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CENTERS FOR MEDICARE AND MEDICAID SERVICES
Medicare Evidence Development & Coverage Advisory Committee

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Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, Maryland

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Panelists

Chair
Barbara McNeil, M.D., Ph.D.

Panel Members
Mark D. Grant, M.D., M.P.H.
Mark A. Hlatky, M.D.
Deborah Schrag, M.D., M.P.H.
Ruth Bush, M.D., M.P.H.
Karl Matuszewski, M.S., Pharm.D.
Nancy Davenport-Ennis, B.A.
Leslie B. Fried, J.D.

HCFA Liaison
Barry M. Straube, M.D.

Consumer Representative
Linda A. Bergthold, Ph.D.

Industry Representative
Peter Juhn, M.D., M.P.H.

Past Administrator
Thomas A. Scully, J.D.

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Panelists (Continued)

Guest Panel Members
Jean Slutsky, P.A., M.S.P.H.
Michael A. Jacobs, M.D.
Sean Tunis, M.D., M.Sc.

Executive Secretary
Michelle Atkinson

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PANEL PROCEEDINGS

(The meeting was called to order at 8:10 a.m., Monday, October 22, 2007.)

MS. ATKINSON: Good morning and welcome, committee chairperson, members and guests. I am Michelle Atkinson, executive secretary for the Medicare Evidence Development Coverage Advisory Committee. The committee is here today to discuss evidentiary priorities for the Medicare program. The following announcement addresses conflicts of interest associated with this meeting and is made part of the record. There are no conflicts of interest for today's meeting. We ask that all presenters please adhere to their time limits. We have numerous presenters to hear from today and a very tight agenda, and therefore cannot allow extra time. There is a timer at the podium that you should follow. The light will begin flashing when there are two minutes remaining, and then turn red when your time is up. Please note that there is a chair that says next speaker, and please proceed to the chair when it is your turn. For the record, the entire panel will be voting today. The voting scores will be available on our web site following the meeting.

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I ask that all panel members please speak directly into your mikes, and since we have a few number, we're going to have to share today. And lastly, please everybody, if you could, discard your trash in the trash cans outside. And now I would like to turn the meeting over to Dr. Barry Straube.

DR. STRAUBE: Good morning. I'm Barry

Straube, I'm chief medical officer for CMS and also the director of the office of clinical standards and quality, and want to welcome the panel as well as all the members of the audience.
This is quite a unique meeting of the MedCAC and I want to thank Dr. Steve Phurrough, who is the director of the coverage and analysis group, as well as the staff of that group for putting this meeting together.
Previously in the past, certainly up until the '90s, Medicare paid for everything generally that the FDA approved as safe and efficacious, but starting in the mid 1990s there was an emphasis on gathering evidence and making evidence-based decisions on coverage policies here at CMS.
I think if you look at the history over the last seven or eight years in particular, we've

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made as an agency some significant advances. First there was an expansion of the clinical research policy that started at the end of the Clinton administration where we attempted to broaden coverage and make sure that Medicare beneficiaries had access to clinical research trials.
After that was implemented and over the first five years, including the input by a number of people sitting on the panel here, the Agency developed a concept of coverage with evidence development, where again, the broadened coverage by covering technology services and devices that had a preponderance of evidence that would suggest it ought to be covered but didn't quite meet our evidentiary standards, so we put in place a process through which registries and clinical trials would be able to participate.
We continued to focus through work at least for medicine with many, many other organizations, including AHRQ, on comparative effectiveness, and Section 1013 (inaudible) portfolio working with AHRQ to gain information on comparative effectiveness.
There's many other things that I could

talk about, but I hope I've made the case that we're

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focusing more and more on the development of evidence so we can make wise coverage decisions, but also so that we can use that evidence to educate physicians, clinicians and beneficiaries on the appropriate use of that technology. So this panel this morning is somewhat unique and again, I thank Steve and the team for even coming up with the concept where we're going to look at evidence prioritization, and so bear with us as we go through today because we're treading on new ground, but continuing the charge towards the use of evidence when it comes to coverage in medicine.

With that I'm going to turn this over to Dr. McNeil who I think may have some comments and will introduce the panel.

MS. MCNEIL: Well actually, I think Barry has said most of what I wanted to say as introductory remarks. This is a new approach for MedCAC and I think it's also going to be fairly tricky for us because it's really, the whole approach today is going to represent a mind shift in how we think about things.

People have traditionally talked about the burden of disease, the cost of disease, the prevalence of disease, the incidence of disease, disability days, whatever. Those have typically been

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how we've thought about lots of the things that we do, but we're really down one level deeper this time, as Barry said.

It's going to be important for the speakers and the panel to keep their eye on that ball that we're looking at, that we're looking at particular clinical services, so at the end of the day we can make a priority list of them for CMS. That's going to be the challenge. Hopefully by the time the speakers have finished their remarks, we'll have quite a large list to digest and discuss.

As Michelle mentioned, we have a lot of speakers, we've got a large panel, there will be lots

of discussions, and I'm afraid I'm going to be fairly brutal in keeping panelists to their time. So if you think you're going over, if you think right now you have 20 slides for 15 minutes, you might want to start deleting. But with that, I think I would like to start introducing the panel quickly.
I'm Barbara McNeil, from Harvard Medical School.
DR. GRANT: I'm Mark Grant, from the Blue Cross Blue Shield Association.
DR. HLATKY: Mark Hlatky from Stanford University.

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DR. BUSH: Ruth Bush, a vascular surgeon from Texas A&M.
DR. MATUSZEWSKI: Karl Matuszewski, University Healthcare Consortium.
MS. DAVENPORT-ENNIS: Nancy Davenport-Davis, Patient Advocate Foundation.
MS. FRIED: Leslie Fried, ABA Commission on Law and Aging.
DR. JUHN: Peter Juhn, Johnson & Johnson.
DR. BERGTHOLD: Linda Bergthold, consumer representative and Medicare beneficiary.
MR. SCULLY: Tom Scully, with Welsh, Carson, Anderson & Stowe.
MS. SLUTSKY: Jean Slutsky, with the Agency for Healthcare Research and Quality.
DR. TUNIS: Sean Tunis, with the Center for Medical Technology Policy.
DR. JACOBS: Michael Jacobs, orthopedic surgeon.
DR. MCNEIL: Thank you. And now Herb Kuhn, the deputy administrator of CMS, would like to say a few words.
MR. KUHN: Thank you all very much for coming together today for this important meeting, and as indicated before, it really is a chance for us to

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look at the evidentiary priorities in Medicare coverage. One, I want to thank Barbara McNeil for

chairing this group and for taking on the responsibility here. I also want to thank Barry Straube, Steve Phurrough, Barbara McNeil, and all their colleagues for putting together a very different type meeting. I also want to thank the guest panelists, particularly Tom Scully and Sean Tunis, a couple CMS alumni, Tom being our former administrator and Sean being the former medical director here and also director of clinical standards and quality, for being back to share their own thoughts on this as we move forward.

You know, as you think about these meetings in the past that we've had before here, mostly what we brought together was a panel to consider a specific evidence and coverage issue, but this meeting is different, as you've heard before, and as you'll see as we move forward today, because it's really a chance for us to think about and look at and learn what are the challenges to CMS as we go forward, and I think Barry provided a good summary of why we need to be thinking about that.

So at the end of the day the outcome, you'll hear this again, will be a list that you come

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up with to help us think about a list of research priority projects that will not only contribute to the body of medical evidence that's out there, but also really have a great amount of help in terms of providing the needed services for Medicare beneficiaries as we go forward with this program. And we couldn't think of a better way to kind of have that discussion than to bring that forward before the folks here at MedCAC.

So again, thank you to the members of MedCAC for being here to take on this issue, thank you for our guests for being here to offer their advice, and for everybody that's here to participate in the meeting in the room, this will mean a lot to us. I think it's a lot of heavy lifting for one day, but I can't think of a better group to try to accomplish it. So again, thank you all for your participation, we do appreciate it.

DR. MCNEIL: Thank you, Herb. Are there any questions before we start among the panel? Okay. Then why don't we start with Rosemarie Hakim, who is going to present some background information of a very generic, very general nature. So Rosemarie, you're on.
DR. HAKIM: Can you hear me? Today I want

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to talk about some major costs to the Medicare program. And before I start I just want to say a couple of things, one is because Barbara will cut me off, that heart disease is by far the biggest cost to the program. I think you get the picture.
Also, I want to warn you that most of my slides look like I was buying property on Park Place in a Monopoly game.
The first slide says that most of the changes, recent changes in the Medicare population in the last 25 years occurred in the disabled and in the oldest of the old. So that if you look at the blue bar, the number of disabled in the Medicare population has doubled while the number of patients over 80 has been steadily declining.
In this slide we see where most of the money goes. Physician and supplier costs are $83 billion and about 700,000 for about 33 million people. Hospital costs of 80 billion and about seven-and-a-half million people have had hospital services. The next most expensive is skilled nursing facilities, followed by home health agency services.
This slide gives you the most important discharge diagnoses. If you look down at the circulatory system diseases, we're spending about $33

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billion on that. The next most expensive is respiratory system, hospital discharges.
Looking at, this slide just picks out several of the numbers for heart disease. The biggest hospital diagnosis, which is not the same as procedures, is atherosclerosis, at about $7 billion.
If you look at MI and other ischemic diseases, they

come in at about 5 billion. CHF is really expensive, 5 billion, and stroke and cerebrovascular disease is about 4 billion.
Now this is procedures for heart disease. All surgeries are about 25.5 billion. Removal of coronary artery obstructions, which is mostly stenting, is nearly 4 billion. Coronary bypass graft is 3.5 billion for fewer people than for stenting. And cardiac cath is 2 billion, also for about the same number of people that are getting stented. In the bottom you see surgeries involving insertion of pacemakers or ICD are about 2 billion.
This slide shows hospital stays for fractures, which total about 3.7 billion, and the most expensive part of that is fractures of the femur. And interestingly, poisoning by drugs and biologics is about $230 million for about 49 patients, 49,000 patients.

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Digestive disorders are not quite as expensive as the other things. The most expensive are cholethiasis and diverticulosis, followed by enteritis and colitis.
These are all surgeries on the musculoskeletal system. Total knee replacement was the biggest one and affects the most people. Second most expensive is reduction of facial fractures. Total hips come in fourth at 1.2 billion, and disc surgery is about $200 million.
This shows outpatient services which by far is chronic renal failure, mostly for dialysis. Respiratory services therapy is about 9 million, or I'm sorry, 900 million, followed by chronic ischemic heart disease services.
The most affected patients are those who -- I'm sorry -- the most served patients are for screening, hypertension, diabetes and cardiac arrhythmias.
Okay. This is a slide that shows you how respiratory therapy is the biggest part of hospital procedures.
This shows you home health agency

services, which are headed by treatment for circulatory system disorders followed by diabetes.

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Musculoskeletal comes in third at 800 million, followed by skin care at almost 800 million. Next, the final slide shows you differences in admissions to skilled nursing facilities. We have the nursing homes. In 2000 the biggest reason was hip fracture and that's changed. The two most common reasons for admission are now heart failure and pneumonia. Admissions for acute stroke has changed dramatically. And my final slide shows the differences between physician services in total and per person services per year. The highest costs are all hospital outpatient visits and consults, totaling about $12 billion, and ambulance services and hospital evaluation each come in at 6 billion. Cataract removal is about 2 billion, and payment for oxygen concentrators is the fifth highest. Now the per patient payments go to mostly injectables. Rituxan is $14,000 per patient, radiation treatment delivery, again, about 14,000 per person. Remicade, Neulasta and ESA are also up there, and wheelchairs come in for almost $4,000 a person. So that's it. If you want to look up these statistics yourself, we have them on our web

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site.

DR. MCNEIL: Rosemarie, what is ESA.

DR. HAKIM: It's erythro-stimulating agents.

DR. MCNEIL: Thank you. Any quick questions for Rosemarie? Well, this is the umbrella. She provided the data on really the costs at the aggregate level as well as numbers of patients that are involved in the Medicare pool, so we can pick up on that as the overview, and we're going to be looking for surfaces under those various diseases and conditions that we

want to identify.
So with that, we will move on to Peter Savage, from the office of the director of the NHLBI.
DR. SAVAGE: Thank you. I have the slides in front of me here, but -- there they are, okay.
What I'm going to try to do in the next 12 minutes is to talk very briefly about some area where there's gaps in information, particularly from translating information that comes from previous research into things that are useful for clinical care. And I want to start with a couple general comments.
This is obviously an oversimplification,

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but asking the question of what traditional clinical trials tell us, they tend to be designed, many of them, to focus on finding the cause of a disease, finding the maximum benefit of optimal therapy, provide limited adverse event information at the time that drugs and devices are sometimes cleared for sort of clinical use. The clinical care environment, however, is often very different. Patients have multiple diseases, they're on multiple drugs. More and more in the elderly, the drug combinations are a source themselves of problems. The type of therapy is less intense, the follow-up can be less complete than in a trial, and so problems can emerge that aren't seen in the trials.
There's a wide variation of patient response to treatment and that has multiple components, the healthcare system itself, patients and how they behave, the overall environment in which they work, they live. And in many cases unexpected adverse events emerge years after a drug has gone on the market, and the troglitazone controversy that just made the news a few months ago is one example of that.
And what I want to talk about in several of the slides that are coming is the need for

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practical studies where the research is actually

close to what will be implemented in clinical care settings. It involves both cases in which there should be some sort of a systematic tracking or observation to monitor for benefit and harm, and also of necessity some randomized clinical trials that have a very practical orientation. And the system itself needs to be fairly agile in order to respond when problems are identified.

One of the big areas despite the fact that it's been around for more than 50 years is hypertension control. It's the major cause of cardiovascular disease worldwide. It actually is a major contributor to myocardial infarction, to stroke. Congestive heart failure, which you could see from the previous talk, accounts for an enormous amount of expenditure.

Is an expensive clinical trial evidence of the benefit of treatment? Major benefits have been achieved, as you can see from slides that everybody is probably familiar with in terms of the course of cardiovascular age-adjusted death rate, but even now the minority of patients achieve optimal control, control according to guidelines. And as guidelines are being tightened up further, that number actually

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in some specific cases is even less. And there are multiple causes, as I mentioned just a few minutes ago, and progress is lagging in certain subgroups of the US population.

What are a couple of things that we need to do? We need to improve our tracking and surveillance of data to monitor trends when the clinical study comes out about some way of improving treatment of hypertension, what impact does it have in the real world. We need to evaluate the interventions for hypertension treatment in multiple clinical settings, with a goal to achieve control rates that will be seen in some of the best systems.

It's obviously very different whether you're dealing with a big, well organized system such as the VA, or even a chronically underfunded system such as the Indian Health Service, where there's a

whole structure of care providers and various people to assist them and people to reach out to the patients in the community, and a single practice or a small group practice or a small clinic in a poor urban area.
And there's a clinical trial that's in the process of being worked on, it hasn't been approved to go forward yet, but at the NIH, looking at the

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treating blood pressure to lower limits, lower levels in high risk patients to see if further benefit can be achieved. It's going to be called the SPRINT trial if it goes forward.
A major area for prevention, as again was highlighted in the previous talk, is heart failure. The target result of our prior success, people are staying alive that would have died from their myocardial infarct, and people with heart failure are living longer. It's a major cause of morbidity and mortality. Prevention is critical. If something can be done to prevent people from moving to the advanced stages of heart failure, the treatment is easier, hospitalizations are reduced.
The major causes of heart failure are hypertension and coronary artery disease with loss of myocardial mass. So again, it goes back to the link between what we were just talking about. And there's a disproportional impact of heart failure on minorities, and we need trials and ongoing surveillance to see how we're doing.
Specifically, we need an effort to, studies to increase efforts to control known congestive heart failure risk factors. As I mentioned, there are things that we just talked

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about. There's also a feeling that a major area that needs further research is diastolic heart failure.
The current recommendations for heart failure with impaired systolic function are quite detailed, but for heart failure with preserved systolic function, diastolic heart failure, the main recommendation that

has strong evidence is blood pressure control. And there are a series of other things recommended but that are relatively nonspecific.

NIH has a trial that's ongoing called Top Cat, which is looking at the use of beta blockers and ACE inhibitors and receptor antagonists to try and provide specific benefits to patients with diastolic heart failure, but the general way in which it should be best treated needs to be evaluated in more detail looking at the drugs that are used in systolic heart failure, as well as corticoid receptor antagonists.

Vascular imaging is a major area and there's a set of questions that really need to be addressed by any new technology that comes along and some of the ones that are out there on imaging tests. What is the clinical usefulness of the new test, what does it actually add to what we already know? What are its advantages, what are its complications, what are its costs? Does it replace or add to the

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procedures that are done for current assessment? What are criteria to have it actually accepted and paid for in practice?

And the question we have to ask, I think, is the question of whether some of this fascinating technology is driving practice rather than the actual clinical needs of the patients with disease driving more refinement of the technology and careful testing to see what really helps.

One of the areas in particular right now is CT angiography. There are trials needed to look at its utility in diagnosis and prognosis, what are its advantages for disease progression assessment? Is traditional angiography still needed? One of the negatives is that even though there's been some improvement, there is a substantial dose of radiation, the utility for screening is uncertain, and it's not optimal for repeat exams. Trials are needed to look at its utility so that we actually know whether it can be used to prevent cardiovascular disease, or can be used to refine the treatment in such a way that actually impacts upon clinical

outcomes.
Now one of the questions is what is the
optimal group in which this needs to be looked at.

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There are people with very low risk factor patterns
where doing a test is unlikely to produce much if any
benefit. There are people that already have risk
factor patterns that are known in advance of such a
test that they begin the maximal therapy, and so
again, it might not make much difference. And so
there does need to be an identification of some type
of intermediate risk patient group to see whether or
not it can be, it can contribute to a better clinical
outcome.
And it was pointed out to me in the course
of putting this together that the NCI's lung cancer
screening trial is an example of a more systematic
approach to looking at technology.
Drug-eluting stents, to some degree, and I
think this is a little bit of an exaggeration
obviously, is an opportunity missed. The development
of drug-eluting stents addressed a major problem with
the bare metal stent. It was obvious that rapid
clinical adoption could be foreseen. It was also
obvious that clinical trial results that were
available in the beginning when the stents were
approved were inadequate to really understand the
long-term safety and efficacy of this technology.
There was some concern expressed at the

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beginning about the possibility of late events, but
it's obviously become greater subsequently, a few
years ago, and one of the residual things now is the
fact that patients may need longer-term anticoagulant
therapy and if that's true, the cost projections and
projected savings from the drug-eluting stents,
obviously that whole question is substantially
altered.
Clinical questions remain unanswered about
long-term complications, the appropriateness with
severe disease. It's an evolving technology and new

stents need to be evaluated quickly because they may not have the same adverse effects. Congestive heart failure, or rather chronic obstructive pulmonary disease, I will go over very quickly. There's an NHLBI study regarding oxygen supplementation and the group suggested that we really need to look at whether or not pulmonary rehab would be valuable in patients with moderate to severe COPD or following acute exacerbation. Blood diseases, my last slide shows, I'm going to move ahead here, there were some practical research questions about the impact of storage time on the characteristics of blood, optimal transfusion triggers, blood transfusion, how many should be given

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to what target, what's the difference in clinical outcome depending upon the risk, and what is the cost effectiveness. So in conclusion, there has been major progress on several chronic diseases. Cardiovascular disease, I may be somewhat biased, but I would say it's a very good example. But it also shows, as you look at the current status of cardiovascular disease, that the complexity is reduced by progress. Costs of the benefits achieved are high. We need a better understanding to optimize prevention. We need better ways to apply and assess clinical trial evaluated treatments in real world settings. We need more research in clinical environments. Thank you.

DR. MCNEIL: Thank you very much. That's a terrific list to start us off with. Okay. Let's move on to the NCI with Martin Brown.

DR. BROWN: Thanks. That was a great talk by Dr. Peter Savage because it actually, the same themes are the things that we encounter at NCI, so I will touch on some of those same ideas, I think. So -- I'm sorry, I had two sets of slides, so I just wanted to must sure this is the right one here. We were asked to list five topics of concern in evidence gaps. I know at CMS you're

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interested in diseases that are prevalent and have a high expense to beneficiary ratio, so it puts us in kind of an odd situation because as you know in regard to treatment, cancer is, you know, according to who you ask, 50 diseases or 100 different diseases, and the treatments are very heterogeneous and increasingly tailored. And so any one treatment is not very common actually, not very prevalent, and it's not a very large expense in and of itself. If you add them all up, cancer of course is a major expenditure by CMS, probably almost 20 percent of CMS reimbursements.

But there are, the procedures that are cancer-related that are more prevalent and also are pretty big dollar expenditures are cancer screening and surveillance, because a population that receives screening, of course, is not just the population of the diagnosed cancer patients, but potentially the entire segment of the population. So that's one area where I think there's some real, and again, a very dynamic technological development going on in that area.

Another area is the area of pharmaco-surveillance of drugs, which as you know are increasingly being developed. And not only do we

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have new drugs being developed which are quite expensive, but increasingly there are diagnostic and prognostic biomarkers which, the question is, is it just a drug, is it just the treatment drug, or is it just a package of prognostic and diagnostic biomarkers and the drug itself which should form the service that should be the topic of a coverage decision, and if that's the case, how would you do it.

The other area I just wanted to mention, supportive therapy, as you all know, that's been an area of obvious concern that we just, the ESA, and there's some evidence that the stimulating factors may be an issue too, but there's unrecognized adverse events.

And so in terms of evidence gaps, again,

this is sort of repeating what you just heard, we have randomized controlled trials for some screening modalities, but two questions emerge. Number one, how do those apply to older populations that CMS covers, especially very old populations with shorter life expectancy and more comorbid conditions that may have not been represented in a trial, that is eligible for treatment, or participation in trials as well.

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And number two, what about screening modalities that are not the ones that were represented in randomized trials but are technological extensions, either of the trial evidence, or are technological variants of screening modalities? So here's just an example of that, colorectal cancer screening. You know, the original trial involved guaiac fecal tests and currently in addition to it, there is a chemical fecal test, and I know there was interest beyond this, and there is now an emerging CT colonography, and I expect this may be the subject of a CMS coverage decision in the future. They are looking at fecal DNA tests and there will probably be several others within the next years. There's even the possibility of a serum, blood serum test for colorectal cancer screening. So what do you do about, you know, how do you go about a coverage decision, what kind of evidence is sufficient when you don't have the original mortality endpoints clinical trial which are hundreds of millions of dollars and 10 to 15 years of time, but is it sufficient to use certain kinds of modeling or extrapolations from that data to single out. Of course in lung cancer, as you just

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heard, there is an NCI CT screening trial that will have results sometime in the future. Another broad area that I think is of relevance is what I call the triad, pharmaco-surveillance, (inaudible) and others.

