I'M KIND OF ENTHUSED ABOUT
25 ASTRAL. ASTRAL HAS A LOT, IT'S THE LARGEST TRIAL UP

00277

1 TO NOW. IF YOU LOOK AT THAT, THOUGH, THE TROUBLING
2 FEATURE TO THAT ARE IDENTITY CRITERIA. I MEAN,
3 BASICALLY (INAUDIBLE) SO THERE'S NOT A FIRM
4 INDICATION FOR REVASCULARIZATION. THE CLINICIANS ARE
5 UNCERTAIN AS TO WHAT TO DO. WELL, RANDOMIZE THEM.
6 AND THEY'RE UNCERTAIN AND IT'S UNLIKELY THAT THEY
7 WILL BE CERTAIN IN SIX MONTHS. THAT'S SORT OF AN
8 IMPOSSIBLE THEORY AND I THINK IT'S ALMOST CERTAIN
9 THAT WE'LL GET A GROUP OF PEOPLE WITH SUBCLINICAL
10 LESIONS, AND I THINK THE REAL POTENTIAL DOWNSIDE IS
11 THAT WE'LL GET TRIALS WITH INADEQUATE POWER.
12 DR. SCHWARTZ: (INAUDIBLE) IN THIS
13 COUNTRY. THERE IS A BIG TENDENCY TO GO FOR
14 INTERNATIONAL AND MULTINATIONAL TRIALS WHICH ARE GOOD
15 TO SOME DEGREE, BUT I THINK IT'S BECOME INCREASINGLY
16 DIFFICULT TO DO LARGE RANDOMIZED TRIALS IN THE UNITED
17 STATES. A LOT OF COMMERCIAL INVESTIGATORS ARE
18 FINDING IT'S EASIER AND FASTER TO DO THESE IN EUROPE
19 IN PARTICULAR, AND WHILE THAT HAS, THAT HAS SOME GOOD
20 ASPECTS TO IT, IT DOESN'T ALWAYS ADDRESS THE
21 QUESTIONS IN THE WAY WE WANT THEM TO DO IT.
22 I THINK ONE OF THE THINGS, MARCEL, THAT
23 NEEDS TO BE REVISITED BETWEEN NIH AND YOU GUYS, AND
24 AHRQ OR FDA, IS TO LOOK AT WHAT'S HAPPENING WITH
25 LARGE RANDOMIZED TRIALS IN THE UNITED STATES TO

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1 FIGURE OUT A WAY TO REDEVELOP THAT INFRASTRUCTURE SO
2 THAT WE CAN PLAY A LARGER ROLE, BECAUSE THAT'S ONE
3 REASON WHY WE'RE GOING TO CONTINUE LACKING ANSWERS TO
4 OUR SPECIFIC QUESTIONS.
5 YOU KNOW, THERE ARE CERTAIN THINGS THAT
6 ARE USEFUL ACROSS THE WAY, BUT THERE ARE A LOT OF
7 THESE ISSUES THAT ARE NOT QUITE DEFINED THE SAME WAY
8 IN EVERY COUNTRY AND EVERY CULTURE.
9 DR. GARBER: OKAY, THANK YOU. DOES
10 ANYBODY WANT TO MAKE ANY COMMENTS ON THE POINTS AT
11 THE END ABOUT TRIALS? WE'VE ACTUALLY GOTTEN AROUND
12 TO MOST OF THESE IN OUR DISCUSSIONS IN THE OTHER
13 QUESTIONS ALREADY. THIS IS YOUR LAST CHANCE TO
14 SPEAK.
15 MICHELLE HAS AN ANNOUNCEMENT AND THEN I'LL
16 HAVE ONE.
17 MS. ATKINSON: I JUST WANTED TO SAY TO THE
18 PANEL MEMBERS, THE SHUTTLE IS HERE TO TAKE EVERYBODY
19 TO BWI. AND THEN ALSO FOR EVERYONE ELSE, IF YOU
20 COULD PLEASE PICK UP YOUR TRASH, THERE'S TRASH CANS
21 OUTSIDE. THANK YOU.
22 DR. GARBER: LET ME -- I WANT TO THANK THE
23 SPEAKERS WHO ALL DID AN EXCELLENT JOB AND IT WAS
24 EXTREMELY USEFUL TO US, BECAUSE YOU REPRESENTED
25 DIVERSE PERSPECTIVES, AND YOU ALL CAME LOADED WITH

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1 FACTS, WHICH IS EXACTLY WHAT WE NEEDED FOR OUR
2 DELIBERATIONS. YOUR PRESENTATIONS WERE RIGHT ON
3 TARGET. I APOLOGIZE TO THOSE WHOM I CUT OFF, BUT
4 THAT'S MY JOB AS CHAIR. I DON'T NECESSARILY RELISH
5 CUTTING YOU OFF BUT I DO RELISH FINISHING ON TIME.
6 AND THEN I WANT TO THANK THE PANELISTS FOR
7 DOING AN EXCELLENT JOB. YOU WERE WELL PREPARED FOR
8 THE MEETING, GREAT QUESTIONS, GREAT DELIBERATIONS. I
9 APPLAUD YOU AND I'M SURE CMS DOES AS WELL.
10 IT'S BEEN A REAL HONOR AND PRIVILEGE TO BE
11 CHAIR FOR THESE PAST TWO YEARS. AS A REGULAR MEMBER
12 I WILL BE UNLEASHED, SO I CAN SAY WHAT I REALLY
13 THINK, BUT I REALLY DO APPRECIATE EVERYTHING THAT YOU
14 ALL HAVE DONE FOR ME. THANK YOU.
15 (APPLAUSE.)
16 DR. SALIVE: ON BEHALF OF CMS, I WANT TO
17 THANK ALAN AGAIN FOR HIS STRONG TENURE AS CHAIR, AND
18 I WANT TO THANK ALEX FOR HIS SERVICE AS VICE CHAIR.
19 I WANT TO THANK ALL THE PANELISTS FOR COMING, AND I
20 KNOW YOU ENDURED A LOT TO GET HERE, AND THANK YOU FOR
21 ALL YOUR DELIBERATIONS.
22 WE WILL BE POSTING THE VOTING UP ON THE
23 WEB SITE VERY SHORTLY AND ULTIMATELY WITHIN ABOUT A
24 MONTH, WE DO POST THE TRANSCRIPT AS WELL, SO EVERYONE
25 CAN LOOK FORWARD TO THAT.

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1 THE MEETING IS ADJOURNED.
2 (WHEREUPON, THE MEETING ADJOURNED AT
3 2:55 P.M.)

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