There's sort of three concerns here. In terms of pharmaco-surveillance, when we start to look at data in the actual world of access to various large databases and we find long-term adverse effects that weren't evident in the original trial, you know, what do we do? Do we simply put restrictions on a drug or device or technology that's already been approved in the past, and what evidence do you need to do that. So the focal point, for example in our viewpoint at NCI is the recent understanding that HRT therapy did not have some longer benefits that it supposedly had, and in fact is a risk factor for breast cancer. And of course there was, you know, there has been a large decrease in the use of that therapy as a result of that information. But if you're asked from a coverage viewpoint what kind of evidence would you need and what kind of restriction would you want to place on such a drug that was already in practice, I think that's a very important question. And there are other examples of that sort

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of phenomenon.
On the other hand, there are common drugs which may turn out to be preventive for cancer, for example. Through the same type of surveillance research you may find evidence of that, and then how do you respond to that kind of evidence?
And finally, as I already mentioned, this whole area of clinical practice in which you have so-called tailored therapies, we have diagnostic and prognostic biomarkers. And the question of how you move from relatively small studies in a highly selective population who typically are younger without comorbidities, to large older populations, and what kind of package combination of drug therapy and diagnostic/prognostic markers might be the subject of that actual coverage decision, I think is a very complex and increasingly important question.
So that actually, I have pretty much covered my slides, I think. So that's it.
DR. MCNEIL: Thanks very much, Martin.
We'll keep plowing ahead and then hold questions for

our last speaker. So Susan Nayfield from the NIA, is she here? How about Michael Schoenbaum.
DR. SCHOENBAUM: It would be great if I could speak off my own slides, though, and not

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Susan's. Thank you.
So, I want to thank the committee for organizing this I guess unique session, and also for including the National Institute on Mental Health in this. I know that the focus in this session is on evidence to support coverage and quality improvement, so I will be brief with the context.
This slide shows the distribution of disease burden in the U.S. and Canada and shows here in the blue wedge that 30 percent of the burden at the population level is attributable to neuropsychiatric disorders, and fully half of that is attributable actually to medical disorders. For the Medicare population in particular, it's important to note that the number of Americans with mental disorders in the Medicare age range is projected to rise quite substantially over the coming decades due to a combination of demographic trends and improvements in treatment.
Now in the last few years there have been several comprehensive analyses of priorities for improving mental health care, in particular by the Institute of Medicine, by President Bush's New Freedom Commission on Mental Health, and also by the U.S. Surgeon General. And I will be drawing on their

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recommendations and of course on our evidence base, which was the basis for many of their recommendations.
The reports identified many common priority issues for quality improvement both across mental disorders, and between medical and mental health disorders, so I think you will recognize some common themes in what I will talk about and what some of the preceding and presumably subsequent speakers will talk about.

I'm going to illustrate our comments here by focusing on two particular conditions, depression and then schizophrenia and psychotic disorders. Just, again by way of brief background, depression is common in the Medicare population, it's four percent overall in the Medicare age range, 10 percent in primary care settings, and 15 to 40 percent in patients with comorbid medical illness. And it's important to note also that the prevalence of depression rises with the severity of medical illness. Also, 15 percent or so of SSDI awardees have a primary causal disability of depression or psychotic disorder.

The clinical features of depression inhibit care pretty directly actually. They inhibit

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appropriate care for depression. They also inhibit care for chronic illness. It is easy to think if I were old and sick and bereaved and, you know, unemployed, I would be depressed too, but it turns out this is actually a fallacy, that even in elderly populations with significant medical illness, other life risk factors that, you know, that one would expect to be associated with depression, that even people like that respond to depression treatment and in fact they respond to depression treatment at rates that are very comparable to working age people, younger populations.

So, depressed patients have more severe medical illness, they have higher rates of disability, they have up to twice as high rates of mortality, and they also have substantially higher medical costs compared with other like or similar patients without depression. Importantly, most cases of depression can be treated effectively in general medical settings, but currently half of Medicare beneficiaries with depression are not recognized or treated at all.

Among those that are treated, care is often ineffective, which is not to say they receive no care, they actually receive the wrong care or they

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may receive subtherapeutic doses, or they may start therapeutic doses and discontinue. And the end result of this is that overall, only one in five patients with depression in the Medicare population currently get better under prevailing practice standards. So usual care, thus, is not effective. That is, simply providing coverage for efficacious treatments which Medicare largely provides now is not adequate for, you know, improving outcomes in Medicare beneficiaries with depression. What is effective is a proactive system of care, collectively called collaborative care which includes the elements here on the slides. So obviously screening and assessment leads to patient identification. Patient education and activation. Treatment, which is already largely covered under Medicare, meaning antidepressant medication and brief structured psychotherapy, common behavioral therapy and other similar directed type of therapies. And then an important active ingredient to an effective model is care management in the general medical setting to support treatment, to get people on an appropriate treatment plan. But then what's really critical is proactive tracking of outcomes. Once you've started a treatment plan, you reassess

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the patient periodically to see if the patient has improved; if the patient has improved, fine, you can continue what you're doing. If the patient has not improved, you do something different. And the care manager turns out to be integral in activating the provider, the clinician to do something different, to change treatment if the patient is refractory. Another key ingredient here is mental health consultation to the general medical provider. So you don't necessarily need to send the beneficiary to a psychiatrist or a psychologist, most elderly people with depression don't want to go to a mental health specialist, and it turns out not to be necessary to send them most of the time. If necessary, or course that's important too. But what

is essential for improving outcomes of care, it turns out, is having a mental health specialist available on a consulting basis not to the patient, but to the general medical treatment team.

So again, together, this model is referred to as collaborative care, and based on 30 or more randomized controlled trials, effectiveness trials across multiple population groups in the United States, collaborative care has been shown to very substantially improve outcomes. In fact, I guess the

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short version of the rest of this slide is that collaborative care essentially doubled the effectiveness of usual care for depression. Importantly, collaborative care also seems to be largely cost neutral, and even cost saving in higher risk populations. This slide shows trial results for depression in diabetics over two years, with a negative impact on cost. The costs were actually lower in the intervention group. So based on this kind of evidence, the President's New Freedom Commission explicitly recommended that public and private care cover the core elements of collaborative care.

Why is that important? Because Medicare and most other insurance do not currently cover what the President's commission referred to as the active ingredient, the core elements of collaborative care. And in particular, Medicare and other plans don't cover care manager time, particularly via telephone contact, which turns out to be an element of almost all of these trials, and as you know is relatively cost effective to deliver, it is certainly an active element of these interventions that is typically unreimbursible. Now a specialty consultation, similarly, if you send a patient to a mental health

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specialist, that's reimbursible, but if the primary doctor consults with a mental health specialist about that patient's case load, that is not reimbursible, again, without face-to-face patient contact.

Screening is reimbursible under some circumstances. Outcome tracking is not explicitly reimbursible. That is, if you do a hemoglobin A1c on a diabetic, you can submit the results of the hemoglobin A1c. But if you do the depression equivalent of a hemoglobin A1c, which is something like the PHQ-9, a structured assessment, that is not directly reimbursible. So, okay.

So we know that this model works and it works in heterogeneous practice settings across diverse patient populations. What is it that we still need to learn? What are the priorities that argue for new evidence? And the answer there is basically lots of ways, there are lots of things we need to learn to move towards population-based delivery of a model like this.

For instance, what are the best ways to deliver, to implement collaborative care across different practice settings? So big practices typically can support an internal practice care manager, but solo or small practices, which AHRQ says

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I believe accounts for something like 50 or 60 percent of primary care visits currently, may need to contract with a third party to provide services like this, because they just don't have enough of a case load to support their own care managers. And then the question is, should that third party be contracted by the practice so that there's a linkage from the practice to the provider, or should it be contracted by Medicare as, for instance under the current Medicare Health Support pilot program? What linkages work well in those situations?

Similarly, what kind of plan change is effective for doing this on a population level? Should it be fee per service or, you know, each contact or each consultation? Should there be a case rate based on a month or a three-month or six-month management? Should there be beneficiary cost sharing? There's some evidence about issues like this, but I think for population level applications we need more evidence.

The warning means I have two minutes left, is that right?
DR. MCNEIL: Exactly. You might want to move ahead in your slides.
DR. SCHOENBAUM: Yeah, I understand. I'm

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actually going to stop with depression. The issues with schizophrenia we can talk about separately, and they are actually conceptually very similar, okay. So the third issue is how can we incentivize quality? If we want people to do this, if we want to spend money on this, what are the right outcome measures, what are the right incentives to get people to do it, via PQRI, CPT category two codes, other ways to capture the core elements to see if appropriate care is being delivered. And then again, moving further out on the research frontier, extending this model to the whole patient so that we have effective depression modules, we have effective depression in diabetes, depression in heart disease and so on, but really we want to treat any of the diverse range of conditions that a patient might present with, and currently we don't know very much about diabetes.
Possible leverage points for developing this evidence, obviously coverage decision, procedure codes and quality measures, again, PQRI. Ideally we want information systems that generate these things short of a full-blown electronic medical record.
Demonstrations and pilot programs, I mentioned Medicare Health Support, which is ongoing; the

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Medical Home demonstration, which is impending; the DIAMOND initiative, which is a Minnesota initiative that CMS could join and actually had joined via Medicaid but not via Medicare, and so on.
NIMH is available to work with CMS on any of these initiatives. Thank you very much.
DR. MCNEIL: Thank you very much. Can we then assume, if you could fast forward to one of your last slides, the same conclusions would hold for

schizophrenia?
DR. SCHOENBAUM: Sure.
DR. MCNEIL: Okay, fine.
DR. SCHOENBAUM: Should I describe those?
DR. MCNEIL: No. Only point out which slides would be relevant for us.
DR. SCHOENBAUM: So what's relevant is slide -- oh, I actually don't have them numbered here, so it's one, two, three, four, five from the end, titled Effective Strategies Exist. And again, it highlights evidence-based models for improving the reach of efficacious treatments for schizophrenia.
DR. MCNEIL: Thanks very much. That's on page ten.
Okay. Why don't we go on to Judith Fradkin, from NIDDK.

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DR. FRADKIN: Am I supposed to push something or are you going to bring my slides up? The NIA representative is here now.
DR. MCNEIL: Okay. Well, why don't you go ahead. It must be the Cleveland Indians exerting their revenge.
DR. FRADKIN: There we go.
First of all, I would like to thank you for inviting me to present at this important meeting. I just want to take a minute to give a different perspective than Dr. Hakim on the contribution of diabetes to Medicare costs, because most of the costs of diabetes are not for the care of diabetes per se, but because patients with diabetes have so much of an increased risk of cardiovascular disease, of fractures, of pneumonia, of infectious diseases. And so if you look here just as a footprint of the percentage of Medicare patients who have diabetes, which is 21 percent, versus the cost to Medicare of taking care of people with diabetes, which is 31 percent of your budget. And you see that for ESRD it of course is even a greater increase, going from one percent of the population to 6.2 percent of the costs. So I think when you represent the costs simply as a cost of caring for diabetes,

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that really underestimates the importance of diabetes both to the Medicare population and to the CMS budget.

Now I think everybody knows that the prevalence of diabetes is very high in older people 65 and above. In addition, it's substantially increased in people with disabilities. And looking at the incidence, you can see that the problem is only going to get worse as we move into the future.

The good news is that we have done a study, the Diabetes Prevention Program, in over 3,000 people which included 20 percent over 60 and 45 percent minorities, which showed that lifestyle modification, weight loss of about seven percent could reduce the risk of developing diabetes by 58 percent. And in the population over 60, the effect was actually greater; it reduced the risk of developing diabetes by 71 percent.

So that brings us to issues related to how best to translate those findings to try to prevent the phenomenon that diabetes is potentially going to overrun our healthcare system. And I think, first of all, we need better methods to identify those at risk for diabetes. There are 54 million Americans with pre-diabetes; practically none of them know they are

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at risk and, therefore, they're not being advised by their physicians to do these kinds of changes that can in fact prevent the risk of diabetes. So I think we need to develop algorithms based on data from longitudinal studies, from CMS data, to help decide who are the people in whom preventative intervention should be delivered.

We also need to develop more cost effective behavioral therapy. In the Diabetes Prevention Program, the therapy consisted of 20 individualized one-hour sessions. Clearly it's not going to be feasible to provide that for 54 million people. So we need to develop ways of group delivery, Internet delivery, delivery in community

settings. We're doing a study now which looks very promising delivering these key interventions at the YMCA. Most Americans live within ten miles of the YMCA. If those kinds of things do occur, we're going to need a model to pay for them.
Bariatric surgery has increasingly been shown to affect both mortality in diabetes, but I think there are a huge number of unanswered questions with regard to bariatric surgery, particularly related to the impact of timing of the procedure, the level of obesity, when in the course of disease it

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should be done, and how that affects risk, benefits, costs, and development of diabetes.
And finally now, there is clearly a huge interest in the pharmaceutical industry in developing weight loss medications. I think that when those come on, we're going to need to look at long-term effect on hard outcomes rather than short-term effect on weight loss.
Now we've also shown that glycemic control can dramatically reduce the risk of microvascular complications, and for type one diabetes it's been shown that it can also reduce the risk of macrovascular complications. So again, there are a number of questions related to how we should try to control glycemia in diabetes. And we really, at this point it's very hard for people who are on insulin, for example, to bring glycemia down to near normal, but the question is, should we start glycemic therapy earlier when people have milder diabetes when it's much easier to control the diabetes, and would in fact starting therapy earlier preserve the beta cell and make diabetes easier to control in the long term?
Another glaring piece of information that we need is a head-to-head comparison of the various therapies for glycemia, using cardiovascular disease

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and other heart outcomes. Clearly this has been getting a lot of attention recently in the media.
Clearly for people who develop diabetes at

a younger age, we want to get their A1c as close to normal as possible, because they have many, many years to develop the complications of diabetes. But for patients who develop diabetes at an older age where they may have a limited life expectancy, I think we don't really know what is the optimal level of glycemia as assessed by A1c that will be associated with better quality of life and better functional outcomes.

Also, we need to learn how to maximize the benefits from self glucose monitoring. We really don't have strong data in patients on oral hypoglycemic as to which patients can benefit from that, how it should be done, how physicians and patients should take the information that they get from self glucose monitoring and translate it into changing their glycemic therapy.

Here I just want to show you that, again, in blue patients with diabetes versus, in white patients without diabetes, and you see the cardiovascular mortality is much greater. You also see that in men in patients with diabetes, the rate

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is dropping, as they are in the general population, but in women it's not so clear that rates of cardiovascular mortality are dropping parallel to the general population in women with diabetes.

And I think this raises a number of questions, given that cardiovascular disease is the cause of death in two-thirds of patients with diabetes, about some of the issues that Peter mentioned, how best to improve blood pressure and lipid control in the primary care setting. We need to find ways to increase the utilization of low cost effective therapies such as aspirin, influenza vaccinations, to prevent the complications of diabetes.

And we need to find better ways of monitoring utilization. So in many of the patients with diabetes, some aspects of diabetes care such as aspirin or influenza vaccination can't be measured because they have no way of measuring it when people

are getting flu shots from all sorts of sources and so there is nobody who can really be held accountable. And I think given the importance of some of these comprehensive care aspects, we need to find ways of measuring it so that we can actually assess whether patients are getting it.

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I think also for many patients with diabetes who are on polypharmacy and may be taking 10 or 12 medications, we need to figure out better to enhance adherence to medication. And a variety of things have been proposed, such as a polypill. Blister packs have been studied in the military, where people get all their medications for a given day in one blister pack. So if they get a monthly blister pack, it could make fewer medication errors and enhance adherence. I think these are some of the kind of practical issues that we need to study for patients with diabetes.

Amputations actually are decreasing in patients with diabetes, and that's one of the few pieces of good news, but it's really a tremendously understudied area when you consider that about one in 100 to one in 200 elderly patients with diabetes will in fact lose a piece of a limb each year. And I think we need to lock at approaches for preventing limb loss. Again, therapeutic shoes and socks, the value of those I think needs to be studied further. In particular, I think we need to find better ways to identify and educate high risk patients. It's been proven that in these kinds of programs where you identify patients with early

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neuropathy and give patient education, can in fact prevent ulcers and limb loss, and this is something that, again, we need to learn how to implement in the general care setting.

We also really do not have any rigorous studies comparing approaches to healing of ulcers in terms of offloading, methods of debridement, use of biologics, indications for angiography and

revascularization. All of these are areas that are very much understudied. And finally, I think it would be really important to identify predictors of ulcer healing, to know whether a person should proceed to amputation or whether they might be able to be salvaged. Just as diabetes dramatically increases the risk of cardiovascular disease, so does kidney disease. And Peter Savage already mentioned a study in planning, SPRINT, to try to look at optimal strategies to slow the progression to cardiovascular disease, which will include a large sampling of patients with chronic kidney disease. This is clearly something that is an understudied area. We know that chronic kidney disease increases the risk of cardiovascular disease, but we know remarkably little about specific therapies to prevent that.

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I know Medicare is very interested in the fistula first program, but again, I think if it is related to early placement of a vascular abscess, particularly how far in advance of such conditions like diabetes where there may be poor healing, optimal timing for initiation of dialysis. GFR is not a perfect marker of uremia; do they study markers that could help determine when patients should start dialysis methods to reduce cardiovascular disease in end stage renal disease patients. And also questions about how best to evaluate pretransplant patients. Some studies did huge cardiovascular workups, others did practically none, or at least not as large invasive workups, and the value added of that needs to be studied. And finally, I just want to close with urologic data which, not that urologic procedures are part of my institute's mission. These don't cost Medicare patients so much, but they cost Medicare patients huge amounts of money in out-of-pocket expenses, particularly for incontinence, and also, they are a major cause for admission to nursing homes. And so some of the issues that we need to

study are now that we have minimally invasive surgery

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both for HPH and for female incontinence, guidelines for who should get these kinds of surgeries need to be established. Many urologists accept a urodynamic evaluation, but I don't think we really have strong evidence with regard to the role of urodynamics in evaluation and treatment of lower urinary tract symptoms.

And then finally, optimal urologic treatment for spinal cord patients, studies comparing intermittent catheterization versus indwelling catheterization, because there are different costs in terms of personnel and supplies, but we need to know which will do better in terms of development of infection, which is in fact the major cause of death in spinal cord patients who die from urosepsis.

So I'm going to conclude by saying that NIDDK would love to work with CMS and to develop studies to address some of these subjects, and we really welcome opportunities to do that. Thank you very much.

DR. MCNEIL: Thank you very much. That's a terrific list to help us start our discussion. All right. Susan Nayfield arrived so we will wind back a little bit and go to the NIA. Hopefully we can get her slides.

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DR. NAYFIELD: Thank you for the opportunity to be here on behalf of the National Institute of Aging. We are a small institute with much overlap in terms of disease focus. The presentation I'm going to give relies more on the independence of older people, preventing nursing home admissions, and maintaining an independent lifestyle.

The goal of the National Institute on Aging is maintaining independence and health in old age, and the challenge for us today is to identify areas where additional evidence could lead to better targeting of coverage. We're interested in effective services being delivered to our older patients either

by expanded coverage or better focus of current coverage. The critical services we've identified rely on, or focus on prevention of falls in elders, structured exercise programs to maintain walking ability and independence, post-acute stroke rehabilitation, coordinated management for transition and medical rehabilitation services following hip fracture, and therapies for unexplained anemia in the elderly. The first problem, falls, 30 percent of people over age 65 suffer a fall each year, and this

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increases to 50 percent over age 80. 50 percent of these falls, half of these are recurrent falls in patients who have had a previous fall and should have been recognized as at risk for additional falls and injuries. They are a major cause of hip fractures and a major independent determinant of functional decline. The risk of skilled nursing facility placement increases by three-fold for first falls and ten-fold for falls with injury. Falls are a condition in which there are multiple risk factors, medical disease, medication, environmental factors such as home hazards or footwear, and cognitive function actually does contribute to the list of variables for a risk of falling. The service that we're interested in is a coordinated multidisciplinary risk factor screening and intervention program for community-dwelling elders. The Cochrane review in 2003 recognized the efficacy of the multidisciplinary programs and of the individual components of these programs. And through work by Mary Tinetti and our fall prevention center at Yale, there is a Connecticut Collaboration for Fall Prevention currently being studied, and the results of this will be published next month.

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A variety of professional societies have addressed this issue, guidelines for fall prevention

have been established by the American Geriatric Society and endorsed by the American Academy of Orthopedic Surgeons.
What we find is that while components of the services are currently covered, they are not widely provided, and they are not provided in a coordinated manner. These services involve evaluation of gait and balance, review of medications, review of footwear, a home inspection for risk situations, and to coordinate not only these evaluations but the interventions to help fix the problems is a major issue.
The additional needs for evidence you see here. We feel that we need to know how changes in coverage could improve outcomes, is there an alternative administration of current coverage that could help fall prevention and initiate these coordinated programs? How can we increase the dissemination about the benefits of this and current coverage to the physician population who see patients at the risk of falling?
The second focus, structured exercise program to maintain walking ability, it's amazing

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that the loss of ability to walk a moderate distance can have such a dramatic effect on the independence of older patients. Low physical activity, as manifest by very little walking, is a strong predictor of severe disability. And while there are numerous current recommendations for exercise in general, there is lack of evidence for the efficacy of a specific program for specific problems.
The structured physical activity program designed to maintain walking ability has been in a pilot phase and results are now in from that, it is called the LIFE study, Lifestyle Intervention and Independence For Elders, conducted by Dr. Marco Pahor, who is now at the University of Florida in Gainesville. This started as a center-based aerobics, strength, balance and flexibility exercise training that was transitioned into home-based maintenance with periodic follow-up by a trained

professional.
The pilot study found good adherence
improved physical performance in 424 patients over
age 70 years, actually in the intervention group,
which was half of that 424 patients. And there were
trends toward lower incidence of major mobility
disability.

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Additional needs for evidence include a
full-scale clinical trial which is under development
by NIA now that looks at long-term functional and
health effects as well as cost effectiveness. It
would be most helpful in this undertaking to have
this viewed as a clinical intervention and considered
for clinical trial participation.
Post-acute stroke care. Over half of
stroke patients are unable to walk at hospital
discharge, and this impaired ambulation leads to
falls, fall-related injuries, hospital readmission,
nursing home placements, and contributes to physical
decline. What's most important is that the clinical
course following a stroke, particularly in older
people with a variety of comorbid conditions, varies
from patient to patient, and patients may not have
apparent problems early in their course, these may
become more obvious as the patient transitions to a
familiar home environment or to a rehabilitation
facility.
So we feel that the integrated and
coordinated aspects of post-acute rehabilitation
services need to be tailored to the individual
patient needs. This has been examined by numerous
Cochrane reviews and they found that an extended

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home-based rehabilitation program and physical
therapy was beneficial in improving functional
independence following stroke.
We have found in studies by Studenski and
Duncan that 50 percent of patients with limited
ambulation have meaningful improvement in lower
extremity strength and gait velocity with post-acute

stroke rehabilitation. Gait velocity is a very interesting predictor here, because the ability to walk .4 of a meter per second limits an individual to within-the-home activities. Moving that up to .8 of a meter per second means that they can ambulate in the community and return to a more usual community discourse.

We also know that following the guidelines that are in existence doesn't improve care.

So while many services are currently covered, they're not widely provided, they're not well integrated and coordinated. They are time limited, they are limited to certain time periods following the event, and they are insensitive to individual patient course and needs.

So the areas for additional evidence are on the effect of the following on improving outcomes: Changes in coverage, alternative administration

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policies for current coverage, and again, the need for increased information dissemination about current coverage to promote the use of currently available services by community physicians for stroke patients.

Studies on coverage for integrated and coordinated services should guide us further, particularly focusing on patient-tailored programs, cost effectiveness, and payment for quality programs.

A fourth area that's a bit of a hot topic right now is anemia. Over 10 percent of patients age 65 years and above are anemic by World Health Organization standards, and this increases to 20 to 25 percent of patients ages 80 plus. Recent work by Jerome, et al., has shown that about a third of these anemias given a standard workup are nutritional, about a third of them are related to anemia of chronic disease or chronic kidney disease --

DR. MCNEIL: Dr. Nayfield, you have two minutes.

DR. NAYFIELD: And a third are unexplained despite clinical evaluation. Anemia, even mild anemia is associated with a variety of bad outcomes as you can see here, and with a focus on unexplained

anemia, we believe that increased responsiveness to this were precursors to EPO in aging as one of the

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causes.
So the question becomes, can we treat anemia, unexplained anemia in the elderly? Currently we use erythropoietin. There has been a lot of clinical experience with it, it is controversial right now in terms of its complications, particularly a high incidence in patients with kidney disease. However, these are patients without kidney disease. In the future there are non-traditional ESAs and other approaches to targeting cytokines, hepcidin, HIF, or other mediators.
You can see the evidence here. There have been a number of fall studies, particularly in the frail elderly. Patients with heart failure show that you can increase hemoglobin with erythropoietin and increase physiologic measures and functional status.
The additional needs for evidence involve large-scale clinical trials to establish efficacy, dose and schedule, exploratory studies, and coverage for clinical trial participation. NIA is going to establish a consortium on unexplained anemia in the elderly to help address these issues, and many of these studies will begin shortly.
Very quickly, the last focus is post-hip fracture care, particularly on the transitions

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between care and the coordination of care that most hip fracture patients endure. This is a very vulnerable population as you can see; over half do not return to pre-fracture function. They average three to four transitions in the first six months compared to, 20 percent have five or more transitions, and these transitions are often associated with adverse drug effects, falls, and fragmented or sub-optimal care.
So the service we're interested in is integrated and coordinated post-hip fracture care.
The evidence is here. There are guidelines that

exist, for example, evaluation of hip fracture patients for osteoporosis and treatment with bisphosphonates; however, this is not widely used. And there is also the need for additional evidence in these areas.

Finally, again, as other speakers have echoed, there are opportunities for collaboration. We can design our studies best to answer your questions if we know what evidence you need and where you think the gaps are as well as we do. Thank you.

DR. MCNEIL: Thank you very much. Okay, Dr. Koroshetz, neurological disorders and stroke.

DR. KOROSHETZ: Very good, thanks very

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much, it's a pleasure being here today. I'm representing the National Institute of Neurologic Diseases and Stroke, and we were asked to prioritize, we cover about 600 diseases, the prioritization means that we've got to be pretty stingy on about 598 of these.

I'm going to probably concentrate on cerebrovascular disease because it seems like it may be of most interest to this audience, and I'm going to talk about two themes.

The first theme I think in terms of research gaps is that we have, we have suffered because we have a lack of evidence about how community practice parallels clinical trial results. I think that's a general theme I would like to point out, and the example I would use is carotid artery revascularization for asymptomatic stenosis. This is a fairly well-studied area. The clinical trials have shown the natural risk of stroke is pretty low, it's about two to three percent per year, endarterectomy is of benefit. However, the benefit is related to the fact that the operation has an extremely low procedural rate of stroke and death, less than three percent, and the patient has to live a certain amount of time to reach the benefit, given that the stroke

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and death rates are about the same as the annual

rate, and that's considered to be about five years to show benefit.
The problem is that the clinical trial results are known, then when it goes into clinical practice it becomes an extremely common procedure, and we have no real data on how it's operating in the real world. There are a lot of big concerns. Some people who have looked at Medicare databases, the suggestion is the mortality rate, which is the only thing one can get out of those databases, is excessive, and suggests that possibly the entire United States general efforts to limit carotid artery disease stroke may not be benefiting patients as a whole. That's a question that's still out there and we don't know the answer.
It was brought up even further in the recent SAMPRIS trial where there was an attempt to compare endarterectomy to stent in patients who have difficult surgical risks, and the thing about that trial, it showed that most of the patients, about two-thirds were asymptomatic patients, and the complication rates from either the endarterectomy or the stenting procedures were higher than one would have wanted to recommend a patient to undergo any

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procedure. The question then raised again, whether in the real world patients are being submitted to these procedures and that there is no net benefit potentially in that arm, because of the high risk patients that are now being operated upon.
The second theme I wanted to bring out is that for us in the neurologic world we're dealing with patients who have conditions that may cause severe damage to their quality of life or cause death. So talking to those patients about the options is a very difficult situation. The patient is going to want, if at all possible, to try to make the deficit go away, in other words -- I'm sorry -- make the risk go away, whether it be a berry aneurysm in the head, arterial decompression, carotid stenosis. If they meet a proceduralist and that proceduralist is confident about their ability to

make their problem go away, the patient is generally going to go in that direction. The question is, to really make it an educated decision, one has to know what the risks and the benefits are of these procedures.
And this has been a problem in PFO closure where you have a hole in either the left or right side of the heart. A third, almost a third of the

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patients have this hole. So the patient has a stroke, they are found to have a hole, the question is, do you close the hole. It's a real quandary for the patient. Statistically, a stroke due to that hole is incredibly, incredibly low probability. For a patient with a low probability of an event, you have a patient being very nervous about their anatomy and the lack of data with regard to what is the best way to proceed.
Carotid stenting we talked about.
Intracranial clot removal is another device and a new procedure that's out on the table for patients with acute stroke, and again, we don't have data, although it's being used.
Intracranial stenting, when the stenosis occurs inside the brain, patients have little option.
Stenting intracranially is now being studied.
Surgical epilepsy versus medical therapy is another major procedure that's on the table in terms of when the procedure is indicated, and this is removal of epileptic focus to try and prevent further epilepsy in a patient.
In terms of research gaps concerning clinical services and stroke, I think it was mentioned by Dr. Savage about the problems with

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atherosclerosis being, you know, a major source of health problems. And one question I think we're going to face in the future is screening for atherosclerosis. For patients who die of a heart attack or die of a stroke, but that's not the disease they die of, the disease is atherosclerosis, now you

can diagnose atherosclerosis. We have very good imaging techniques where you can determine if you have athero in the neck and the heart, and the femoral arteries and the aorta.

The question is going to come to the table fairly soon, when do we put money into screening for those procedures, intervening with primary intervention before someone has an event. Most of what we are doing now is general health, kind of education and guidance and risk factor reduction, but we're not really diagnosing atherosclerosis, which is the real killer, and we can screen for it. There are now, you know, trucks that go around to churches and parking lots and malls where you can have screening procedures, patients will pay money to know if they have atherosclerosis. The quality and the impact of those screenings need to be tested.

We talked about carotid disease so I'll skip over. In terms of the cumulative nature of

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stroke we now have a therapy which is similar to what we had in the heart in the '80s, which is intravenous thrombolysis, it's been shown to have some benefits and reduce disability, reduce movement of patients from the hospital to a nursing home, so I think it's cost effective to the Medicare system in general. However, the costs to the hospital itself, the acute hospital has to put a lot of money into the proper administration and care of these patients, so there is a need to examine these costs, and they seemed very responsive to doing that just a couple years ago.

The issue we still have is how to get this therapy out into the community, so that's a big clinical service gap. Currently in the United States if you have a stroke, what happens to you depends on where you have your stroke. If you happen to have it near a very experienced stroke center, you'll get the treatment. But most patients are not going to get the treatment, only about two to three percent of patients will get intravenous thrombolysis for their stroke. Some of that relates to the fact that they

don't get to the hospital in time, but a lot of it is because the hospital systems are not organized across the country yet in a uniform manner.

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Another issue that's coming up is what is the appropriate treatment and diagnosis workup for a patient with transient ischemic attack. A transient ischemic attack in its purest form is a period of time when your brain is ischemic but your deficits go away before there's any real significant damage. The trouble with it is that there is really no good way to know whether a person's spell is due to ischemia or not, and therefore TIA is often used as a term for a whole bunch of different spells and that makes its treatment difficult. The question now is can we increase the specificity of diagnosis and then target specifically those patients for more intensive workup and treatment to prevent a stroke, because TIA, a real TIA patient has a very high risk of stroke in the next two to three weeks after their event. This is a warning sign. We need to be able to specifically diagnose it and then diagnose a treatment.

When they fail reperfusion therapy, a patient has a major stroke, there's usually a clot inside one of the blood vessels in the brain. Intravenous thrombolysis, as I mentioned, is useful. However, these big clots are very resistant to the intravenous therapy, which led many people to try and

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go in with catheters to try to move the clot either with drugs or with a clot retrieval device. This really needs to be studied because these procedures are very, extremely risky procedures involving catheterization with patent's injection of dye, and there's lots of problems that can go on during these intracranial procedures.

NINDS is currently running a trial of patients who get TIA in a randomized intra-arterial versus medical management after the intravenous therapy.

The advance, one of the advances I think we're going to be seeing is new stroke imaging coming into emergency therapy. This is done in many centers now and it's a basis of studies that are trying to expand the time window of intravenous thrombolysis past the current three-hour window. The idea there is that if you have a specific imaging technology and select those patients who can still benefit even though it's past three hours, versus a large portion of the patients in whom the stroke is already done by three hours and could no longer benefit. The only way to deal with these patients currently is through imaging, but this needs to be proven in randomized trials.

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We mentioned chronic atherosclerotic disease, a big problem in patients with diabetes and African-Americans, Asians, and we currently have trial now to randomize patients to medical versus intracranial stenting.
It's important for these procedures that you recognize that once a registry has been established in the hospital, that that is a magnet for patients to not go into a clinical trial but instead go into a registry. You have to re-examine, what is the use of these registries, and when do they become an impediment to real randomized clinical gathering, a big problem for the NINDS trials.
It was mentioned, the difficulty with rehab after stroke, what is the appropriate rehab.
If it was treatment of a berry aneurysm that ruptured, or a subarachnoid hemorrhage, very high mortality rates, it's not clear whether surgery or endovascular technology is important, and unfortunately what the patient gets is determined by where they go, as opposed to being evidence-based.
We talked about PFO closure, and just to a mention, there was an attempt to do a clinical trial of PFO closure, the clinical trials could not enroll, and the FDA changed their requirements. There's a

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clot retrieval device which is used for acute stroke the first couple of hours after stroke. There was a series of patients and it was shown that if you pulled the clot out of the patients, the patients did better, as opposed to if you went in and didn't pull it out or you were unsuccessful.
That led to FDA approval of the device, but there was no randomized trial. The mortality rate in those series is about 50 percent, which is the highest you see in any trial. So it's not clear, you know, what is the net benefit. Sure, it works, it will help people if you can get the clot out. The question is, how much risk are you putting them at in attempting to try, and without a randomization technique, there's no way of doing that.
In many of these procedures we may have to, you know, because it's so difficult, we may have to go to some sort of a daisy analysis to get these trials done, to get some evidence as opposed to just a randomized one-for-one trial.
So, lots of other things, cardiac arrest, hypothermia, there's been a few trials but it's not really spreading across the country as it should, or maybe we need another trial.
I think my time is running out. I think I

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will end up with this last slide to kind of summarize my ideas. We need some mechanism where people can innovate to develop new technology, and that comes from the use of these devices and treatments in the community, but that's got to go through safety and performance testing, Phase Two trials, Phase Three trials. The more leakage we have in safety and performance to Phase Two, the more chance we'll never get the answers out of Phase Three, and that's kind of the theme I wanted to bring out today. Thanks very much.
DR. MCNEIL: Thanks very much, Dr. Koroshetz. You might have noticed that he had some new slides, so we will be making copies of those for the panel as well as for the audience. Thank you very much.

So now we have Dr. Turkeltaub from arthritis and metabolic disease.
DR. TURKELTAUB: Good morning everyone, and I thank the panel for inviting us to participate in this program. My remarks obviously will be involved with those mission statements or those mission areas that our institute is involved with, particularly osteoporosis, osteoarthritis, with osteoarthritis of the knee as a separate entity, and

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back pain as well. So, I would like to say that I don't envy the work of the panel identifying priorities in all of these very important areas. Osteoporosis is extremely important in this population. We're aware that it's a major problem and that there are risk factors, some of which we know, some of which we don't know yet, and some of which can be at least avoided. We know that a third of women over 65 have spine fractures, 15 percent of white women will have hip fractures, as has been covered by my colleagues, and that they can be treated and prevented if discovered before the major bone loss occurs. And so what we're doing and what we would recommend be done is that there be a good education related to providing the coverage and to providers of what can be done to prevent osteoporosis, and this has to be done from the earliest stages.
We know that the Surgeon General recently had a report that was put out on osteoporosis and there are many publications out there, but as previous speakers have indicated, information that may be out there may not be used. And so that becomes a major issue with regard to this population and the reality of the situation.

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The educational materials need to be enhanced, and they do provide us with some opportunities for additional research as part of the materials. Where should they go? Why aren't they being used? How are they accessed by diverse

populations? Are they targeted to the right populations? And do they really make a difference even when they are looked at? So we spend a lot of money on these materials in all of our areas of prevention, I think, so why aren't we having the effect that we felt we should?

With regard to educational programs, there's also little follow-up, so we really do need to look at prevention strategies, whether or not these prevention strategies are followed. We need to look at lifestyle changes and how we can best get people to incorporate lifestyle changes. This is for heart disease, cancer, stroke, anything that we want to look at.

The skeletal risks associated with smoking, for example. How many people are aware of that? And the need for calcium and Vitamin D intake, and who hasn't heard about Vitamin D these days? A big hot issue. What are the outcome measures that actually determine the effectiveness of prevention

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programs and how do we measure these? Is it different in men and women?

So, research opportunities. Who to treat and what to treat them with. Dexascan, although Dexascan has been used for many years now, there are still many issues related to even the use of Dexascan for determining the level of bone involvement in individuals. How are they interpreted, how are they standardized, how and when should they be used, in what population? There are some guidelines out there indicating women at age 50 should have a Dexa, but how often should they be followed up? What about the men, is that the best way of discerning bone density in males? Do we have the appropriate standards for comparison?

QCT is one of those procedures that is covered by Medicare, but we're really not sure whether QCT is an appropriate measure. Is it necessary, is it better than Dexa, is it better in men and maybe not in women? What are the standards for QCT? So we need to make recommendations with

regard to that.
Identifying markers is a big issue at
NIAMS, we are looking at markers for most of our
disease conditions. What markers will be predictive

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of fracture risk? What biospecimens can we look at
that would give us an indication of who might be at
greatest risk and what needs to be done for them and
at what point in time? Obviously a 50-year-old and
an 80-year-old with similar outcomes from a Dexascan
may need different treatments, and so we need to look
at age relation in treatments that are used.
Predicting fracture risk using both MRI
and ultrasound, looking at bone quality. Bone
quality is more than just mass or density, we're also
looking at bone strength. And so there are new
technologies that are being developed to look at bone
strength as well, which will give us better
indication of risk for fracture. So we're looking at
those types of technologies.
And looking at genes that affect bone mass
and can be targeted in the development of
osteoporosis therapies so that, what do we find that
stimulates bone growth? There are certain
populations where we see high density bone, we see
them in certain individuals. There's high density
bone on Dexa. But what causes that bone to be more
dense in some than in others? What can we find in
that population that will provide information for us
to continue the development of interventions?

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And then what to treat them with. Use of
bone morphogenetic proteins to stimulate fracture
healing or bony fusions would be very helpful in
developing methodologies for working with this
population, preventing fractures of the back or
fractures of the spine and so forth.
Combination therapies are what we're
interested in evaluating. The regimen of Vitamin D
and calcium, and in fact what are the best doses of
those. The low dose hormone in spine therapy,

hormone therapy and alendronate, for example, because these will decrease the amount of each of the components of the dual therapy and decrease the side effect chances or problems associated with them. Parathyroid hormone and alendronate, and cholesterol lowering statin drugs, maybe that will be a two-fer. Start them on the statins and you get better bone quality.

And then of course behavioral studies related to nutrition and exercise, and that is very important also in terms of shaping the type of lifestyle people live.

Now, osteoarthritis. Osteoarthritis is a very interesting question. Why do some people who do not have complaints of pain on x-ray actually show

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changes that indicate osteoarthritis? And vice versa, people who complain of pain don't have any changes showing up on x-ray. That's something that we found looking at our Osteoarthritis Initiative, in fact.

Cartilage is an understudied tissue and so we need to look more at cartilage. What is it made of and how does it change, what causes it to change during osteoarthritis, and how does it break down, and then how can we prevent that breakdown.

Actually in looking at and understanding this condition we also have to look at the opportunities that the Osteoarthritis Initiative has created for us. The Osteoarthritis Initiative is a research resource that NIH has, we have developed it with the National Institute on Aging, and it together with some of the databases at CMS might provide us with some additional information that we might be able to use.

Now looking at cartilage, we might look at, for example, the relationship of SERMS or the use of raloxifene on joint cartilage to see if that has any impact on the ability of the cartilage to sustain itself. We have had some studies looking at the use of doxycycline and the ability to prevent the

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destruction of cartilage, and we do have specimens that can be used for other researchers to maximize. We're looking at the effects of bisphosphonate on symptoms and pathophysiology, and in fact we do need to look at pathophysiology. How can we prevent rather than just treat. And then of course tissue engineering, one of our big areas of concern, how can we in fact develop the scaffold that will allow cartilage to regrow. When we look at research opportunities related to osteoarthritis, we also looked at identification of risk factors and prevention. Behavioral changes have been talked about, what do we do about obesity and exercise habits? We start with the young and we work to old age, but we need to look at these and see what can change behaviors. Clinical trials. Treatment of pain is very important to these issues. How much exercise is beneficial and how much is too much? And again, the effect of Vitamin D on knee OA.

DR. MCNEIL: Dr. Turkeltaub, you have two minutes.

DR. TURKELTAUB: Yes, thank you. When we look at OA, we're also looking at the evidence report

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from AHRQ, and I notice somebody from AHRQ on the panel. They recently came out with a publication that reviewed intra-articular viscosupplementation, oral glucosamine and chondroitin in combination, and arthroscopic lavage or debridement for knee OA. And yet, the best available evidence does not clearly demonstrate clinical benefit. So the recommendation that NIAMS supports is to have clinical trials that are multi-center and that are RCTs. So we have many opportunities for research in knee OA, from looking at the types of invasive surgery and joint prostheses that can be used to investigating the role of exercise in protecting the knee. In terms of back pain, we'll do this quickly although it's probably the major area, as

anyone among us know, or don't know somebody who has back pain. But we're looking basically at the effectiveness of surgery versus nonsurgical treatment for low back pain. We've had a major study that's indicated that there are times when surgery is as effective or not as effective as not having surgery, so it's still up in the air. What do we do about it? How can we determine and at least try to predict who is going to benefit from this type of procedure? So predictive elements are very important,

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and that gets back to some of the biospecimens and the ability to have predictors in that area. Disc degeneration, who will get it, how can we prevent it? Who will better benefit from the lumbar fusion or the use of artificial discs? Who can tolerate the use of artificial discs, what material is best to be used in that arena? And then disc arthroplasty or degenerative disc disease at the cervical and lumbar spines.

These are all the major issues that we're looking at right now that will, we feel, have a great impact on the Medicare population, and we look forward to working with you on these.

DR. MCNEIL: Thank you very much. So let's see, I think Dr. Ferris appears not to be here; is that correct? So I think what we'll do, my sense is there will be a fair amount of discussion to drill deeper into some of these presentations in order to get some greater specificity on some of the clinical service that might be relevant to the major bullet points that were mentioned by many of the speakers. But before we do that, what I would like to do is ask for our public, those individuals from the public who wanted to speak, to start. So the first one will be Steve Glassman and Daniel Resnick,

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who are both orthopedic surgeons, and they will be followed by Randy Burkholder and Ann-Marie Lynch.

DR. GLASSMAN: Good morning. My name is Steve Glassman, I'm an orthopedic surgeon from

Louisville, Kentucky, and I'm here on behalf of the Professional Society Coalition Task Force on Lumbar Spine Fusion. My conflicts are that I'm a consultant and receive royalties from Medtronic and I receive research support from Medtronic and from the Norton Healthcare System.

The Professional Society Coalition Task Force has been formed by the constituent societies which represent the vast majority of spine surgeons in the United States. The purpose of the task force is to advocate for and promote an improved evidence base with regard to lumbar fusion surgery. The task force is also intended to provide improved communication with CMS regarding available evidence and the efforts of our members to improve that evidence.

As we're all aware, lumbar degenerative disease is a common clinical problem and the burden of the disease in the Medicare population is growing with the aging demographic. Many existing treatment options, but surgical and non-surgical, are resource

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intensive. As an example, AHRQ data suggests that the number of fusion procedures grew by 73 percent from 1997 to 2005. At the same time insurance claims data documented substantial increase in the use of epidural steroid injections, which is a non-surgical alternative which also faces the problem of the widespread use despite suboptimal proof of efficacy.

Based on these issues and the fact that spinal fusion has been used as a comparative standard for newer technologies, CMS convened a Medical Coverage Advisory Committee on fusion about a year ago. At the MCAC meeting there was disagreement about the inherent quality and appropriate interpretation of the existing literature, but there was broad agreement that the evidence base was inadequate for most fusion patients.

A major limitation which might be improved through collaboration with CMS is the lack of any reasonable diagnostic specificity in our present coding and data collection system.

The primary question of last year's hearing was whether spinal fusion was an effective treatment for low back pain. The problem is low back pain is a common symptom, not a diagnostic entity. So asking whether fusion is helpful to low back pain

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is like asking whether antibiotic treatment is effective for shortness of breath. In either case the answer will be completely dependent on the specific etiology of the symptom.
One consensus conclusion of the MCAC hearing was that better studies comparing surgical and non-surgical treatment are necessary. The inherent problem is that our preferred study design, a randomized trial, is not well suited when comparing these treatment options. The dilemma is that failure of conservative treatment is regarded by most surgeons as a prerequisite to fusion surgery. Therefore, if a patient is randomized before they fail conservative treatment, they don't have standard surgical indications and may not be good candidates for surgery. If on the other hand a patient is randomized after they fail conservative treatment, then the non-surgical arm of the study is simply repeating the treatment modalities they've already failed. This inherent dilemma is the likely explanation for high unilateral crossover rates which have plagued most RCTs for spinal fusion. Additionally, there's little available evidence supporting our standard medical treatments for lumbar degenerative disease, and therefore a

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consensus non-surgical regimen isn't readily available.
We believe that by working in collaboration with CMS, the difficulties in balancing methodology and clinical relevance can be bridged such that future studies generate data which is considered meaningful by a broad range of stakeholders. At the conclusion of last year's MCAC hearing, CMS expressed its intention to work with

professional societies and others to improve the available evidence base. Our goal is to pursue that collaboration.
Since last year's meeting there have been several studies that have added to the existing evidence base and improved our understanding of appropriate roles for fusion. The most notable, which was just mentioned, is the SPORT study, and NIH-funded randomized controlled trial. Although some controversy exists with regard to study methodology, SPORT has clearly raised the bar with regard to evidence for spinal surgery.
I would now like to turn over the podium to Dan Resnick from Wisconsin, to talk about potential avenues of collaboration.
DR. RESNICK: Hello. My name is Dan

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Resnick, I'm a neurosurgeon from the University of Wisconsin. My conflicts are that I am a consultant for Medtronic, I've received research support from the American Association of Neurological Surgeons and Congress of Neurological Surgeons.
At the conclusion of the MCAC meeting in November 2006 we were charged by CMS to basically get our house organized. Representatives from every major spine society have gathered in order to form the lumbar fusion task force. We have representatives from the North American Spine Society, the Scoliosis Research Society, Congress of Neurological Surgeons, the American Association of Neurological Surgeon, and the American Academy of Orthopedic Surgeons, so basically every spine surgeon in the United States is represented by this panel.
The purpose of this panel is to serve as a clearing house and advisory panel for outcomes research regarding lumbar fusion surgery and the treatment of low back pain by either surgical or non-surgical means. The makeup of the panel draws from all specialties related to the surgical treatment for low back pain, to include both skeptics as well as proponents of lumbar fusion. We've included curmudgeons as well as innovators in terms

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of the treatment of spinal disease. And what we hope to do is partner with CMS and with the other funding agencies to try to answer some of the funding problems, in terms of identifying effective treatments for these modalities. One of the main problems we have, as Steve alluded to, is we don't know who is getting fusions and why in the Medicare population. Lumbar fusions were, the literature base reviewed at the MedCAC panel specifically dealt with a 40-year-old patient population with degenerative disc disease. That's not who the MCAC or CMS is interested in, and does not reflect the fact that Medicare patients receiving this care are almost always being treated concomitantly for another disorder such as lumbar stenosis which limits ambulation, which you heard is a major predictor of morbidity in that population. Such as a radiculopathy, such as compression fractures, which are another source of morbidity. So we need to know who is getting treated for lumbar degenerative disease in the Medicare population, and we need to consider methods to improve the specificity of the diagnostic description in order to enhance the analysis.

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The main message we want to convey to this panel is that while lumbar fusion doesn't appear to rank more than a rounding error in terms of the overall expenditures of CMS when you look at the other disorders being considered, we feel very strongly that lumbar fusion in the Medicare population is something worthy of investigation. We are here and ready and willing to partner with the CMS and the various funding agencies, and we share your enthusiasm for providing strong evidence-based and effective treatments for our patients with low back disorders who are in the appropriate demographic for CMS. Thank you very much.

DR. MCNEIL: Thank you very much.

Dr. Weintraub, is he here now, from the AHA.
DR. WEINTRAUB: Good morning and thank you very much. I'm here representing the American Heart Association this morning. I have a number of industrial grants but no conflicts as far as this presentation is concerned.
So, which disease represents the greatest burden for Medicare beneficiaries? We've heard about it all morning, haven't we? It's cardiovascular disease. It's the number one burden, it's the most common cause of death in our society. The number of

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beneficiaries consuming resources will be greater for cardiovascular disease than for any other entity.
One in three American adults have some form of cardiovascular disease. The most common, as you've already heard, is hypertension, and of course which is most common in the Medicare population.
What are the most common diseases?
Coronary artery disease is the most common source of death, acute myocardial infarction. This has actually decreased over the last 40 years by some 40 percent or so but there are still in the range of 800,000 acute myocardial infarctions in the United States every year, and most of those are going to be in Medicare beneficiaries.
Congestive heart failure is actually the most common cause of hospitalization in the Medicare population, and consumes resources similar to that for coronary artery disease.
Arrhythmias, particularly atrial fibrillation, are also a major problem and a major source of resource consumption. And of course stroke is as well and is the number three cause of death after cardiovascular disease and cancer.
Our major risk factors are all well known to you and require intervention really throughout

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life, and those are systemic arterial hypertension, hyperlipidemia, obesity and glycemic problems. And while we've done well with other risk factors, not as

well as we should in the control of hypertension and hyperlipidemia, obesity has actually gone in the other direction and has been getting worse, especially in young people. And as obesity has increased, of course Type II diabetes has increased with it.

Cardiovascular disease is our number one cause of mortality, has been on the decline, and this has been going on for years, since the 1960s, but remains our number one cause of death.

Cardiovascular disease is responsible for over 800,000 deaths per year, 36 percent of all deaths are caused by cardiac disease. Heart disease is our number one killer, and stroke, as I just said, is number three.

You also have lots of people who are surviving coronary artery disease. We heard that from Dr. Savage earlier this morning, more and more of our patients are surviving, and since they're surviving, one of the things that has come along with this is an increase in the number of patients with heart failure, and there our situation is not quite

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as good as it is in the treatment of heart attacks or risk factors.

While we decreased the in-hospital mortality over the last number of years from heart attacks from some 15 percent more to a rate of 7 percent, the long-term consequence are again not so good and, well, it says here, 38 percent of patients who have a heart attack will ultimately die of it.

If you think in long enough terms, people who have a heart attack, ultimately we know what the cause of death in most of those people is going to be.

And so while we've done well in risk factors in some areas and not as well in many of them as we would like, some things are increasing problems. The aging of a population, especially as the baby boomers move into the Medicare population over the next several years. We have rising obesity rates, especially rising obesity rates in young people, as I have already noted. We do have improved

outcomes in heart disease. One of the things that we are seeing is also improved outcomes in congenital heart disease.
Now we're so focused in cardiovascular disease in the Medicare population that congenital heart disease sometimes is overlooked and it really

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shouldn't be. Congenital heart disease is the number one cause of birth defects in our society, and as we've done better in the treatment of congenital heart disease, we now have large numbers of adults with treated or partially treated congenital heart disease, somewhere in the range of one million adults now with congenital heart disease who also require care.
So, which diseases and their treatments are the costliest to the Medicare program? Overall cardiovascular disease, overall costs of cardiovascular disease in our society, a really stunning number. In 2007, some $432 billion. And here's a little bit of a breakdown of these costs: Coronary heart disease, 152 billion; stroke, 63 billion; hypertension, 66 billion; and heart failure, 33 billion. Now we see this figure for heart failure and I think it's really an underestimate, because some of those costs have really shifted into coronary artery disease.
So heart disease being the leading cause of hospitalization, especially in Medicare beneficiaries, while we have decreased cardiovascular events, we have increased procedures rather dramatically, from 1979 to 2004 by 432 percent, a

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really rather scary number. In 2004 there were 6.3 million inpatient cardiovascular procedures.
Cardiovascular disease, we have an error here, because it says $29 million, but it cost $29 billion, but it's only three orders of magnitude off.
And here are our procedures. PCI, some 663,000 procedures. Coronary artery bypass surgery, 215,000. 638,000, that's probably low, for

diagnostic cardiac catheterization. And valve surgery and pacemakers also remain quite common.
DR. MCNEIL: You have two minutes.
DR. WEINTRAUB: Okay. So overall costs of cardiovascular disease, very high, as you see here, estimated costs to Medicare. We also are spending a lot on prescription drugs in the Medicare population, some 15 billion in 2003 anti-hyperlipidemic drugs, 8 billion.
Where are our deficits in knowledge?
Certainly about congenital heart disease.
How do we approach the problem of increasing the evidence base? We do need additional research funding, basic, clinical and healthcare delivery. And I would add, epidemiologist and outcomes investigator funding, as I think Dr. Savage from NHLBI would agree, is not what we would all want

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it to be.
What diseases and their treatments are most critical to the evidence base? Acute myocardial infarction, how to treat it, how to deliver care remains a major source of concern, as does congestive heart failure and how to use more advanced forms of therapy such as ventricular assistive devices.
Arrhythmias and the use of ICDs remains expensive and an area of investigation. We need more research in peripheral arterial disease and we need to learn yet more about stroke, its prevention and care.
So thank you very much for listening to me this morning. Any brief questions?
DR. MCNEIL: No, we'll hold the questions. Thank you very much. So the next speaker will be Randy Burkholder, from PhRMA.
MR. BURKHOLDER: Thank you. I'm going to be speaking without slides briefly this morning. My name is Randy Burkholder, I appreciate the opportunity to speak to you today on behalf of the Pharmaceutical Research and Manufacturers of America. We represent the nation's leading pharmaceutical and biotechnology companies, and they invest $433 billion annually in research and development.

25 As a result of that investment, each new

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1 medicine brought to patients is backed by extensive
2 scientific and clinical research, and we strongly
3 support the development of such evidence to support
4 good decision-making in healthcare. We appreciate
5 the opportunity that CMS has provided for us to
6 provide input on this topic today.
7 I would ask CMS and the advisory committee
8 to consider three basic points today. Two of those I
9 believe have already been addressed by a number of
10 other speakers, so I will move over those more
11 quickly. One of those is the value of considering a
12 broad research agenda, one that looks not only across
13 the healthcare system and the range of interventions
14 and care processes, and management delivery
15 mechanisms that can impact patient outcomes, but also
16 at questions that can give us insight on how we can
17 do a better job applying what we already know works
18 in healthcare.
19 The second point that I think has been
20 brought out already that I again will touch on
21 briefly, is the utility of considering a broad range
22 of policy mechanisms in relation to this research
23 agenda and research priorities.
24 The third point and one related is the
25 value of CMS and MedCAC considering what has already

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1 been generated through existing priority-setting
2 mechanisms as they go about their work today.
3 So first, briefly, CMS and MedCAC should
4 consider all aspects of healthcare delivery that
5 affect patient outcomes. This includes not only
6 pharmaceuticals and medical technology certainly, but
7 also processes of care and approaches to care
8 management and delivery. The concept of a broad,
9 integrated, research agenda base is not a new one,
10 but it is one that has yet to be fully translated in
11 practice in the United States.
12 John Eisenberg, as I'm sure many of you
13 know, the former director of the Agency for

Healthcare Quality and Research, made this point in a 1999 article in JAMA when he said, the organizational and structural changes to the healthcare systems should be subjected to the same rigorous evaluation that would be used for a new drug or device. More recently, Doctors Elliott Fisher, Michael Coe and Don Burwick, among a number of others, have made similar arguments in recent years. Addressing this issue just earlier this month at the Institute of Medicine, Dr. Fisher from Dartmouth Medical School said we need better evidence both about biologically targeted interventions, but also

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about care delivery. I think it is critically important that we broaden that focus to include evidence-based care management and evidence-based care delivery. Research that's recently been conducted and supported by both AHRQ and Case Western Reserve University demonstrates the effect of increasing co-pays on patient adherence. That offers just one example of a way in which evaluations at the care delivery benefit and design level can benefit patients and ultimately benefit the healthcare system. This study found that the effect of raising co-payments from six dollars to ten dollars resulted in increased patient noncompliance with prescribed treatment, leading to a $125 million reduction in drug costs annually but also an increase in costs overall of $360 million annually as a result of increased complications. So secondly, CMS and MedCAC should look to existing priority-setting mechanisms. Under the effective healthcare program for comparative effectiveness of research, AHRQ and CMS have established a set of priority conditions as the focus of HHS research efforts. AHRQ is to be commended for the implementation of an open and transparent process

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for receiving input on research priorities under this program.

In describing this effort at a listening session in 2006, CMS officials explained that the two agencies had jointly selected ten conditions affecting Medicare beneficiaries. MedCAC should consider the public input AHRQ has received through this process and in particular place a priority on those research areas identified by stakeholders but not yet implemented by AHRQ.

Two brief examples of those types of recommendations, again, that illustrate the value of looking at a broad and integrated research agenda as we consider Medicare research priorities. One was the University of Colorado Health Science System, which noted that relatively little attention has been paid to problems faced by older patients receiving care across multiple settings. They noted that most older patients with complex needs often are receiving care from a variety of different caregivers across different settings and that more research is needed on the best and most effective ways to integrate that care delivery. Another effort in this area, attention to strategies to ensure Medicare patients safety would be paramount.

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Similarly the American Heart Association, who we just heard from, emphasized the value of additional research to better understand how we can address the problem of medication nonadherence, noting that this represents an opportunity to improve the healthcare needs of American seniors, as well as to take steps that could save the Medicare program significant funds in the future. And AHA noted that the costs of patient noncompliance with respect to a prescribed therapy are estimated at approximately $177 billion annually.

Third and finally, CMS and MedCAC should consider mechanisms beyond the national coverage process to address research priorities. On some questions of primary importance to Medicare beneficiaries, such as those related to coordination of care and medication treatment adherence, are beyond the scope of coverage policy. And in

addition, linking the conduct of research and analysis that needs to be rigorous, independent and impartial, to a high stake, high impact Medicare process at times can be of questionable utility. We believe other policy mechanisms such as demonstrations which have been cited by other speakers today offer a valuable approach to

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addressing many of these questions.
Again, we appreciate the opportunity to present before the advisory committee today and we look forward to continuing to take part in this discussion. Thank you.
DR. MCNEIL: Great, thank you very much.
So Ann-Marie Lynch, from AdvaMed.
MS. LYNCH: Thank you very much for the opportunity to be here this morning. My name is Ann-Marie Lynch and I am here on behalf of AdvaMed, the Advanced Medical Technology Association. AdvaMed member companies produce medical devices, diagnostic products and health information systems that are transforming healthcare through earlier disease detection, less invasive procedures, and more effective treatments. AdvaMed's members range from the largest to the smallest medical technology innovators and companies.
Thank you for holding this MedCAC meeting and for soliciting public comment on your effort to assist CMS in developing priority areas for generating evidence that will impact the health of Medicare's 42 million beneficiaries.
AdvaMed understands that generating evidence to inform physician-patient decision-making

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is an important matter deserving of full public discussion. We in the medical device industry believe that the needs of Medicare beneficiaries are paramount, and that better evidence will result in improved clinical outcomes and enhanced beneficiary access to high quality care.
AdvaMed asks each member of this MedCAC

panel to consider the following principles as you develop a priority list of research topics:

First, CMS should focus on areas of research that will have an impact on improving care for diseases and medical conditions that are widespread among Medicare beneficiaries, as you heard this morning. Specifically, we recommend that the evidence generation priorities begin with research involving health system changes that will affect the management and delivery of healthcare items, service and procedures. In this context, the priorities include changes to improve chronic disease management.

As you know, and we saw many specifics this morning, an estimated 45 percent of the U.S. population has at least one chronic condition, and at least 60 million individuals have more than one chronic condition. Chronic illnesses are responsible

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for 70 percent of deaths, 76 percent of acute hospitalizations, 88 percent of prescriptions filled, and 72 percent of all physician visits. Healthcare costs are estimated to be two times greater per year for individuals having one chronic condition, and 14 times greater for individuals having five or more chronic conditions.

Secondly, we commend CMS's efforts to conduct this process of developing evidence development priorities in a fashion that allows for stakeholder input through the MedCAC process. Openness and transparency in the determination of research priorities will enhance the credibility and strength of the ultimate conclusions of any evidence development efforts. We urge CMS to continue efforts to involve stakeholders in evidence development priority-setting going forward, and that the stakeholders include patients, physicians, hospitals, and experts from the medical device and diagnostics industry, who often have a unique understanding of specific devices and technologies, among others.

Third, I ask that you note the immense heterogeneity that exists among medical device and

diagnostic technologies. Depending on the type of medical technology you may suggest for a study, there

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may be considerably different study design challenges with very different types of evidence generated for each based on the unique demands and limitations of studying each technology. A one-size-fits-all approach to evidence development for medical devices and diagnostics simply would not work. We urge the MedCAC and the research community as a whole to recognize and make methodological allowances for this diversity.

Fourth, generating evidence on new technologies and procedures can be a challenging task. Medical device technologies, both therapeutic and diagnostic, often pose difficult technology challenges due to their rapid evolution and short life cycles compared to pharmaceuticals. This rapid innovation cycle is the result of constant efforts to make improvements to help Medicare beneficiaries and other patients. To ensure that any research performed is useful, it should be applicable to the current generation of technology.

Finally, new medical device and diagnostic technology effectiveness depends in part on user training and experience. Early assessment of a device may incorrectly state its effectiveness. Accordingly, researchers should consider the effect

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of training and experience upon outcomes, and should only conduct assessments when the technology has an experience base and is widely available. Likewise, those using these studies should recognize the challenges and limitations of evaluating medical device technologies.

Again, we appreciate the opportunity to comment in this public forum and welcome future opportunities to communicate with CMS and the MedCAC regarding the development of evidentiary priorities.

Thank you very much.

DR. MCNEIL: Thank you very much as well.

Now I understand there is nobody from the audience who has made a request to speak. I want to make sure that's correct before we move on. A quiet crowd. Okay?
All right. We've had lots of speakers with very many different points of view. I was trying to keep track of the kinds of things that were being said today and I have four categories, and there may be more. Let me tell you what I have down here.
I have several individuals talking about basic research problems that need to be attacked. That's not our agenda, for example, issues of

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co-payments. That is not the kind of thing that we will be addressing today, or basic level of disease. While these are all critically important to most if not all of the agencies that are here today, we will not be talking about those specific aspects of things.
The second general area that I heard a lot of comments on was the issue of care coordination, and I think we probably do want to talk about that. I would like to hold that discussion, though, until later, because I think that came from many different speakers from many different diseases, and we'll have to figure out how to actually talk about that, because care coordination per se isn't really specific enough for our purposes.
The third general kind of, the third topic or area that I heard discussed was specific clinical services, and I think the representative from neurologic diseases gave us about 20 very specific clinical services that we should consider. Bypass surgery versus medical therapy, there were a whole bunch of things. Those are definitely on our agenda.
And the fourth area was some general clinical areas, like better treatment for acute heart attacks, I think the AHA had some examples of that.

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Those we can talk about in the context of some

specific examples under each one of the generic groups.
So, did I miss anything in terms of the generic approaches? Barry.
DR. STRAUBE: Barbara, this may fall into one or several of the categories, but I heard just about everybody talk about prevention also, prevention and I suppose risk factors or risk predictors.
DR. MCNEIL: That's true.
DR. STRAUBE: So that might be a separate area.
DR. MCNEIL: And actually the other one was surveillance, particularly by heart and lung and cancer, so we should put those on the list and figure out how to make them a little more specific. Okay.
So let us ask questions of the panelists.
So Leslie, I think you --
MS. FRIED: I just had two more things to add to your list that I heard. One is, almost every person spoke about comorbid conditions and I think that's something we may somehow approach. And the other was the optimal strategies to treat people in primary care settings, so it's a broad approach.

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DR. MCNEIL: I think that's part of the first one.
MS. FRIED: I was thinking of the idea of annual physicals or something like that which could be a covered service at some point.
DR. MCNEIL: Well, I don't think we should be looking at coverage so much. I think we're trying to identify high clinical, potentially highly valuable clinical services for which there is an evidence gap.
MS. FRIED: Well, okay.
DR. MCNEIL: I mean, I think that's our charge; is that correct?
MS. FRIED: I was under --
DR. STRAUBE: Well, I think we talked about this at the beginning and I think it's primarily focused on evidence gaps that we would like

to help guide us in terms of where we go forward with our coverage decisions, but it's also in a larger context of evidence that will help us inform patients and clinicians and others how best to use those services.
MS. FRIED: I heard a lot of folks talking about screening and other things, if they were done early that we could then identify, treat and assess

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earlier. So my thinking is, how does that happen if people just go to the doctors when they're sick.
DR. MCNEIL: Okay, got it. Linda, did you have a question or comment?
DR. BERGTHOLD: I think there are sort of two kinds of umbrella issues that maybe are important to all of the things that we're going to talk about that folks mentioned. One was the relative lack of Medicare beneficiaries in clinical trials, the importance of getting more of this population into the trials. And the second is the importance of looking at comorbidities in the trials, so we're not focused on a single condition. So if we could sort of put those two things as, I don't know, overarching, I hate that word, but overarching issues or questions, something like that.
DR. STRAUBE: It comes to mind that we do have some barriers that probably should help us to try to limit what's a very broad discussion. Namely, there are a number of issues that were raised and may get raised that are not part of the Medicare program. Specifically we've used the term screening, and screening services are at the moment not covered benefits. So we have to be a little bit guarded in terms of how much we talk about that particular area,

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because it would be dependent on Congress to add those services before we could even cover them. Preventive services are a good example the same way. When the Medicare program started, there were no preventive services, and those have been added sequentially by amendments to the Social

Security Act such that there are some but not all preventive services added. So in terms of prioritizing things that aren't covered under Medicare, we probably ought to put those on a second panel discussion in the future.
DR. MCNEIL: Sean.
DR. TUNIS: Yeah. Is this an opportunity now to ask questions?
DR. MCNEIL: Well, I just want to make sure that nobody has any other general comments. Yes, Nancy?
MS. DAVENPORT-ENNIS: I just had one general comment, Sean, and then we'll come back right back to you. But likewise, I notice that a number of people did talk about the issue of comorbid conditions, but a number of people also, and I don't know where this would fit, and perhaps it would fit into one of the global areas that have been identified, but there was much reference to the role

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of obesity in the diagnosis of so many diseases, the need for more study of the role of obesity. And also much discussion, particularly from the osteoarthritis community as well as others, about the role of mobility, which and how do you incent choices that enhance mobility.
So if there is a way that we can put these two items under one of the others that have been called out, perhaps within care coordination, within that discussion, how do you go near that, or even specific clinical services, if part of the review on clinical services could include that.
DR. MCNEIL: That's a great comment. Why don't you think about how to do that as we carry on.
MS. DAVENPORT-ENNIS: All right. So I may be interrupting frequently with comments.
DR. MCNEIL: Terrific, that's your role. Let's see, were there any other general comments before Sean asks the first question of the presenters?
MR. SCULLY: Just one other general comment that won't make your agenda, but the biggest

change in the Medicare program over the last four or five years is the fact that we've got 20 percent of people in Medicare participating in screening and

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that number is going to keep growing, and while I know that we don't make coverage decisions there, there are completely different behavioral trends I'm told, like cancer screening, dialysis services, and there's been very little to no research showing whether people are better off or not, especially with risk assessments.

Now that the insurance companies seem to want to find sick people and do lots of preventative care, tracking that and showing what's the difference between, if one of the plans can save 60,000 bucks a year per person per year whether they do provide better preventative care, or whether somebody on dialysis actually gets different care. So whether you agree with the policy, this is a huge growth in this direction, it has probably gone from 20 or 25 in the last few years, and we don't really know if it's a good idea or not, so I think it's a pretty critical thing.

I know you're more focused on traditional fee for service programs, but tracking the parallel behaviors there I think is important to look at.

DR. MCNEIL: Agreed. Sean, do you want to start us off?

DR. TUNIS: Maybe I could make one more

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general comment too to see if this fits into a separate category. One of the things I heard from a couple of the presenters was examples of effective services like coordinated care, falls prevention, et cetera. I think they were recommending evidence development around basically how to get those more broadly adopted, you know, through demonstration programs, et cetera. So I'm wondering, you know, is that sort of within the scope of what we're wanting to talk about, you know, in other words, things for which the evidence of effectiveness exists but they

are under-disseminated or under-utilized, and so you see some kind of a demonstration or other mechanism to try to expand, you know, expand their use.
DR. STRAUBE: No. I think definitely it is, Sean, because it could be done through coverage purposes or processes, but it could be through pay for performance or other incentive programs, public reporting in terms of quality outcomes and results, so I think that's absolutely an extension.
DR. TUNIS: Okay. The question I was going to ask to any of the presenters who care to respond to it, it goes to the issue which CMS faces frequently, which is, there is a mismatch between the timing of rigorous clinical trials and when CMS is

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frequently called upon to make either a payment or a coverage decision. So, I think there are several examples of large NIH-sponsored trials for which it seems to be too late for CMS to do anything with the information.
There was the MIST trial by NIDDK which was a comparison of minimally invasive interventions for BPH to maximum medical therapy. That trial I think is in year two of a five-year trial, and I think we have been paying for almost all those, Medicare has been paying for almost all of those interventions for years already, and you know, TUNA and TUMP --
DR. MCNEIL: Can you explain what those are?
DR. TUNIS: TUNA is transurethral needle ablation, TUMP is transurethral microwave something.
DR. MCNEIL: Okay.
DR. TUNIS: You know, there are several others, and as Tom well knows, they are sort of well reimbursed. And so the randomized clinical trial would be an important priority, I think, for evidence for CMS coverage and payment decisions. You know, but it would have only been useful had that trial been started three or four years ago.

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Now we have a similar situation, if I can give one more example, you know, proton beam therapy for treatment of early stage prostate cancer, following on intensity modulated radiation therapy, following on earlier forms of radiation, and Medicare has already made its payment decisions around IMRT, you know, and may or not make one around proton beam. I think a recent AHRQ evidence review called for large head-to-head studies, but you know, any study started today will be delayed some years. The last thing I will mention is one the presenters talked about the missed opportunity of drug-eluting stents. And we can all, you know, go back to the decision several years ago by CMS to pay kind of a bonus payment for drug-eluting stents leading to, or partially leading to a fairly rapid clinical adaption, and perhaps there was a missed opportunity to generate evidence at that time. So the broad question I'm wondering if any of the institutes could comment on is the feasibility of launching very early prospective evaluations of some of these technologies in time to provide the evidence that Medicare would need.

DR. MCNEIL: That seems like a terrific question. I wonder who wants to be the first person.

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The enthusiasm is overwhelming.

DR. SAVAGE: I think Sean has touched upon a very important issue and that is the process by which the NIH generates the approval for large clinical trials and so forth takes some time. And inevitably a technology, particularly an attractive technology will appear on the scene, and there isn't time to wait five years for a standard clinical trial to be done. So that, I guess the only thing I thought of that, or the only two things I thought of that could be relevant to this, one is to track fairly carefully what's going on in a group of patients in which this technology is being used initially, so if something unexpectedly is going to show up, you'll know about it relatively soon, rather than eight or ten years later when it becomes

apparent to everyone. The other is the question of whether or not if the technology looks very promising, and the drug-eluting stents certainly did in terms of addressing one of the problems that existed with the earlier stents, is there a possibility of giving some sort of approval that would be contingent upon a formal trial going forward and then a final decision as to whether there would be continuous coverage

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after the result of that trial has ended.
DR. STRAUBE: Dr. Savage, that latter comment that you made, that's what our coverage and evidence development policy pretty well addresses. Although I think we have some things we're struggling with in that, in terms of there's probably so many technologies, devices, services, et cetera, that could potentially be at that stage where you want to do that, and we might, the question for Medicare is going to be how many of those are we going to put into coverage for evidence development, and we had intended initially when we opened it up to have it be a rare occurrence. It's seeming as though the demand may be more than what we had expected before, and I think Sean's question partly gets at that. We're hoping that there's ways that industry, the academic community, et cetera, might be able to figure out how to answer the question sooner, kind of knowing what we will end up asking for.
DR. SAVAGE: And I think we had experience with the drug-eluting stents in that it was talked about, finally a group of investigators came in and said they wanted to do a study. We decided it would be better to do a randomized trial than just do some

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sort of a registry. And then the process of getting the application and getting it through the system and so forth inevitably takes long enough so that in the case of the stents, the FDA went ahead and approved the devices and there was an explosion in their use,

and then it became hard to do a study in the United States.
So I think it is, particularly for an attractive technology that looks like it could be a major advance, it is a significant problem. But the idea of letting it go ahead with a final decision to be made when the final results are in could be the best way.
DR. MCNEIL: Can I ask just one clarification question on this? It's my understanding that most of the coverage development approaches have involved registries. Which ones have been RCTs?
DR. STRAUBE: Well, we used registries with the ICD, but we had some problem with off-label use of cancer drug, PET scanning.
DR. MCNEIL: But there are no patients in it, right?
(Discussion off the record.)
DR. STRAUBE: They are not recruiting well

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but they are set up to be used in that manner. Some of this is contingent also, we're struggling with our clinical research policy and what the criteria ought to be for that.
DR. MCNEIL: But just to pursue it a second, so there is a randomized clinical trial on off-label drugs in cancer?
DR. SCHRAG: Colorectal.
DR. MCNEIL: We're sure it's an RCT? Is the NCI here to confirm that, just to answer this question, are we sure this is an RCT?
DR. TUNIS: Which one?
DR. MCNEIL: Colorectal off-label drugs.
DR. TUNIS: Yeah, those were studies that NCI had already planned to launch at the time that the Medicare coverage decision was made. The one other example of an RCT CED, well, other than the NET trial which was the original one in the '90s, that was a randomized trial before CED. The one that hasn't worked so well is the national coverage decision on PET scanning for Alzheimer's disease

which, the coverage policy would allow for coverage for PET scanning for Alzheimer's in the context of a randomized trial, one has been developed, but it has not been able to obtain funding.

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DR. STRAUBE: The other randomized clinical trial was the use of oxygen in the home setting.

MR. SCULLY: Can I just comment on two of these things? Part of the problem here is just bureaucratic unresponsiveness between agencies. I go back to, I think I made up with Sean's help the higher code for drug-eluting stents which created the methods that they had, because we couldn't make it a higher code which allowed hospitals to get paid. Part of the problem, though, was we created that code six months before FDA approved it, because the hospitals were going crazy. Plus there was zero under the law, FDA couldn't tell us anything, and unless something's changed, CMS finds FDA is approving products using the New York Times. And people don't understand that, because FDA can't share anything if it's proprietary at the time. So people come in the day after the FDA's approved something and say where's my code, where's my coverage, and the reality is CMS knows nothing at all in most cases, which is a huge problem. I'll give you another example, where FDA (inaudible) functionally equivalent, which caused quite a little stir, and Secretary Thompson asked

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NIH, NCI to do a study at that time of the appropriate dosages of EPO and how it should be worked. That was four years ago, and then (inaudible) the last six months if they had done something on it for the past four years, but I didn't see any evidence that that happened.

DR. MCNEIL: Okay. So Mark and then Debbie. Mark Hlatky first.

DR. HLATKY: I guess I had a question. Our charge is to look at major gaps in evidence and

what kinds of evidence. The question I had is what kind of evidence should we try and promote here, and I guess I had thought about trials as the primary kind of evidence that most people would accept, but one of the speakers, and I can't remember which one, had mentioned there were some registries which are also very useful, and their point was it seemed to be an either/or rather than a complementary thing. I wondered if we could, I'm curious about hearing what the problem is in terms of the, are the registries going to kill off the trials, is that, do we have a big problem here in terms of gathering evidence and what kind of evidence, if you will, is admissible for this.

DR. MCNEIL: Is there a reason you wanted

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to ask that question?

DR. HLATKY: One of the speakers made a comment about the registries interfering with trials and I'm wondering if I could hear some more about that.

DR. WEINTRAUB: I guess I could expand a little bit. You know, in terms of something like carotid artery stenting, you're talking about something that's really quite politically complicated. You're talking about a new field, like cardiology, coming into a field that was dominated by vascular surgery. So the question that's out there on the table is not just what procedure is better, but which field, which specialty society is going to take over the field. There's a lot of ego there, a lot of politics, there's a lot of hospital decision-making on where the resources are going to go.

So we have, NIH has a randomized controlled trial of stenting versus endarterectomy. We're trying to enroll about 2,000 patients and it's hard enrollment, and yet, you know, tens of thousands of patients are going into registries. And the registries are basically picked up and unfortunately used as a tool to establish turf. And so it really

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complicates the decision-making. And also, you know, if you're a procedurist and you're being paid, you know, a significant amount of money, thousands and thousands of dollars to do a procedure, and then you're asked to randomize, that means your income is cut in half automatically. So I think the registries will kill clinical trials in reality, and so I think they should be really post-clinical trials and they should be put on hold if a clinical trial is out there. Otherwise, you're never going to get the answer. The taxpayer pays tons of money to NIH to do these trials, they don't get done, it becomes more and more expensive. It's just not in the public health's benefit, and the registry should be reserved until after the clinical trials are done. The issue of can you get the clinical trial done in time, that's, as Dr. Savage mentioned, that's a real problem. That's where maybe we need a better coordination between CMS and NIH to get the data out there in time. But it clearly is a slow process and that's an inherent problem too.

DR. MCNEIL: That is a really critical question you've raised, and I'm trying to decide whether we should take time to speak about it or

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whether we should hold it. What do you think, Barry?

DR. STRAUBE: I think continuing on just a little bit might be appropriate if other people have comments.

DR. HLATKY: If I could just follow up on that, I'm sure that one of the issues often talked about is a lot of trouble enrolling, especially for things that are already approved and funded, so I'm not sure if a registry is a symptom or a cause of the problem that is there. I think that in my view, the registries are potentially helpful in addressing this issue that one of the panelists here mentioned about comorbidity. I think what that means is the people who we see in the trials are really not very representative of the real world, and we're much more

interested in real world evidence of what's working and how well it's doing for that. And in that sense, you know, the registries can be helpful, but I think they're both pretty challenging, but I think they can both be, I would like to see both of them go forward, both trials as the best kind of evidence in ideal people, and registries for more real world situations.
DR. MCNEIL: Okay. Does anybody else want to make a comment on that specific issue? Okay,

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Mark.
DR. GRANT: I could echo the previous comments regarding carotid endarterectomy rather than stent, we haven't had the opportunity to evaluate that evidence, and how difficult it is to synthesize it with the absence of clinical trial data when the registries are proliferated. So I think it's a real issue and I think that there certainly does need to be a balance there. And the registries certainly provide valuable information, no question, but they oftentimes don't answer the critical question, is one therapy more efficacious than another.
DR. MCNEIL: Okay. We have a number of people who want to ask questions. Who has a question on this particular point?
DR. BUSH: I just have a comment about the registries. As a vascular surgeon and someone who takes care of patients who are older and have multiple comorbidities, oftentimes in a randomized clinical trial, especially if you have a procedure that's not being done that frequently, you aren't going to enroll enough patients to be able to evaluate in a randomized fashion whether or not we should be doing something to a patient, especially with a new technology. So I would agree that these

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should be done hand in hand, and it's nice to have both data, and it's complementary.
DR. MCNEIL: So Peter, do you have a thought on this?

DR. JUHN: The question I have is really more to do with this notion of the evidence gap and are we looking at the evidence gaps in the context of coverage decision-making or clinical decision-making or both. And I think this is especially important in considering whether we're looking at so-called clean randomized controlled trials versus kind of real world observational type of information. And I think having some clarity around that, I think, will help in going through that prioritization.
DR. MCNEIL: Okay. So maybe Barry, and then we will move on.
DR. STRAUBE: Again, I think that for purposes of discussion here, because this will be so broad, we should be focusing on the evidence gap and its relevance to coverage decision-making. That was the original intent of this advisory committee, although we changed it to evidence development and coverage so that we could take the broader picture in the long term. So I think the focus today should be on, in the coverage arena, but realize again that

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this would also benefit us in the broader picture.
DR. JUHN: In that context, I think then given the current approach to reviewing evidence for coverage decisions, I would say that the observational trial designs are in a secondary position to randomized trial design.
DR. MCNEIL: I think most people would agree with that. Debbie?
DR. SCHRAG: So just to sort of try to put this together, we've heard from all our speakers about gaps in evidence, basic gaps in the clinical evidence and how critical getting those RCTs done are and how the registries are clearly second rate evidence. So then the question is, how do we set up systems to better incentivize Medicare beneficiaries to participate in these clinical trials without violating fundamental principles of research ethics. I mean, that would seem to be a core question. You know, I think those of us who work in a clinic often find that Medicare beneficiaries are

somewhat ill informed about what a clinical trial is, why they should participate in one, and, you know, that itself, it's almost like public education in that population. It's an issue of what's going to be good for them, good for medicine, good for everyone

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to foster participation.
And then just a procedural note. Since so many of these big Phase Three clinical trials are developed with NIH funding, it's very interesting that when you write an NIH grant and protocol, that you go through a quite laborious section describing accrual and enrollment plans for minority groups by ethnicity very specifically, children and women. But yet, really no attention is required to be put into what is your plan for accruing elderly high comorbidity patients, it's not required. So often the very patients who Medicare treats, or covers, are excluded.
DR. MCNEIL: I think that's really a comment you want to have the NIH hear, because they're the ones who make the guidelines on what goes in the grant applications. Did everybody hear that?
DR. WEINTRAUB: I agree.
DR. MCNEIL: Yes.
MS. DAVENPORT-ENNIS: I would simply like to mirror what my colleague has said, but I'd like to add a couple of additional points for consideration. I agree completely that it is extremely difficult to get the senior population accrued into clinical trials, not only because they may have a hard time

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understanding the complexity of what is going to be involved in that, but also there is a reticence on the part of the provider community to try to recruit many of the seniors who have comorbid conditions that immediately preclude their eligibility for going into the trials.
A second point that I would like to bring forward is that for many of the senior population that we serve and that we all read about and study in

this country, household incomes are at such a point that if the clinical trial requires travel, overnight stays, full-time caregiver in attendance, they are immediately precluded from that, particularly if they are a widow or widower, children are in distant locations.

And so as we have this conversation about clinical trials needing to have seniors in them, I don't know how we can have that without addressing part of the concerns about what do we do to get those with comorbid conditions to qualify for more of the trials, and what do we need to do at least in terms of educating the public that yes, if you're a senior and want to go into a clinical trial, there are certain special service needs you're going to need to be helped with, whether through the family or the

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community at large, in order to get the senior approval.

DR. MCNEIL: I think, if you don't mind, I think this has been a great discussion on clinical trials and comorbidities, but I think it's a little bit tangential to the bulk of our charge today. So what I would like to do is put a little semicolon on this discussion about how we enroll patients in clinical trials and how we deal with comorbidities, and whether registries and clinical trials should be done hand in hand or sequentially. And if we have time at the end of the day, go back to some of those generic issues.

But I'm afraid if we keep on this line, we're not going to get at some of the particular clinical services that we need to address, and we won't have the opportunity to ask questions of our presenters, which we actually have time for only for about the next hour. So I want to be parsimonious with their time and our discussion time.

So what I would like to do now is turn over and say what does the panel have to ask about any of the remarks from our panelists or our public speakers that relate to specific clinical services or to the elaboration of specific clinical services that

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would emerge under some of the broader rubrics that some of the speakers gave. Is that okay? All right, then Mark.
DR. GRANT: I'm going to be a little obscure here first.
DR. MCNEIL: Not too obscure.
DR. GRANT: Okay. Or more general. Having spent most of my professional life as a practicing geriatrician, I was surprised not to hear the topics of end of life care, which is of considerable cost as well as interest to Medicare beneficiaries, discussed, as well as the dementing illnesses, in particular Alzheimer's disease. I was wondering if some of you may have comments.
DR. NAYFIELD: Certainly there are a lot of other issues. I am actually an internist and hematologist. I was (inaudible) for years before I was recruited to aging. I am not a neurologist, and while there are needs certainly for care in Alzheimer's disease, I'm really not the person to speak to those, and we really did not have time to include that expertise in our presentation. So that is obviously something we have neglected. In terms of end of life care, I think that is very important. We are working now within, to

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some extent within our Peppers Center programs, to look at some of these issues and to try and identify these better. So we couldn't cover everything and we did pick some of the things that we felt were most pressing. It doesn't mean the other things aren't important.
DR. MCNEIL: Thank you. Does anybody else have a comment? We understand that you had a limited amount of time and couldn't do everything, but thanks for your time.
DR. KOROSHETZ: As a neurologist, I think that the community recognizes this is a major problem, especially when it's linked to use of health service resources, and I think it's a social and

ethical problem. The physicians have a great deal of difficulty, maybe it's not their area to make, you know, pronouncements about it. It may be something that the country has to look at in terms of an overall policy. Clearly in intensive care units, in stroke units, the issues really come up to the physician, and there's a discussion with the family about what's appropriate. It's a long discussion if the discussion hasn't occurred when the patient hits the hospital.
Clearly, I think the low hanging fruit

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here is to try to incentivize physicians and families to try to think about these things before the events happen. And I think a lot of hospitals now are really pushing this kind of discussion, trying to get forms actually on the record for all their patients with regard to their wishes should disaster occur. I think that's probably, it seems to me a place where you can make a lot of progress.
DR. MCNEIL: In line with our charge, perhaps we won't deal with this today, but is there a specific component of end of life care that we should be considering beyond end of life care? I want to drive this committee as much as possible to specificity.
DR. WEINTRAUB: I don't know if it's really attributable to me, but if you were to incentivize physicians to deal with end of life discussions in patients over 65, I think that that would be a major impact.
MR. SCULLY: Related to this, the fastest growing area, as shown in one of the first slides of the day, in the Medicare population by far, is hospice care. But hospice is also the last Medicare payment (inaudible) make a whole lot of sense and it needs to be fixed. And the fastest growing part of

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hospice and the most controversial by a factor of a hundred, is Alzheimer's care (inaudible) huge issue about what research in the next couple years would be

useful to CMS defining who should be in hospice care for Alzheimer's or at what point the diagnosis is, is a gigantic threshold issue for research. And if you're looking for an example in the next three years, my guess would be (inaudible) without the right research, that's about as high as you're going to get.

DR. MCNEIL: Let's see, I think I have Karl next.

DR. MATUSZEWSKI: Mark pretty much covered my question about Alzheimer's intervention.

DR. MCNEIL: Okay.

DR. MATUSZEWSKI: But let me add a side bar, and somebody else talked about it. These various institutes with all their disease states, you know, the 600 diseases, probably a thousand diseases overall, I'm not sure if the focus is life span extension. I mean at some point if we put down coronary disease and look at cancer and other neurological diseases, they're going to have to die of something. But is quality of life, is that ultimately also on the agenda as needing more study,

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maybe in an RCT type situation.

DR. MCNEIL: You have to do that in terms of clinical service, so you have to be specific.

DR. MATUSZEWSKI: We talked about this in the conference call, so for orthopedics, disc replacement, quality of life for the patient, the type of procedure, surgery you're going to perform for that patient depending on whether they're 65 and active or whether they're 85 and immobile, and do those sorts of studies need to be done earlier, perhaps while you're collecting some data for FDA approval, or is that an ongoing commitment? So indeed we have a device that's been approved; is there some way, much like with pharmaceuticals, there are expectations of a Phase Four post-marketing study to provide that sort of data down the road.

DR. TURKELTAUB: Well, if I could just from the NIH perspective let you know about one of our roadmap initiatives, which is the PROMISE

network, which is patient reported outcome measures through the use of technology, and we're developing that now to look at quality of life issues, the way to measure them, what components are important for each different healthcare issue, and how that information can be used to improve population's

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health in general.
So we're looking at quality of life. For the arthritis institute, many of our conditions are not life-threatening, but we are looking at quality of life in particular.
DR. MCNEIL: Mark, did you have a question for somebody?
DR. HLATKY: I do have a question. One of the things that we saw on the AHRQ conditions that was mentioned as a priority was peptic ulcer disease, and one of the slides that we saw was a number of things related to digestive diseases, numbers of people with cholelithiasis, diverticulosis, et cetera. So my question is for the NIDDK representatives here, because I didn't see anything about the digestive tract on the list of research priorities from the agency, and I see a lot of things saying this is a burden, and I'm wondering what areas should be part of it.
DR. FRADKIN: Well, I guess with the 12-minute limitation, NIDDK has so many different digestive diseases, it was really hard to know, you know, where to focus attention. And I actually am a divertologist rather than digestive diseases person, so I could certainly get back to you, or did you have

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a specific question about digestive diseases?
DR. HLATKY: Just as a cardiologist and since we're supposed to be very specific here, I'm not sure I know what the research gaps are in terms of that. I know that, you know, somebody is recommending we should do more on peptic ulcer disease, I see there are a lot of procedures being done. Are there opportunities and gaps that people

know about, or maybe others? It seems to me that ignoring the digestive system is not a good idea.
DR. FRADKIN: I think it was covered a bit by cancer in terms of colon screening, but I'll try to get back to you.
DR. MCNEIL: Susan, I'm sorry, did you have a comment on that?
DR. NAYFIELD: The comment really goes to quality of life. In geriatrics we look at functional status as well and we have entered into a dialogue with the FDA on having measures of functional status being outcomes in clinical trials. That could be useful for drug approval as we look at things, so this is a concept for organized measurements of the physical performance.
DR. BROWN: Can I add to that?
DR. MCNEIL: Sure.

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DR. BROWN: The PROMISE initiative, we have, we support that in the cancer group, but we also have cancer-specific components, and we have also started a patient-reported sort of initiative with our cooperative groups involved in clinical trials. And even though we've all recognized for a long time that endpoints, patient-reported endpoints in addition to things like the obvious things like mortality, treatment side effects, et cetera, are important, it's really, this goes back 20 years, probably longer.
There has been an ongoing sort of discussion and struggle about what are the measurements of patient-reported endpoints that you can get out of randomized trials or also observational data that were, you know, are as rigorous as something like the mortality endpoint and also are clinically meaningful. And I don't think the answer has fully emerged, but it has been recognized in the last couple of years at NIH that this is something that needs to be done, and there is a lot of activity now trying to find the answer to this question.
DR. MCNEIL: Is this on that point?

DR. GLASSMAN: I just had a response to

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your comment about looking for new trials to provide data. I think the point is that that data really exists, and we had a discussion last year about spinal fusion. All the control data which there's a huge amount there out of the IED trials, was discarded because it's part of an industry-sponsored study looking at a device. But even if you would say let's not look at the investigational arm of these studies, let's look at the control arm of these studies, because that's supposedly the standard against which we're measuring it, there are very large amounts of data that have been collected as part of IED studies that we don't look at because it's not, you know, in the RCT design that we want. And I think, as a lot of people have said, that doesn't seem to be giving us what we want in a timely fashion.

I would suggest to you that a big piece of evidence that is part of what you're looking for exists already, you just might have to go back and look at it a little differently than how we've done in the past.

DR. MATUSZEWSKI: I think with some of the IED, the control groups do have that background and you could look retrospectively at quality of life,

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but some of the newer technologies don't. So you often have data that maybe extends only two years out and you're looking at not only device durability, but patient ability to function with that device over five or ten years, whatever the expectation would be for that device to be implanted, that often doesn't exist at the time of approval, and yet a coverage determination has to be made with the hope that indeed it will turn out like that in ten years. But for control groups you're right, there is that data that exists.

DR. MCNEIL: Peter.

DR. JUHN: I wanted to maybe shift gears

just a little bit and ask one of the presenters a very specific question, and this is for Michael Schoenbaum, which is on the whole depression area. And I think I found your presentation quite effective in terms of highlighting the multiplier effects of depression. But the service that you're describing, I was a little unclear what the specific service is that we need and you have identified as having an evidence gap, and therefore additional studies can be done, that evidence gap be filled, and then CMS makes some kind of coverage decision. Can you kind of drill down to a very specific kind of set of, or

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description of the service, and then the type of trials that could be done that could satisfy CMS in the coverage requirement.
DR. SCHOENBAUM: Okay. I'm glad to have an opportunity to elaborate a little bit. I should admit up front that I'm not confident that I understand some of these terms of art quite the way you all understand them. So Barbara, in your instructions to us you kept mentioning, you know, you have to drill down to specific services. And you know, service is the language that everybody is using here, so with a caveat -- I mean, I'll try to respond to Peter with a caveat that I'm not sure that I understand exactly how that is meant in the Medicare vocabulary.
I mean, there's service at the level of treatment per se, is the question, right? Antidepressant medication, structured therapy, those things are already part of the Medicare benefit, practically speaking, right? And the efficacy probably shows that the majority of patients who are exposed to these treatments and complete a therapeutic dose of them actually get better. We also know at a population level that no more than a quarter of Medicare beneficiaries are exposed to

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anything approximating a therapeutic dose of these treatments, so that's treatment per se.

And so in the mental health world, there's been a huge amount of focus on what is it that we have to do to real world practice to make it more likely that patients who present with a condition like depression, when they present at the medical system or I guess there's even community outreach models, but let's say when they show up at their doctor, because most of them do, how does one increase the chances that they will be identified with this disorder and that they will leave with a therapeutic treatment plan?

And at least in the way I use the word service, or I understand the word service even, what we have developed is a very strong evidence base supporting a package of services, again called collaborative care, but this is all based on Ed Wagner's chronic disease model. So where, you know, the patient shows up, there is some process by which the patient completes a screener for depression. If the patient screens positive, then the next step is to engage the patient in doing and assessment. The clinician can do this, but the clinician typically isn't very effective at starting this process.

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And so the gap in the real world that needs to be filled in order for this process to begin is some kind of physician extender role, you know, shorthand, care manager role, to engage the patient. Then you start the therapeutic process, you send the patient home with a prescription. Does the patient fill the prescription? Does the patient stay on the prescription? If the patient discontinues, and about 50 percent of people who start an antidepressant discontinue after 30 days, why did they discontinue? How does the clinician find out?

The standard of care at the moment is you either send the person out to fend for themselves and nobody does any follow-up, or they go out, they start the med, they may stay on the med for very long periods of time. In the Medicare population in trials, we see people who enter trials who have been on an appropriate antidepressant for a year, two

years, they haven't gotten better, right? So to get them better, what you have to do is monitor outcomes. So again, physician extender role, monitor outcomes, play this intermediary between the patient and the provider.
So those are the services. It's finding a physician extender, somebody to engage the patient,

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connect the patient to the provider, follow up, get the patient back if they're not getting better, monitor outcomes.
DR. JUHN: So if I could just maybe for my own sake, this is really about providing payment, if you will, coverage or payment for another part, a member of the care team?
DR. SCHOENBAUM: In essence, that's right.
DR. JUHN: So my question then may be to perhaps Barry then. Is that the type of service that we should be thinking about in terms of something that could be covered by Medicare vis-a-vis this depression area?
DR. STRAUBE: Yeah. Although I think that's a very important area, it actually is somewhat peripheral to the discussion today. Because, I mean, the one area we have gotten into, we talked about this earlier, are bundled services. We do have, we struggle with that. In the population with cardiac rehabilitation, historically we struggled with, and recently we put out a national coverage decision on pulmonary rehabilitation. And this gets into the barrier that I mentioned earlier, that some of these services are not benefits of Medicare clearly under existing statute, so we get into payment and

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reimbursement questions, legal questions, et cetera, as opposed to the evidence part that we'd like to have identified today. I don't know if I'm making myself clear.
DR. JUHN: It's a little challenging, I think, in a lot of the care management descriptions that were actually included in many of the

presentations today. Which is, if those services are not part of the standard, current standard benefit package, then it may make little sense for us to talk about gaps in the evidence in those services, because even if we were to identify those gaps and do some research in those areas, we wouldn't be able to actually cover anything given the current structure. Is that a fair assumption, Barry?
DR. STRAUBE: Yes. That's what I tried to mention earlier, that there were these barriers, including noncoverage. There are simply issues like hearing aids, which are noncovered under Medicare. That wouldn't be a good use of our time.
DR. JUHN: So for the purpose of today, then, we should not consider that in these care management proposals in terms of the evidence gaps; is that correct?
DR. STRAUBE: I think we have to be

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specific about what the care management proposal is, and we need to comment on whether it's covered under Medicare or not.
DR. JUHN: So this one that we just heard would not be covered?
DR. STRAUBE: Under current statute that bundled service, including multiple other caregivers besides the physician and/or other people who would normally be eligible for Medicare reimbursement may not be covered, yeah.
DR. SCHOENBAUM: Just to clarify, I mean, the model actually has been delivered under Medicare in trials. I mean, there's issues of who is the right person to play this role, you know, qualified providers working in, clinicians and so on. But there are certainly circumstances in which these models can be delivered, you know, provided and billed under Medicare, and under circumstances that allow Medicare reimbursement.
The issue as I see it, I mean, I think there may be some ambiguity about some of these details, so maybe I could ask for a little clarification and then sit down. The evidence

actually suggests that, you know, if you send the patient to the care manager, if you send the patient

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to the psychiatrist, those things are all covered services. The problem is, those are expensive things to do, the patient doesn't want to do them, they're not necessary to get the patient better. What there's an evidence base for doing is extending some of these things to telephonic contact, to curbside relationships between physicians rather than sending each patient to the physician face to face. So it's the same providers providing these other services, and maybe those things are outside the scope of the Medicare benefit at the moment and then the question, I guess, is how do you want to handle it. The principles are the same for managing a diabetic patient or for managing a CHF patient. So one way or another, these issues are going to come out.

MR. SCULLY: But realistically, though, the fact is over the last 30 years the problem with psychiatric care is measuring when the dose is appropriate, and every time these things are happening on a fee for service contract (inaudible) today. I'm amazed that (inaudible) the Kaisers of the world should be incentivized to do all of this, and it doesn't work. You should be doing a clinical trial of your own to measure the services that you

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think should be provided as a threshold, versus what Kaiser or some (inaudible) get into the fee for service world (inaudible) follow the money and if you open up the payments to amorphous payments you get an explosion and you get to spending and you get the reaction. So it's not on the subject today, but if there's ever a place where you should be looking at it's Medicare management (inaudible).

DR. MCNEIL: Excuse me, I'm going to exercise my prerogative. I think that this is really important, but I'm afraid we have a very limited amount of time, and if we have time at the end, at

five of 12, we can come back and talk about this again, because I think there are some specific coverage issues here that go beyond the charge to the panel. So while I appreciate the importance of it, if there is some component of mental health diseases, drug X versus drug Y, shock treatments, whatever, and you could bring those up as examples that we could discuss, that would be really helpful.
DR. SCHOENBAUM: And I was focusing on what I focused on exactly because the data of the effectiveness evidence is in the direction I was mentioning and not in -- you know, we need new treatments but that's not where we're at at this

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moment.
DR. MCNEIL: Okay, so I guess we're at different places. So Leslie, did you have a comment?
MS. FRIED: Well, it was to him but now it's sort of broader in that many of the presenters spoke about how we have some good research but it's not being used in the clinical setting. So my question is, and some of the speakers, and I think almost every one of you said it, do we have a gap in research on how to get what we know is good research in the clinical field to the patients in the clinical setting? Does that make sense?
DR. MCNEIL: But I don't think --
MS. FRIED: Well, if there are clinical services that are, that have been proven that are not being used or not being --
DR. STRAUBE: I think, again, this is a noble set of questions and issues that people are bringing up right now, but they all get back to Beth McGuinn's work that shows that about 50 percent of the time, when people go to physician offices, that over time they receive care in accordance with clinical guidelines. So they're doing a horrible job of delivering care. That is not, again, my understanding, and Steve Phurrough can chime in too,

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but if we go back perhaps to the questions that the

panel's going to have to address this afternoon, I'll just read those, it might give people a little bit better focus.

We're going to ask the question on what diseases represent the greatest burdens to Medicare beneficiaries. We're going to ask which diseases and their treatments are the costliest to the Medicare program, and we've had some presentations regarding that. The third question is going to be, what do you consider to be the most important clinical services that address the major public health issues affecting the Medicare population? The fourth question is, in your opinion, what are the major gaps in evidence for the clinical services in question three? Recall that our primary emphasis is on the Medicare population. And the last question asks you to provide a priority list of clinical services for which additional evidence is most critical for the Medicare population.

MS. FRIED: Okay. I would suggest my question went to number three, if there are clinical services which have been proven but for which Medicare patients or individuals are not getting. So that was sort of the purpose of my question.

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DR. MCNEIL: Yes, Debbie?

DR. SCHRAG: I want to try to take your question and make it specific by basically using that as a jumping off point and applying it to a specific clinical service. And maybe this will be a bad example, but that is tobacco cessation and how important that is in the Medicare population. And again, I say that because the data we have in front of us in terms of the killers of Americans in the Medicare population, heart disease, cancer, cerebrovascular disease. Injuries, maybe tobacco is not implicated, but with COPD certainly. So four of the top five, depending on whether you want to include injuries or not, how many people are smoking in bed, you know, clearly tobacco is important. But is there an evidence gap or not when we have to answer number three in terms of important

clinical services? Is there an issue there or is everything humming along just fine? Is that specific enough?
DR. MCNEIL: That is to say, is there an evidence gap?
DR. SCHRAG: Is there an evidence gap on understanding the benefit of tobacco cessation, smoking cessation strategies for the Medicare

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population? Is it an important intervention in the Medicare population, or does it really only matter for 30-year olds and therefore, is it not an issue in our population?
DR. MCNEIL: I have no idea.
DR. SCHRAG: I'm trying to take your general --
DR. MCNEIL: It is specific enough. I have no idea about the answer.
DR. WEINTRAUB: I think the issues that are being raised here about preventive services, both primary and secondary, are relevant to the decisions you have to make, they are certainly relevant to the American Heart Association. The American Heart Association has been so interested in smoking cessation in everybody. I don't know of a single study in elderly patients concerning smoking cessation. Mark, do you? I don't know of a single one. So is there an evidence gap there? I suspect there is.
I think in general we have an evidence gap on how to deliver preventive services in hypertension, in smoking cessation, in obesity, in hypolipidemia, in general I think there's an evidence gap, I think it's true for everybody, and I think

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it's true for injuries as well.
DR. MCNEIL: Thank you very much. Go ahead.
DR. BROWN: You know, I think it's, from what I understand, there are tobacco studies. There's something called five As, which has been

shown to be effective and actually cost effective, and I do think that smoking cessation in a clinical delivery setting actually is understudied compared to smoking cessation, you know, in other settings. And we do have a study that is being conducted by HMOs that were mentioned before, I won't give any brand names out, which is looking at trying to enhance and increase the delivery of smoking cessation in a primary care setting, using electronic medical records, using tailored feedback to physicians, et cetera, and that study is ongoing through a randomized trial and, you know, we hope to have results relatively soon.
However, I'm not sure whether that would be a Medicare-covered service, because it has to do with utilizing the system resources of the HMO, not necessarily something that has to do with reimbursement to a specific position.
DR. MCNEIL: Let's keep it on the list.

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If I could, I would just like to try to turn the dial a little bit to get a little more specific and ask the cardiac people. I was surprised not to hear from either the NHLBI or AHA the issue of atrial fibrillation in the elderly and treatment for that. I would have thought that would be high on your list, but maybe I don't know enough cardiology. Was it on the list?
DR. WEINTRAUB: Actually I did mention, we had one point on the slides on arrhythmia, and we did mention atrial fibrillation.
DR. MCNEIL: I'm sorry.
DR. WEINTRAUB: Atrial fibrillation is a very complex area. As you well know, it's a problem that increases in the elderly. If you look at clinical trials on atrial fibrillation, most of them are people in their 70s, not in their 50s and 60s.
DR. MCNEIL: So is the issue there, are there new treatments for that disease that you would be specifically looking at?
DR. WEINTRAUB: There are new treatments, there are new medical therapies, there are procedural

therapies that are not fully understood and have not been properly subjected to randomized controlled trials. I think the evidence gap in atrial

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fibrillation is as large as anything you're doing.
DR. KOROSHETZ: A major problem with atrial fibrillation is stroke, and so there are a couple very specific issues. One is that the treatment which has been really well studied clearly showed that even in the elderly, Warfarin decreases stroke risk and has overall benefit. We know that the penetration of Warfarin into the elderly community, and mostly with atrial fibrillation in general, is not where it should be. And the problem is the risk, and the inconvenience of taking Warfarin, so I think that's a major issue. There are things that could be really groundbreaking like a new therapy that does not have the same ups and downs of Warfarin. The risks of Warfarin goes up exponentially as the INR level, the level of blood coagulation starts to get too high. And so if you look at large studies, patients are only within range about 60 percent of the time, but 40 percent of the time they are either not protected or they're so high they have a risk of bleeding into the brain. So a better technology to try to get people in range and just get their INRs in range would be a dramatic benefit. The current practice is to get your blood

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checked once every three to four weeks, which has absolutely no evidence behind it, and anybody that's looked at it has already seen that it's completely inadequate. I think that would be a very clear-cut study, to try to look at INR regulation to show decreased morbidity, better compliance in the elderly with this.
DR. MCNEIL: So, would you consider that genetic testing for Warfarin sensitivity would be a clinical service for which more data is needed, or is that pretty much a done deal?

DR. KOROSHETZ: My understanding is that that's currently something that NHLBI is studying.
DR. SAVAGE: I think that the reason we didn't mention it is we thought we were supposed to come up with a few topics, and it was one of a long list of things. It clearly is a very important issue in the elderly and the current therapy is suboptimal. There are potential new anticoagulant drugs that are being developed that would have less problem than there is with Warfarin. The issue of genetics of Warfarin metabolism and whether or not that will be a breakthrough in terms of stabilizing the INR in some way is certainly conceptually an interesting one. I think it's also fairly complex in the

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sense that if you have an entity, anticoagulation, in a drug like Warfarin, where the amount of anticoagulation is dependent not only upon the individual genetic profile of that individual, but also upon other drugs they take, upon some foods that they may eat, whether or not they forget to take their medication some days or take too much some other days and so forth, which is a problem in the elderly with cognitive problems. The issue of whether being able to do a genetic testing and look at the genetic variants that have been identified so far will lead to a major breakthrough in terms of clinical outcomes is very much an open question. There is a clinical trial that is in the process of getting underway now that the NHLIB is involved with, but we didn't think it was something that -- I mean, the other side of it is what was said just before I came up here, which is that one of the problems is that with elderly patients there are a lot of reasons why they're making mistakes with their drugs and so forth, and that in its own right may cause significant problems, they could be problems that are greater than any benefit that comes from knowing the genetics.
DR. MCNEIL: Thank you. Mark and then

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Leslie.
DR. HLATKY: I guess, although I'm skeptical about the genetics and defib, it does raise the whole issue about adverse drug reactions as being a huge problem in all populations and especially in the elderly, and I wondered if there were gaps either in pharmacogenetics in particular or any other interventions to reduce adverse drug reactions in the elderly, is that an opportunity or gap in evidence that we ought to be looking at?
DR. MCNEIL: Ask the audience.
DR. HLATKY: I guess it might be useful, and I wondered if Randy Burkholder or any of the others had anything to say about this.
DR. STRAUBE: I think Dr. Brown mentioned this also with cancer.
DR. BROWN: Well, yeah. I will go with what Peter Savage just said. I think there is a lot of potential in this area, but it's a huge unknown area, especially in the elderly because of all the other factors that he mentioned. There are a couple of examples in cancer that I think are kind of parallel to the Warfarin thing in their level of development and unknowable sort of issues, especially for the elderly.

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Well, I don't want to say too much about this because it's very early on, but we are looking into the possibility at NCI and, you know, cooperating with trans-NIH and trans-FDA to try to do more to establish large, and these would be observational databases that would be capable of tracking -- doing two things. One is tracking late and rare adverse effects from all kinds of drugs. And number two, to establish a resource that could bring in large populations into controlled trials that could advance the early sort of, you know, Phase One, Two kind of studies of these kind of pharmacogenomic agents to a real Phase Three kind of trial, which really hasn't been done very much so far. We have a Phase Three trial at NCI for Onco-DX in breast cancer, for example, that's the only one I

know about.
But you know, the problem is, it's hard to bring in large populations, tissue resources, et cetera, to bring these technologies up to that level of development, but of course they can be approved by FDA without that, and then disseminated into clinical use.
DR. MCNEIL: Just to be clear, the Onco-DX trial is a clear example where the evidence is weak

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but lots of patients are getting the test and the resulting treatments if they're in the intermediate range.
DR. BROWN: Right. It's weak, especially in the middle range, that's the issue.
Just as a side issue, again, what goes on in actual practice as opposed to what we look for in clinical trials and what might be the ideal provision of these things for, you know, guidelines, even in a case like Herceptin, we don't even have a data system in the United States today that can tell us among women who are receiving Herceptin for treatment of breast cancer, how many of them got the test in the first place. And also by the way, is that test any good? You know, that's an area where we have a couple studies that we're starting to do. So I think, you know, that's the most well established sort of, you know, genetically tailored therapy with a test.
But in the next five to ten years, there's going to be a bunch of these combo kind of things emerging, at least in cancer and probably in other diseases also. Yeah, I think that's an evidence gap that needs to be looked at a lot more.
MR. BURKHOLDER: Yeah, real briefly, and

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to go back to what I think the question was, are there gaps or opportunities for those drug-related problems, and clearly the short answer is yes. I think the longer answer to a certain extent speaks to I think one of the fundamental questions that it

sounds like the panel has been grappling with, which relates to where your charge begins and ends in relation to the kinds of evidence gaps and their relation to a particular Medicare policy mechanism that you should be looking at.
I think a lot of the answer on the drug-related problem side, whether it's problems with nonadherence or drug interaction or some of these other things, is that exacts a very high toll on beneficiaries and indeed on Medicare itself. Some of those answers are not the clinical interventions per se but the context of care in which those interventions are delivered.
Just one example, and some of what I hear being said is those kinds of questions are off the table, but I think further clarity around that would certainly be helpful. But just as one example under the part D program and the medication therapy management program that is a part of that is, the real question is that I think we would all benefit

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from more evidence around what kind of MTM program is more effective at addressing those kinds of problems, and what are we getting, can we get more information about those, what can we do to better identify the ones that are effective, those kinds of things that can help answer the kinds of questions I think you're asking.
DR. SCHOENBAUM: Briefly I want to cover the psychotropics, which is a major chunk of the part D benefit, as it is for any other pharmaceutical benefit. So quickly, I think from NIH's perspective that there are three kind of issues I want to raise briefly.
One is that I think that the quality of psychotropic prescribing at the moment, I think from our perspective needs considerable improvement. In many cases this is, whether it's for psychotics or whatever, it's more of an art than a science. There are a range of drugs in a class. There's little evidence that allows you to choose which drug you should try first with this patient. Most patients

will respond to one or another of drugs in a class but may not respond to the first drug or the second drug that one tries, and I think this is certainly an area of considerable research emphasis for us to

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equip practitioners with better guidance by genetic information ideally eventually, other kinds of personalization. In the meantime, via some kind of outcome management that might preclude some of the cost ballooning concerns that Tom Scully invoked. I mean, from our perspective, quality of care in mental health should all be measured in terms of outcomes. If it works for the patient, the patient is getting better, fine. If not, do something different. Don't just keep throwing good money after bad right off the bat.

The second issue is side effects, particularly antipsychotic, which are increasingly used in the elderly population by some -- you know, fairly high and, as I understand it, growing fraction of nursing home beneficiaries are getting antipsychotics for off-label uses. Those drugs actually cause a number of metabolic problems and other kinds of physical problems, and I think improving the practice surrounding those issues is also an area of considerable interest to us.

And then a third issue that I want to mention, again at the risk for going off the map, I don't know whether part D falls into your scope or not, but there are certainly coverage issues for

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psychotropics that affect the part D benefit. So as I understand it at the moment, most FDA-approved psychotropics are in practice being covered by most part D plans, but as I understand it, this is a practice and not a requirement. And we imagine that if that practice were to change over time, then the formulary's choice of psychotropic in a particular plan and changing over time could actually turn out to have considerable deleterious both clinical effects for the affected beneficiaries, many of whom

are cognitively impaired in addition to being elderly, and have a hard time processing changes in their formulary and for whom discontinuation of medications can be incredibly disruptive. And actually, also produce selection effects, kind of first order selection drivers. Plans might, through their choice of psychotropics on their pharmacy formulary, in effect practice cherry picking to avoid people with mental illness.

DR. MCNEIL: Thank you. Sean, Karl, Leslie.

DR. TUNIS: This is a question for Dr. Turkeltaub, if I pronounced that correctly, although I would be happy to hear also from others. The question is, as I listened to the

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charge of the committee for this afternoon in terms of what we're going to be asked to do, you know, what are the major causes of morbidity and what are the current gaps in evidence, et cetera, it strikes me that each of the NIH institutes are doing a fairly laborious process in their own priority setting for, you know, allocating funds to clinical research to identify where are the major areas of morbidity, what kind of studies are ongoing, what is the life sciences industry likely to do themselves, and therefore where does NIH need to get involved. And you know, given that that's almost certainly going to be a much more accepted process than anything that we can do here today, what I'm curious about is what, you know, what part of that process, A, if you could just sort of describe for us a little bit how you go about doing that at the institute, and then sort of what part of that doesn't look at the question from the perspective that the Medicare program might. So that's the basic question, to better understand what you do now and how a Medicare perspective might incrementally add to that.

DR. TURKELTAUB: Well, the arthritis institute also covers skin diseases as well. We have

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quite a broad, not as broad as one of the speakers who had 600 to manage, to choose priorities from. And so really the majority of what we do is investigator-initiated, and we have to determine through the use of panels that we bring in throughout the year for our multidisciplinary panels what it is that are the cutting edge issues that they're looking at, and that's what drives us basically. We will come up with some contracts, but in our agency we don't use that many, the funding is not used in that way. The osteoarthritis initiative is an example of that kind of contracting process which we obviously have put a good deal of money into to get a 5,000-person cohort to be able to look at biomarkers in. But that again is in relationship to what the community brings to us and how we can respond to the community needs. We'll put out broad agency announcements that ask for innovative therapies, but we don't dictate what these therapies will be or in which one of our areas. So in terms of really saying these are the high cost items, this is where we're going to be going with them and this is our long-range plans for those in particular, we don't do those in particular. We have a long-range plan that looks at all of the

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areas that we cover and they are identified within that long-range plan what general issues are being considered.

DR. TUNIS: So, that's actually very helpful. I'm just curious if any of the other institutes take any sort of different approach that's, you know, more top down, I would guess I would describe it as driven by public health priorities and considerations, as opposed to kind of investigator initiated and sort of scientific opportunity.

DR. NAYFIELD: Well, at NIA we of course like to identify the big items and focus on, as to what we can do with those particular challenging areas right now. Some of them need research, some of

them are at the point that they could just take off, so part of the question is too, where each of the problems stand in terms of compliance. Are there some that are just sort of trying with a little bit of input into research to really make contributions that they're real close to? And we do try to guide out applicants in the types of grants that they submit by various funding initiatives and we can target areas, particularly those in which there are specific gaps to be filled or in which there are

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just, you know, really the time is right to get in there and do things. And so part of what we need to know, I think, is where the gaps are, not only in the science, but in answering the questions about the science and whether we would find it useful.

DR. MCNEIL: Okay. I'm looking and see we have about six minutes left. We have questions from Karl and Leslie and --

MR. SCULLY: Can I follow up real quickly with one question?

DR. MCNEIL: Sure.

MR. SCULLY: I know you've talked about (inaudible) used to drive crazy when I was foolishly involved in sports for a while was rheumatoid arthritis, but it always drove me crazy that Medicare at the time was probably 80 percent (inaudible) switch drugs, because that (inaudible). Now you have part D (inaudible) in the rheumatologist's practice and a patient's like to tell you which drug you take and when you take it and how it's reimbursed, so (inaudible) doesn't make a hell of a lot of sense to me. But that's a huge issue for docs and for patients with arthritis, I believe it's the third or fourth highest expense for Medicare as far as drugs go, and I know for a fact that Barry doesn't have the

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staff to have somebody just take a look at those behavior patterns and see what's happening, and that could be a huge impact on the Medicare program, I think.

DR. MCNEIL: Quickly.
DR. TURKELTAUB: We are looking very closely at the different types of combinations of medication that can be used to prevent exacerbation, for anywhere from juvenile arthritis to seniors and how the medications can be used in those populations. We're looking at it.
MR. SCULLY: (Inaudible).
DR. WHITE: My name is Richard White, I do joint replacements. I came a long way and I wanted to make a couple comments.
DR. MCNEIL: Sure.
DR. WHITE: I think of all the questions, the five questions that are listed, I think the first, second and probably the third questions have all been answered and are really, no one has a controversy. But in terms of the purpose of this, Dr. McNeil, you have tried to keep everybody on target, is the evidence gap in provided services. I was a little disappointed by all the presenters in the various areas, that they didn't say

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that these are provided services that you already cover where we feel in our specialty we have an evidence gap. Those are the people that should have come forth and told you what those evidence gaps were. You're providing services that are weakly supported by evidence.
On the other hand, there are some that are very strongly supported. I think the only one that really brought it out, and we all know about it, is carotid endarterectomy and the whole controversy with respect to that. So I would have liked to have seen all these various areas say these are the provided services, we really are weak in these areas. Obviously we sometimes provide covered services where we don't have strong research.
Secondly, I think that the inclusion of Medicare patients or beneficiaries in RCTs is very critical. In what we do it's about 67 percent of our enrollees, and I probably wouldn't underestimate their abilities. Our Medicare patients at least in

our RCTs are probably the most informed and the most compliant, compared to our irresponsible people that are usually under 65 years of age, and so we're pleased to have them in our studies.
Finally, I think I certainly would agree

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that the RCTs are very important, but at least in total joint replacements the biggest mistake we see is the tendency to totally ignore registries, and many times we see RCTs starting, that even the weak information we get from registries clearly demonstrate that an RCT should never have been started with that hypothesis.
I think the other thing that all these various areas do is also come to you where the evidence is not an evidence gap but it's so strong that a covered service should not be covered. I think the best two examples are in orthopedics, and that is the debridement arthroscopy of the knee in osteoarthritis, that's a covered service that should be not covered, and also diagnostic arthroscopy of the knee is a service that should not be covered, because the evidence is very strong and just doesn't support that.
But I'm encouraged by the panel and curious to see what the discussion is this afternoon.
DR. MCNEIL: Great, thanks. Karl.
DR. MATUSZEWSKI: I had a question related to a response about 15 minutes ago, one of the dangers of this format, but drugs not to be used in the elderly, those exist in the literature. You have

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drug interactions that are on all package inserts. I think that's a real challenge, and maybe the research is designing precision support whether it's software, whether it's electronic medical records, that take into account these combinations, the comorbidities, the physiological functions. We all know that the elderly have different functioning kidneys and livers, and I think for one clinician to be able to interpret that in their practice with the drugs that

are available and the drugs that are coming out now, is almost an impossibility. So I think, particularly for the Medicare Advantage plans, it almost should be a requirement by CMS that they take those factors into account, and I think that those circumstances, whether adverse effect from drugs or drug interactions could be minimized in the future with the appropriate research and stipulations by CMS.

DR. MCNEIL: I have quickly, like two minutes left, so Leslie, then Linda, and Mark will be it, unless there's a burning topic.

MS. FRIED: I do have a question for anyone out there. Is there a gap in evidence for the use of occupational therapy, physical therapy or speech and language therapy to slow deterioration of

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function with degenerative diseases? Because it's a constant problem for people who are Medicare beneficiaries who are often getting denied services because they're not going to improve in function, but for those who may slow the deterioration or maintain function? Do people understand the question? Is there a gap of evidence?

SPEAKER: I think so, yeah. I think you're right, but let me put it this way. I have never seen anybody get worse from occupational physiotherapy and the nervous system theoretically improves with practice and so we, there is now more and more science to the actual biological effects of rehab therapy and, you know, exercise and muscle strength development, but it's very hard to tease apart exactly what part of the rehab therapy is going to do, so I think it is needed.

DR. MCNEIL: Okay. Linda.

DR. BERGTHOLD: What about eyes?

DR. MCNEIL: No, we were not going to do eyes today because we don't have an eye guy here. Blindness is probably one of the key things we should worry about, but unfortunately we don't have him here today, so I think we're going to have to put that whole area on the back burner and have CMS figure out

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how to deal with it. Let me make a suggestion about how to proceed because it's not obvious, at least to me. The panel has a discussion period after lunch, and we will not be in general asking you for input. We may ask a question or two, but in general we've heard from you, you had wonderful opportunities to make your remarks, we will now be discussing among ourselves.

What I would like to do, however, is the following. I have been trying and I don't know whether I was able to do it, to capture some of the specific clinical services that have been mentioned by various people, and Michelle is going to plug in a number more that were on some of the slides. These are going to be printed out and given to the panelists for our review when we come back after lunch. Also, they are going to be put on the screen, presumably in about 15 or so minutes, however long it takes to type these in.

We're going to try to do it now, and so your job will be to look at that list and see if we missed anything egregious in terms of specific areas that you either mentioned and in my hurried nature I forgot to put in, or that you forgot to mention.

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Now I've also put up on the slide a bunch of things at the top that relate to surveillance, comorbidities, end of life, delivery of preventive services, quality of life, fees for Medicare beneficiaries, and RCTs. I just put those there, we did discuss them, and at some point they will be the format of another CMS panel, but we're not going to get involved in discussing them too much, if at all, in the after lunch session.

I hope this works. I can't think of any other ways to start grinding through a list. This will clearly not be the last time we approach this, but hopefully it will at least get us started. Does this seem like a reasonable approach to people?

Okay.
I understand we're all on our own for lunch. The cafeteria is downstairs. We will be back here at one o'clock. Thank you.
(Luncheon recess.)
DR. MCNEIL: I would like to change things around a little bit from what we proposed before lunch. You now have in front of you a list of 105 or so specific items that have been identified either in the course of the talks by panelists directly, by questioning or whatever. So this is really a mammoth

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task and I want to remind everybody that this is the first step of a multistep process, so if something doesn't make it, whatever that means, that doesn't mean it's dead, it just means that we're trying to develop an approach of getting at this very complicated problem and to do it for the first time. So nobody should go home seizing if your very favorite thing isn't here.
Hold on, Steve has something else to say.
Maybe you should --
(Dr. Phurrough and Dr. McNeil conferred off the record.)
DR. MCNEIL: Okay. So this is now going to be a complicated exercise and I hope -- so, is one good or one bad?
DR. PHURROUGH: One's bad.
DR. MCNEIL: So here's what we're going to do. There are 105 items here. You are to rate each one of these on a rating scale from one to five where one is bad, make sure, one is bad, because I already messed it up, and five is good. So it's an inverse NIH score. And in addition, you are to circle the 25 favorite ones, the ones that you think are your very favorites. And you're also going to put your name on your sheet of paper, since this is a public meeting

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and we need to know who is saying what.
So, we're just going to do this for the first round, no questions, no discussion, just to see

where we are. Yes, Debbie?
DR. SCHRAG: Using what criteria?
DR. MCNEIL: What qualitative criteria, what you think are the most important clinical services that the Medicare population would benefit from, and for which the data are absent or weak.
Yes, Karl?
DR. MATUSZEWSKI: To clarify, the one through five is on the presence or absence of data, so a one would be bad, there's not enough data, and five would be there is some data?
DR. MCNEIL: No, because we haven't gone into the level of data for each of these.
DR. MATUSZEWSKI: So in terms of marking each of the 105 topics on a one to five scale, I need a basis for what is bad and what is good, and number three being sort of in the medium.
DR. MCNEIL: Right.
DR. MATUSZEWSKI: Is it from what I think its clinical value is?
DR. MCNEIL: Clinical benefit, yes.
DR. MATUSZEWSKI: Clinical benefit. So

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evidence has nothing --
DR. MCNEIL: Well, the assumption is that for most of these, unless I'm wrong, the clinical data on many of these are absent or thin, otherwise they wouldn't have made the list; is that correct? Is there one here that you think, where the data are compelling?
DR. MATUSZEWSKI: I would disagree with that. I think for some of these the data are fairly robust or reasonable.
DR. PHURROUGH: Barbara, can I make a comment?
DR. MCNEIL: Sure, Steve.
DR. PHURROUGH: This is to assist in answering question three. What are those things that you're going to recommend to Medicare that Medicare should tell the research world, here's what you should focus on. And so a five says yes, you should tell the world that you should focus on this

research, and one says no. So whatever criteria you decide that is, if it's high value that's important, there's not a lot of evidence, the goal is what do you think, or what do you want to recommend to us that we should tell the research community that they should focus on out of these 105. So rate them all

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and then choose the 25 that you want most. And that's all the criteria you get.
DR. MATUSZEWSKI: I got it now. So five is focus on this like a laser, and number one means forget about it.
DR. PHURROUGH: One may be important, but may not be something that we need to tell the research community focus on because, as you said, we may have all the evidence that we need around that particular issue.
DR. MCNEIL: Mark.
DR. HLATKY: I thought I knew what I was supposed to do, now I'm confused. I thought we were going to try to go directly to question four in our charge, the places where there were gaps in evidence. So if I thought, just to pick something, CT lung cancer screening, if I thought, gosh, we really need a lot more evidence in that, I would give it a five. That's not to say whether I thought lung cancer was important, a big problem or not, but did I think there was a gap of evidence. So are we answering question three, which says, what are the most important services? I could see an important service for which we have no gap whatsoever in evidence.
DR. PHURROUGH: It is question four, I'm

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sorry. Question four is, what are we trying to tell the world that we want Medicare to focus on. So it's a combination; you will need to have answered question three in your mind as to where the gaps in evidence are.
DR. HLATKY: So some internal algorithm like this is a big problem that has a big gap, so I give it a really high five rating.

DR. PHURROUGH: Yeah.
DR. MCNEIL: Is that clear for everybody? Yes, Peter?
DR. JUHN: (Inaudible.)
DR. MCNEIL: Well, I may have been wrong.
DR. PHURROUGH: Obviously people disagree as to whether there is enough evidence or not.
DR. JUHN: I thought that we were (inaudible).
DR. MCNEIL: Well, since there are two different questions, let's figure out which one we're going to answer. One is that, and one is the second one that Mark and Steve just mentioned. Steve, which one do you want us to do?
DR. PHURROUGH: Again, the goal here is for you to tell us what we should tell the research community, which things should we focus on. So

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that's where we want you to aim at, what should we be focusing on.
DR. MCNEIL: You know, maybe one thing we should think about is let's put the questions aside, because they may be causing us a little bit of trouble for the moment. And say what, let me see if this is right, what do we want to tell CMS to advise researchers via the NIH and AHRQ about areas that they should focus on in terms of the care of Medicare beneficiaries? Is that it?
DR. STRAUBE: Yep, and maybe to amend that, taking into consideration several factors, which includes those things that you think are important clinically that address health issues in the Medicare population, those areas that have gaps in evidence as far as we know from the presentations and our own personal experience, and any other criteria that somebody might want to suggest.
DR. MCNEIL: And then you're going to circle your favorite 25. Okay, let's give it a shot, we'll say ten minutes.
(Panelists recorded results on sheets which were picked up and tallied by staff.)
DR. MCNEIL: Has everybody finished, for

better or worse? Okay. This is a complicated list

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and it may be an incomplete list, there may be some inaccuracies on it. Mark Grant has suggested that item number 93 is kind of a non sequitur, oxymoron, whatever. But that aside --

DR. MATUSZEWSKI: That was my favorite.

DR. MCNEIL: So the question is now, it's a little bit hard to know how to proceed from here on in, because as I said, this is going to be a multi-step process. So the talliers are out there, or Steve is the tallier, Steve is tallying the 25 favorites. And with any kind of luck, there might be some congruence among that; on the other hand, there may not, this may be a scatter plot, but at the very least we will have a list.

At this point maybe what we should do, since it's going to take him a few minutes to do that, is comment on any of these that we think would benefit from more specificity that we might think about including at a later time. So for example, Leslie raised the issued of vascular disease imaging.

MS. FRIED: Ruth.

DR. MCNEIL: Leslie didn't do that, Ruth raised the issue of vascular disease imaging, correct?

MS. FRIED: Yes.

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DR. MCNEIL: And the question was, what is vascular disease imaging, when we talk about that, are we talking about everything, or do we want to be quite specific and say we're looking at newer modalities, Doppler versus contrast angiography versus MRA versus CTA? That would be the kind of area where we might want to add some specificity. So is that worth doing at this point or do we want to just wait for Steve to come in and tell us we have the top 25, and everybody can go get a cup of coffee? Yes.

DR. JACOBS: I'm new to this forum, and I would like to thank the speakers for their concise

presentations, but I'm a bit perplexed inasmuch as given the general big picture. I don't, from nine-minute presentations on topics for which I have essentially no familiarity other than one or two, I don't feel like I have any information base to decide what the problems are, let alone moving to the next step of where the information gaps are, because I'm not familiar with two or three of these topics as an orthopedist. And I would think, since you're obviously talking about large amounts of money to direct, on the one hand I would think you would need subcommittees to refine the different areas and

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better triage what a group of people knowledgeable in that area would recommend.
I mean, I really have very little understanding of the mental health needs of the elderly, and these topics to me are based on my reading of the New York Times, as somebody said earlier, frankly, and I would think we need to get subcommittees to distill the problem areas and then you need more information from the other folks as to where these evidence gaps are. I mean, I can't begin to have enough information to comment on anything but orthopedics here, and I'm not sure why I can even remotely triage these other issues based on a simply designed superficial assessment of what are major health factors, let alone the key issue that was raised of where are the information gaps?
What is Medicare paying for that is not substantiated by the data, as opposed to what Medicare is paying for that is substantiated by the data, which caused a confusion just a few minutes ago as to how we should rate things, as to what we were rating, whether they were information gaps or health care issues.
DR. MCNEIL: I think what we said, correct me, but two factors. One is we have a

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multidisciplinary panel and a multidisciplinary audience, and virtually every institute from the NIH

represented, and you heard presentations from them with their perceptions of what is important. So you're right, you can't be expected to know about depression in the elderly, but you do have some ability to judge data and to listen to a discussion, and to make assessments, probably better made in orthopedics than psychiatry, but nonetheless we are hopeful that this is a committee that has had a broad enough experience with the healthcare system that they are able to make sense of these.

The question of what we were making the ratings on, I thought we had said we were going to make a rating on a one to five scale in terms of our perception of the importance of these to the Medicare beneficiary using some intuitive calculator or intuitive algorithm. And we didn't quite specify with or without evidence at this point.

Now what we're not talking about here is having Medicare throw a lot of money at the top 25 problems, if I'm correct. That's not what's on the table. What's on the table is to identify those areas that would be in need for evidence for which Medicare might then be in a position to provide these

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clinical services to the elderly. So this is not meant to be, as I understand it, and Barry can correct me, a vehicle for him going outside and writing a check 25 times to the various organizations that would be involved in whatever these services are; is that correct?

DR. STRAUBE: Yeah. I think I'll go back to what I said at the beginning, and that was this is the first time we have ever approached this topic, this is completely new and different. And Steve and the team have come up with the presentations, asking the panel to try to go through the exercise that Barbara just mentioned. What I'm learning from this, and I think Steve and the rest of our staff are too, is that trying to prioritize things is a difficult process.

And maybe, Barbara, part of what we should do while we're waiting for the tally is, and I sensed

people at the beginning were interested in this. We had a whole number of topics suggested that we don't really get to go through this exercise. I had several that somehow didn't make it onto the list. And a full disclosure for those of you who don't know me, I'm a nephrologist and a transplant physician by training and practice, so ESRD and CKD got mentioned

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numerous times. Again, we spend 21 billion in the Medicare program alone on ESRD in totality, so to me those should be on the list, and I could think of five or six things under each one of them that we could list as areas just like we listed on this sheet.
There's some more generic things we haven't talked about this morning, too, I was talking to Sean at lunch. But from the agency standpoint, we've put a tremendous focus going forward on health disparities and how should that factor in to prioritization to where is the need. We focused on disparity of age certainly, but what about race and ethnicity, what if we focused on gender, what about income, and all the other disparities?
So if we're looking for filling the gap for the time thing here, Barbara, maybe the panel might want to start to brainstorm a little bit on how we think about tying these in more than just this list, and to verbalize to CMS that we want them to be able to go back to the research communities and say here are the things that our panel felt were areas that you might want to focus on. And that's one thing we could get out of this, with the caveats and limitations of, do we have enough information to make

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that. So I'm raising, maybe we should expand a little bit the thought process beyond just this.
This exercise probably would be interesting, but should we be thinking a little more broader. Well, one would be just to throw it open. The question was how to do it, and first is to have some reaction about that.

DR. MCNEIL: Mark.
DR. GRANT: And this is meant to be a generic comment regarding along the lines of, maybe not along the lines of, maybe not so much race and ethnicity, but I think one we haven't talked about much is that most of the evidence that we have to support various treatments, therapies and diagnostics predominantly have been derived from a relatively young to younger old group of individuals, and the oldest old have been under-represented in the least if not the most. And so that not just the comorbidity issue, but also the fact that the 85-plus-year-old group, which is expanding at probably the most rapid rate among the Medicare population, that group really needs to be addressed, and I think specifically, in answering a lot of these questions. Some of them pertain directly to them, some of them do not, but from a geriatric

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perspective, I think that's really critical.
DR. MCNEIL: Peter?
DR. JUHN: I just had a question that's kind of linked to what Mark just said, but really trying to think of our deliberations today and how that fits into continued dialogue which I think is going to happen. I mean this is really the first, if you will, of a series of conversations you and your staff will be having with others. Can you comment a little bit on how the output from today will actually kind of help you with the next steps in this process?
DR. STRAUBE: Just off the top of my head, I think there are several ways. Again, it was mentioned about work groups and again, I suspect that we may come up with issues that we will want to get more expert opinion, not necessarily through a formal MedCAC process but through more resource, less intense telephone conferences, et cetera.
In my mind, and Steve is tallying, he runs the group on a day-to-day basis, one of the things I can think of that is helpful is when we start off the beginning of the year, and Sean was asking the question earlier, we have to prioritize what we're

going to consider in terms of national coverage decisions, so we come up with lists. And this is

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one, perhaps one way of prioritizing at the beginning of the year, both by taking things off the list because the amount of evidence isn't there, but also possibly putting it on the list to generate a discussion, including the one at a MedCAC meeting specific for that topic. So that would be one example.
I think Steve's example of wanting to be able to work with our colleagues at the various branches of NIH and with industry in terms of where are the areas that we should try to collaborate together with more emphasis. And that may include getting the Hill to support things, or whether we can cover it under our clinical research policy, or whatever the value is of focused research on these particular topics. So those are two things.
A third area, we're involved with quality metrics and going down the various healthcare lines, particularly at AQA and HQA nationally, in the process of measurement. People have talked today about wanting to know where the gaps are and unless you have data, you can't focus on them, so we will be developing in parallel a quality metric development process to focus on those areas that need more information.

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So that, just off the top of my head --
DR. JUHN: And that is helpful. And I think to my colleague's earlier question about some of these topics really being not considered, I think you have to get the process started sometime.
DR. MCNEIL: Nancy.
MS. DAVENPORT-ENNIS: There is an additional comment that I would make. I agree so much, Peter, that the way we move this forward is to collaborate, and you were sharing the collaboration across all of the different agencies within NIH as well as with industry, certainly there will be

collaboration with providers.
But in interviewing a lot of our case managers to be prepared for today's discussions, one of the ideas that they asked that we advance is that as you're trying to survey agencies, industry providers to answer some of the questions about where do we focus resources of the agency, where do we move forward, to look at the role of the nonprofits in filling some of the gaps that currently do exist.
And let me give you an example of a gap.
Just a mere ten years ago if we had a stroke or heart attack patient, or any heart disease patient, we could fairly quickly and easily create a system of

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support for that patient, whether it needed to be long term or short term, whether they were insured or uninsured. Today the resources to put together that same patchwork are very reduced from what they were even two to three years ago. So when we look at something such as what federal programs are there to help with that process, there are gaps.
And so as you look at the results of today, I think that you will find great strength and a lot of resources for the agency by looking into the nonprofit community to see what can be done to help them fill in some of those gaps, whether in services or in research.
DR. MCNEIL: Thank you. Typically we're not having too many audience comments, but if you can make it a one-sentence remark, that would be great.
MR. BURKHOLDER: I'll make it just a few sentences and again, thank you for indulging me. I only wanted to come up because Dr. Straube, I think your description, or your answer to Peter's question is important to get clarity on.
What I heard you saying was the way CMS would use this would likely be in the context of a national coverage policy-making in one form or another, which is very different from what I heard

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Dr. Phurrough saying, which sounded more like CMS

going out to the research community and saying these are the issues that we think you should be looking at. I guess I would just like clarity, or I think clarity would help on that, because it holds very important implications for the kinds of questions that are on this list. For example, should drugs covered on part D be on a list that relates to CMS national coverage decision-making, probably not.

DR. MCNEIL: Thank you.

DR. STRAUBE: Again, I was speaking to the context of prioritizing, Randy, how we look into evidence priorities, which is what I thought we came here to talk about, not necessarily to -- that's not the priority of this meeting. I was asked how we might use that information, and I don't think we're going to get into a debate about it.

MR. BURKHOLDER: But I just, if we can get a, it's this answer or it's this answer.

DR. STRAUBE: We're going to use it for all of the above, okay? But the primary reason for coming here was, as Steve articulated, to be able to advise the research community on where there might be gaps that the research community might look into. But we will use it for other reasons.

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MS. FRIED: Are we still talking?

DR. MCNEIL: We're still talking.

MS. FRIED: Because certain things that we talked about that were not on the list because they're outside our scope, I think is worth considering for the future MedCAC, and it really goes to the issues of optimal settings for certain treatments and for not only the primary care setting, but I think we talked about transition like from a hospital to a nursing home back to the community. I think we find, we get a lot of comments from the folks who sort of get lost. They get shipped to the hospital and then they're out, and there's a lack of transition and there's a lack of really good discharge planning, and it really affects their overall recovery from whatever their condition is, but it's particularly true if someone has cognitive

impairment, be it dementia, depression, or any other mental impairment.
There is just sort of this loss of transition, and nobody's held responsible really.
You know, someone's treated in the hospital and then discharged, and then they're discharged either to home with some healthcare, or to assist, but there's no real transition, and I think that really is

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important both for the Medicare program and for the quality of life of the individual, and for the caregiver, because they often get shipped back to the hospital because of a lack of good discharge planning and transition.
DR. MCNEIL: I would like to just mention one experience that I've had recently that bears directly on the topic so far, and that is I have been chairing a committee for the IOM on highly effective clinical services, or the identification of highly effective clinical services for which data might or might not be available, and I raise this as a potential approach for CMS.
What we did, without going into all of the gory details which are not public, was to ask the various plans, the Wellpoints, the Aetnas, the ECRIs, the Winifred Hayes, the Blue Cross TEC, AHRQ, all of the major evidence development groups, what clinically effective services were highest on their list that were most in need of some kind of decision-making for their beneficiaries or their clients.
And what was just enormously striking was the fact that virtually all of those agents, all of those groups were evaluating the same thing within a

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given year period. Within a 12-month period, somehow they all identified the very same 20 or 25 items that have risen to the top of services for which they needed an answer, and in many cases the data were not there, as a matter of fact in most of the cases the data were not there.

And the way they seemed to have identified these services was through individuals in the field saying, you know, we've heard about whatever and we need to get a coverage decision on that, or they just noticed claims coming in. So that might be one way that you could think about, you probably do that already, but it was just striking to see the absolute one-to-one match across six or seven groups. Oh, it was Tom and then Debbie and then Mark, is that where we were?

MR. SCULLY: (Inaudible) stuck with, which is, the reality is cost and size, and that's hearts and strokes, orthopedics, where the vast bulk of the dollars go obviously. But one of the things I think are driving this may be, just to slice it a little more, are things like ICDs. There's a lot of focus on ICDs, we pay differently for ICDs regardless if it's the same thing. I remember when I was here, there was different levels for the ICDs, I could get

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a $9,000 Rush ICD where I could get the same thing with a $32,000 unnamed Minneapolis ICD.

MR. MCNEIL: Unnamed?

MR. SCULLY: I won't say any names, it begins with an M. But anyway, when you get down to looking at those kinds of issues, those are important issues, you know, what is the right level? In MRIs and PET scanners, we were paying for upgraded CTs the same as a brand new PET scanner that was more costly to the manufacturer. You know, things like that when you get to imaging, there are vast arrays of different types of MRIs, CT scanners and PET scanners out there, and we pay the same price for all of them, and I think that's a coverage issue. You know, should we be paying the same thing for a ten-year-old low grade MRI as we do for the brand new one that's much better? Those are big coverage issues that I think are in many ways, both financially and patient-wise, more important than some of the things that have gone on.

One of the other things, somebody mentioned this morning that you probably won't bring

up but I will, because I'm here to be difficult, are coverage issues like Avastin, which is a great drug for many purposes, but apparently it's about to be

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pulled off the market for macular degeneration, because the same company has another drug coming on that costs 20 times as much that's very similar.
DR. MATUSZEWSKI: Let me clarify, not pulled off the market, restricted distribution.
MR. SCULLY: Restricted distribution, and is that an appropriate thing for the Agency to look at? I mean, these are taxpayer dollars and patient issues, and should those coverage issues, even though it's technically a dollar issue, there's no place else that does it. FDA doesn't look at it. Those are important issues for the Agency to look at because they impact patients, they impact Treasury, they impact consumers, and the FDA says it's not their charter to look at them. And I don't think anybody else can look at them and I think as a result of that, it's important for CMS to look at that kind of stuff.
I also think it's important for CMS to look at coverage issues like tie-in medications. Barry knows better than anybody that some of these things on the cancer side, where some companies tie one drug to another. FDA can't look at that, CMS can, as an insurer. I think those are coverage issues that the Agency has to look at.

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DR. MCNEIL: Karl.
DR. MATUSZEWSKI: Barbara, just a quick comment on what you got in your project in the other tech assessment organizations, the responses. I wonder if it was somewhat temporally related to what was on their plate in the immediate vicinity. I'd be curious if any of the responses that they gave of things they wanted evidence for were technologies that were approved and in use for a longer time, for greater than five years.
DR. MCNEIL: No, these were all brand new.

DR. MATUSZEWSKI: These were all recent. So what they basically read you is sort of their top 20 list of things that are on their plates right now. I think in terms of CMS's and Medicare's needs, if there are technologies that have been approved for a long, long time for which no evidence exists, or for which there's a lot of practice pattern variation, and for which we may need some evidence that's going to determine is this a one, a three or a five. And so what those other organizations gave you, I mean that's good for the budget that came out this year, but it's actually probably no help in 90 percent of the things that are done for Medicare patients.
DR. MCNEIL: I think you're right, and

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the other question is we don't see every movement. So let's see, Mark and then Debbie.
DR. HLATKY: I'm trying to think of how all this is going to be used and be useful, and especially if we're saying these are gaps in evidence that should be addressed. I can see two things, we have people from the NHLBI here, and they know stuff, because I'm a cardiologist, they know heart disease really well, and they probably could pinpoint better than anybody here what things are bubbling up and seem right in terms of research. But it also strikes me that at the end of the day there's not enough dollars to fund everything and it might be helpful for them, you know, everything else being equal, to say the one that seems to maybe be more helpful as an issue for CMS or public health, you know, these kinds of things, it's a tie-breaker for things like that. The other one that strikes me is that there is, as much as I respect the NIH, I think they have certain areas that they focus on and other ones that they don't. I can see here that this question that came up on appropriate use of hospice care is probably not on the radar screen anywhere within NIH. And I wonder if CMS could help raise that issue and say look, this is something that maybe falls in

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between the cracks given the way the Institute is put together, and you know, you really need to raise it up higher.
Or maybe, I don't know, I'll pick on NIDDK -- that's the wrong one. For orthopedics, I mean, I think maybe there's a big issue on basic biology, maybe less so on the technology of joint replacements, but maybe that's a huge issue for use here, and maybe more public dollars should be devoted to looking at that issue as opposed to not having it done in a rigorous way.
So I'm just trying to say where can we, you know, this kind of exercise with feedback to the funding agency can be helpful, it seems to me it could be in those close situations, where in other ones they could say here's something that, you know, we find a big variation and all kinds of stuff, and there's no evidence, and we're worried about it, and why aren't you guys studying it.
DR. MCNEIL: Okay. So we have, ready for prime time, Steve.
DR. PHURROUGH: Okay. There were 14 ballots. The top 20 had a cutoff score of four or five, or above.
DR. MCNEIL: What does that mean?

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DR. PHURROUGH: I'm sorry. If we went with a score of four or less, four people saying this is important, we got almost the same thing, so we're only using the top 20, because the top 20 got a score of five or more, so here they are.
Number one was number 56, that had 11 votes.
Number two was number 51.
Tied for three was number 50 and number 1.
Tied for four with seven votes was number 6, number 28, number 52, and number 105.
Six votes, number 16, number 22, number 40.
And the last group is number 7, number 11, number 15, number 24, 25, 26, 58 and 69.
So hopefully that adds up to 20 things

that I called out.
DR. MCNEIL: So orthopedics and neurology didn't make the list; is that right, didn't make the top 20?
DR. PHURROUGH: As part of our follow-up, we will take all the ratings and average those and they will be on our web site to see what the average number is, because the ratings did not have that much distinction between them. The voting for the 25 ones

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you were most interested in did have greater distinction than the actual ratings you gave them.
DR. MCNEIL: So maybe we can take a look at this and see to what extent we think there's some face validity here.
DR. JUHN: Just to clarify, this is where the vote was five and the number of folks that gave it a five score?
DR. PHURROUGH: No. This was the 25 most -- this is how many voted for the 25.
DR. STRAUBE: Steve, is there any way we can somehow quickly put that onto a Power Point slide?
DR. PHURROUGH: No. Maybe before we're done, but not quickly.
DR. TUNIS: So, could I add, just as a first pass comment, when you look at all these, you know, each one of them has a good reason to think that there are evidence gaps there and there would be some importance to further research. So, you know, nothing sticks out at me as an unwise investment of resources to study.
Let me just take one to kind of illustrate where, you know, there is still a lot of work to do in terms of specifying what kind of evidence is

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needed. So you know, one of the ones that came up is the effectiveness of CT angiography, presumably for coronary artery disease. So there's a whole, you know, nest of questions you might ask about that: Its clinical utility for screening patients with

chest pain in the emergency department; there's the clinical utility of use as a screening test in low risk patients; there's initial diagnostic evaluation of patients at intermediate risk. And then you still have to ask the question of, do you want to do a registry or a randomized trial and what kind of clinical outcomes would you be looking for. You would be looking for true sensitivity and specificity over alternative diagnostic tests, or do you really want to show that the test, you know, reduces long-term cardiac events like acute MI or cardiac death.

So there's, you know, no quibble at all with that as being an important topic for study, and you have a national coverage review underway on that particular topic. But, you know, some of the work I have been doing for the last 12 months, we've been struggling with trying to come up with what are the important unanswered questions on exactly that topic and what study would be needed to sufficiently

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address that question, such that decision-makers would feel comfortable using the technology, and it's way hard.

DR. MCNEIL: Right. I don't think we thought it was going to be easy. No, I think you added something really important, Sean. These are not even quite the titles of a chapter of a book, they're very, very high level, and any level of specificity would require a ton of work and there would be multiple subdivisions under that, and you gave us a number of really cogent examples for the CVA one. Mark?

DR. HLATKY: I have kind of a process and outcome question. You said at the end we could rate what, 25 on the list, and this number is not that high, if I counted correctly. And I wondered if the panel after hearing that says well, you know, now looking at the entire portfolio that came out of this, I mean it's a little bit of a Delphi thing, is there something that maybe we ought to raise up? We have a few more spots, you know, some things that

were on the bubble.
For instance, one thing I rated highly,
and I notice they were all on the left side, maybe we
all started on the left and kind of got beat on the

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right. You know, one down near the end that I
thought was pretty important was treatment to slow
progression to chronic kidney disease. I mean, renal
dialysis is a huge problem, you know, if we can
prevent kidney disease, that's a big deal.
I mean, if we have another couple to give,
are there any that aren't rated that we, you know,
somebody would advocate for here saying, you know, we
have a couple others that we could recommend.
DR. MCNEIL: Well, we do have a few slots,
we could do it. The question would be how would we
do it.
DR. HLATKY: Well, I don't know what the
process is for getting there, but I just, I can't
help but notice, I wonder if it's really true that we
think there is nothing on the right side that needs
to be on the list.
DR. MCNEIL: There are several on the
right side, Mark. There are four actually on the
right side.
DR. GRANT: I'm surprised that none of the
orthopedic issues made it to our top list.
Primarily -- well, in large part they have a
tremendous burden of morbidity, we have effective
treatments, we know they're common.

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DR. MCNEIL: Well, people voted in several
different ways.
DR. GRANT: I know we voted a little bit
intuitive, but you know, hip fractures, for example,
to the best of my knowledge we haven't made a dent in
hip fractures over the past 20 or 25 years.
DR. MCNEIL: But that's not on the list.
DR. GRANT: That's not here, I know, but
osteoporosis is, and treatment and prevention of
osteoporosis is, I would think, optimal approaches to

that would be important, and also osteoarthritis, which is extraordinarily prevalent.
DR. MCNEIL: Okay. Why don't we hold that thought, and then Karl, and then I'm going to make a suggestion.
DR. MATUSZEWSKI: You can't let any of the Marks go in front of me, because the orthopedics, again, unbelievable that there weren't some check marks in that area.
DR. MCNEIL: You had your choice.
DR. MATUSZEWSKI: I did, but not enough people, three or four of the five. But that is an incredible disability, incredible dollars, incredible development occurring, and just not a whole lot of long-term --

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DR. MCNEIL: Let me make a suggestion. It's clear that that's the case. Tom, did you want to comment.
MR. SCULLY: If you look at it, it's pretty close to the reflected dollar value of the (inaudible) hear as much controversy about coverage as some of the others, so some of these other things are extremely controversial, and there aren't a whole lot of orthopedic procedures that payment won't be made, and I think the controversies surrounding that area are much less than some of these other areas, which are probably less.
DR. PHURROUGH: I can tell everyone what the next 14 were.
DR. MCNEIL: Sure. We're going to hear the next 14.
DR. PHURROUGH: The next group of those was 14, which is why I didn't include them, because that would take us to 34, and there are a number of the orthos in that group.
But I'll start at the top. The next group was number 4, number 13, number 17, number 19, 35, 38, 42, 49, 61, 72, 81, 85 -- I missed 70 -- 88, and 93.
DR. MCNEIL: Okay. So we have four

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orthopedics, right? Debbie, you wanted to say something, right?
DR. SCHRAG: This is just a procedural, or a process question. And I wonder if this wouldn't be helpful if CMS perhaps internally did this before we undertake this exercise again. As I went down this list, I found myself wanting to separate these items into things that are covered and things that are not covered. So just looking in the top box there, CT lung cancer screening is not covered yet, so there is a sense of urgency because there are people pounding at the gate to get that covered, and clinical trials are in process, as an example.
There are other things that are already covered that perhaps should go to the graveyard and should become uncovered, which is a whole different set of issues, requires different types of studies, different types of implementation, and also you have different types of evidence available.
So I wanted to see this list reformatted by whether it's covered, if it's covered or not, and then for those items that are covered I wanted to see just a ball park blue sky dollar amount and number of patients amount. You know, the information that we received in the background packages reformatted in a

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column next to each one of these, how many lives, ball park rounded to the nearest three million beneficiaries, and dollars rounded to the nearest something, for those items that are already covered. Obviously you can't do it for something that's not covered, but perhaps a projection if CT screening were to be covered, what would the impact be, I don't know, for next time.
DR. MCNEIL: They may not be able to do that for everybody, just because of coding issues and the lack of specificity of the words here, but some of them they certainly could.
DR. SCHRAG: And I guess the reason for that, I think that might make the task easier and I would just hypothesize that if that evidence were

presented to all of us, it might make the task easier and it might make the internal reliability of our scores go up.
DR. JUHN: I would agree, but I would also say that I'm actually quite impressed with how much progress we've made given that this is a list that was just presented to us a couple hours ago.
DR. MCNEIL: We're a good group, Peter, good audience, good group. What do you expect? So one way of proceeding, I'm not sure how

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Barry and Steve would feel about this, would be if you went back with these and kind of elaborated a little bit on what Debbie was saying, and that is go into a little more detail about what actually each one of these meant, and whether or not they were areas that seemed to be appropriate for your decision-making.
DR. STRAUBE: I think what Debbie is bringing up is what I was trying, while Steve was doing the tally, trying to outline a process of how we do prioritization. And this morning when we first started and people were going through their presentations, I made some notes here about prioritization categories and I think Debbie, that's where you're coming out here. The two obvious ones at the top were high volume, high cost, so looking at volume versus cost might be information that would be helpful to everybody to try to help prioritize, including us.
Some of these other ones are potentially more remote, but the setting perhaps, is it in one setting or is it more than one setting, so it would have more relevance across the board. And that would get back into the care coordination piece, we could ask the specific question, does this unanswered

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question have any influence on either improving or worsening or care coordination, or if care coordination is absent, does that have some effect on this.

The hospice care piece was a separate one, I don't know how I fit that into categories, but maybe it would. The pharmaco-surveillance piece I think is one of the prioritization categories, is there some genomic or pharmaco-surveillance or pharmaco-vigilance component to this that would either make it more important or less important. Prevention is the other category, just focused on prevention. And then risk factors, are there mitigating risk factors that would make it a higher or lower priority in terms of the types of patients that we're looking at. I don't know if that sounds clear, but I was looking, are there other things to what Debbie suggested that maybe ought to go into the mix for prioritizing these.

DR. MCNEIL: Yes.

MS. FRIED: The problem, and I understand where she was coming from. The problem is there are

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a lot of covered services, for example if you look at the rehab services which are covered in theory, but for which a lot of people don't have access to. So the problem with, following strictly that format causes a problem. And similarly, you could use that same theory with hospice care, there are restrictions and I think -- I mean, the way it's listed here is very broad, but what the appropriate use of it, even though it's a coverage issue, isn't.

DR. STRAUBE: So Leslie, is that an additional piece of evidence that we need, in terms of evidence about access?

MS. FRIED: Absolutely. Access is a big issue even for coverage purposes.

MS. DAVENPORT-ENNIS: Dr. Straube, I would like to add to the access piece that as we look at the list that you just provided to us, which I think is very cogent and seems very logical to me, if we look at something like a care coordination piece which, that piece normally deals with access issues

too, that service often will deal with hospice issues, pharmaco-surveillance, coordination of drugs to make certain that we're not dealing with toxic side effects just due to drug combinations. They also work a lot in the area of prevention and trying

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to get people into screening.
And so as you look at the one entity on this list for more study and you look at a care coordination piece, that study, if asking the right questions, may indeed give you a lot of information in the other areas that we're all talking about as it related to access.
DR. STRAUBE: By the way, I left off my health disparities thing that I mentioned early, that clearly needs to go in there. And there's another one too that I'm interested in. I mean, all of us being consumers or representing our parents or other relatives as patients, we always ask these questions from a provider or payer or employer or academic perspective, but what about the patient-centered perspective? What do our beneficiaries think are the questions that they need to know? That may be different perhaps than what we're asking.
DR. MCNEIL: I would have thought some of the rehab stuff and the post-treatment would be in there.
DR. STRAUBE: It could be, but within each one of these priorities is there a factor in terms of the evidence gap, do we need to be asking researchers to consider at least the needs of patients with their

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questions.
DR. BERGTHOLD: I think that would be very helpful, and I would hate to think that I was the only, that the two of us are the only ones on the panel who thought about that. But you know, taking out the coordination of care and the setting issues removes, frankly, a lot of the urgent issues from a consumer's point of view. I mean, you know, somebody was saying, well, what do we know about mental

illness in the elderly? We all have mothers so we should know that, right, we should know about mental illness in the elderly, dementia and so forth. I mean, we have our experiences. But, you know, what my 92-year-old mother needs is not necessarily better drugs, but better coordination of care. She goes to the emergency room last week because of a drug interaction. So when I'm looking at this list I'm thinking, you know, we need better information about drug interactions and better information, for example, about just prescribing drugs for frail, small, elderly people who can't take regular doses. But having said all that, I think it would be very helpful to give this to a panel of broader consumers or beneficiaries to, maybe all of them, and

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say from your personal perspective, which of these is most important.
DR. MCNEIL: So you would take basically the list, Linda, or some version of it --
DR. BERGTHOLD: Some version of it, maybe more in English, you know.
DR. MCNEIL: Right. Karl.
DR. MATUSZEWSKI: Over coffee when we were waiting for the Starbucks guy to open up, a group of us were talking about what's really most important, and we were trying to project ourselves into a Medicare beneficiary age, and it really centered on three major areas. It was reasonable functioning, it was mobility and it was cognition, so those three major areas. And I don't want to live to be 100 if it's in an ICU bed and you're going to keep me there for six years. If you could sort of assure that I could live to 80 and have those other three things, then I'm a happy man. If I die from an aortic aneurysm, then that's the way I want to go, quickly. My second comment was, I wanted to compliment all the institute individuals who spoke about the, sort of what are your bad children, tell us your five worst kids so we can really take a whack at them here. And you know, the neurological

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institute has 600 and, you know, all my kids are bad, none of them are really exemplary. But it would be curious on some of the things that we came up on our list today if some of those individuals from institutes say yeah, we've got about three or four trials in progress that we know about, so in a year or so we are going to have some answers, so at that point you want to take those off the table. And then the final thing is that we talk about evidence gaps. I mean, an evidence gap exists for every single disease state. I mean, the next time a new technology comes along, a new discovery in terms of pathophysiological processes, you know, the evidence gap for every single disease state is self-perpetuating. And I was a little surprised that drug-eluting stent long-term safety came up because, you know, I can't wait for the next meeting in Spain that's going to uncover about ten more different meta-analyses on that. I'm not worried about the evidence for that. That's going to evolve, you know, use is down, I'm good with that. The cardiovascular community publishes like crazy, and if there's a little problem, I know there's going to be about three or four RCTs in the next six months about that. What I'm really worried about here is like

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orthopedics, where, you know, I know there's one orthopedic individual in the corner, but they just don't publish as often, and the quality of those trials sometimes is not very good. And there's some other clinical specialties that have suffered from the exact same problem. And those are where it's just a black hole in terms of if it's working or not.

DR. MCNEIL: Peter, did you have a question? No. Leslie.

MS. FRIED: I just wanted to respond. Something that didn't come up today was the issue about caregivers and the role that they play. There's a current (inaudible) the caregiver and the family caregiver assessment tool which is coming out

of CMS, but they put out the tool but not really talked about when it's going to be used. And so when we have people who are in hospitals or nursing homes or somewhere else, the role of the caregiver is huge when it comes to rehab from any reason to some post-acute care, and that sort of got lost, because they're so important to the care for Medicare beneficiaries.
DR. MCNEIL: I think we've had a lot of really good points made. I also think we may be winding down in our additions to the general content.

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So what I would like to do is ask each panelist whether they have anything new to add, not repeating anything that's been said already, but is there any new concept that they would like to put out on the table, or any new level of specificity that they would like to add. I really don't want to go over past ground, so we'll start with Mark.
DR. HLATKY: I just want to echo what was just said about some areas just generically being understudied. I tend to think that actually pharmaceuticals, because of the regulatory requirements, we tend to know a lot more than we do about devices or diagnostics, and especially these other things when we get down to the other areas like coordination or something. If you just look at the quantity of evidence, there's some areas that have an investigative tradition, and I think cardiovascular and cancer are two areas that are updated a lot, and there are other areas that just seem not to get too much at all. I do think it's important and we need to shine the light on a problem that's really very, very important to this age group and to the Medicare beneficiary population. It just doesn't seem to be getting as much attention, and it may be whole areas like you said in terms of orthopedics, or renal

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disease, or some other areas.
DR. MCNEIL: Debbie.
DR. SCHRAG: Just a way to get that

information, just, you know, announcing of Medicare data themselves. There was earlier mention of a registry program but at a very high level, the fee for service claims themselves get 30,000 feet up, but they give a lot of information, although with no granularity, about what's actually happening and what services are being utilized. But the research community, there's a lag, often a three to four-year lag, they're not linked with Medicare. There's all kinds of enhancements that might be made so that those data resources were linked more quickly, that that data were kept more current, to inform this process.

DR. MCNEIL: We've heard that many times from many, many investigators. Karl.

DR. MATUSZEWSKI: One area that I'm not sure quite fits the rules of what we're supposed to be talking about is patient and clinician education/communication, so that we have disease states, we have a test that may have some options or alternatives right now and at least in the commercial research community, comparative effectiveness is a

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very important measure, and I think that is something that some of the institutes should get involved with. So lay out what are the various options for BPH and what are the risks and benefits of each of those. And that way it gets to how the clinician can be educated, not just the surgeon or the primary care individual, or the individual who is going to provide watchful waiting, but communication, and then for the patient to find out so that they go in and know that there is not only one way to proceed.

DR. MCNEIL: Great. Nancy, do you have anything to add?

MS. DAVENPORT-ENNIS: Yes. We talked a lot today about new therapies and the information that we need to have in terms of evidence gap, and there is one area that we did not address at all, and it is the consumer willingness to participate in the cost shifting that's happening. It is not an unusual question for us to have consumers who are in Medicare

to say how much is this going to cost and how much am I going to be responsible for, and what's the ultimate benefit if I agree to this particular therapy? And if I have a stage four disease and I've relapsed twice before with cancer, is this a time for me to begin another regimen of care or is this a time

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that someone needs to have the courage to begin to talk with me about end of life.
So I think as we move forward in the discussion to the master list, Dr. Straube, that you were adding, I would like to see an area added where there is consumer confidence in entering into the cost discussion and what is their participation going to be in that.
DR. MCNEIL: Thank you. Leslie.
MS. FRIED: No.
DR. MCNEIL: Peter.
DR. JUHN: I just want to applaud CMS's efforts in actually getting this process started. I mean, this is obviously not a perfect process but I think it is a process worth embarking on, and I'm actually looking forward to what the next steps will be.
DR. MCNEIL: Good. Linda.
DR. BERGTHOLD: I want to make one comment about comparative effectiveness, only because it's interesting that it does come up as some of the top choices where we were asked to rate something where you looked at various treatments for a given condition. From a consumer point of view, this is the most difficult. Part of our decision-making when

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we get a condition is, how do we know which treatment is effective when there's been so little research.
So I'm very glad to see that a lot of those things came up high on the list.
DR. MCNEIL: Tom, you must have something to add.
MR. SCULLY: I would just say that CMS has no research budget left. I think it's 75 million, of

which 65 million went (inaudible) no research budget. So unless AHRQ and the other agencies actually coordinate with CMS, this is kind of a fruitless exercise. A lot of people don't understand that. They are all part of HHS, which people who work at HHS often forget, or at least they used to. But going back the other way, somebody asked about data sharing for Medicare back to the agencies. CMS (inaudible) other researchers and also electronic health records (inaudible) information and start getting stuff out there. This attention about privacy is wonderful, but you can't run a healthcare system if you're hung up about privacy. And at some point the Secretary or whoever, has to be sharing data between other research institutes and Medicare, and populating electronic health records for things like cancer, if they keep on adding layers of

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privacy, we're going to be in the stone age.
DR. MCNEIL: Thank you. Jean.
MS. SLUTSKY: Sitting between Tom and Sean, I'm mostly passing the mike, but I guess the only comment I would have is when I look at this list, one of the things that really strikes me is the whole issue of applicability. There may be areas where there are trials ongoing or trials that have been done, but generalizability to the elderly and the old elderly is probably a missing piece, and it's important to keep that in mind as we prioritize this further.
DR. TUNIS: Maybe this goes into the category of a suggestion for next step in the process. You know, I think most of the topics that came up here on this list are topics that aren't radically surprising, you know, depression, coronary artery disease, et cetera, so these are known to be big issues for Medicare, so we know we're in the right ball park.
You know, I think one underappreciated resource for identifying evidence gaps is the AHRQ EPC reports because they review everything we know now, and they're pretty good about identifying those

25 things that we don't know that are important, because

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1 the way they actually develop their reports is they
2 first ask their technical expert panel, what are the
3 important questions, and then they go back and
4 collect all the evidence, and then what's left over
5 is the stuff that's important for which there's no
6 evidence.
7 So it seems to me you could take three or
8 five of these that the group seems to think was
9 pretty important, you know, see if there's an AHRQ
10 evidence report, there is one for carotid disease,
11 which was the number one topic. And you know, look
12 at their future research needs section, and perhaps
13 then convene a group like this or something to kind
14 of look at those to see what's missing that the AHRQ
15 report has identified.
16 But I do think a lot of the work about
17 where the evidence gaps are has actually been done
18 and perhaps more effort needs to go into actually
19 prioritizing, you know, where to invest your money.
20 But I think you could try that at least as an
21 experiment and see how far you get.
22 DR. MCNEIL: Thank you. Michael.
23 DR. JACOBS: Well, I was just going to say
24 what Sean said, which actually was said already, that
25 there is more expertise out there that needs to be

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1 mined to give you a better feel for where you turn.
2 And it may be out there, it may have to be gathered,
3 but that's pretty much what Sean said also.
4 DR. MCNEIL: Okay. Well, are there any
5 final remarks from anybody?
6 DR. STRAUBE: I just want, these are very
7 helpful comments, number one. Number two, if you
8 refer back actually to the paper Randy Burkholder
9 submitted and spoke to, that was very much in line,
10 Randy, with what I was thinking early on in the day
11 myself. And he makes some of the comments that you
12 all have just reiterated. The first one you'll see
13 there, the AHRQ list for HHS priorities, but these

were ten conditions that we submitted from CMS at the beginning of the comparative effectiveness, Section 1013 of MMA. And it does overlap tremendously with what we've done.
And as Sean suggested and Randy suggested too, going back to the AHRQ comparative effectiveness studies, and there may be the ability to query some of those people about some of the areas we talked about today.
Randy also put down, you know, the need to have a broader role, that's what I was trying to get at, that there are other categories, other priorities

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that we should be probably addressing and listing out, so I think actually that's something that we can consider as a group at the staff level here as to what, given all these categories, what we would be thinking about into the overlap of these other categories. So this has been very helpful from my standpoint.
DR. MCNEIL: Well, I think that we will be synthesizing all this information, and are we going to get it back, Steven, in some fashion to comment on? Okay. That will be great, and then I guess you'll tell us whether there are subsequent marching orders; is that right?
DR. PHURROUGH: You may have to come back to see me.
DR. MCNEIL: Well, I suspect most of us would love to come back to see you. Uh-oh, Karl doesn't want to come back.
DR. MATUSZEWSKI: I just have a quick question for Steve. When the panelists were filling out their votes, did you notice that there were some people who just had to consistently give everything a four and five, or did you see that everyone was sort of spreading out their ones and twos and threes?
DR. PHURROUGH: I only looked at the

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circles, I was busy counting circles.
DR. MATUSZEWSKI: Because I think a

panelist said there might have been some topics that they weren't sure about, and I wonder if it might have been a good instruction to leave those blank. Or you know, sometimes when I thought it was pretty good I just put down a three, and I really kind of focused on the two ends of the scale.

DR. MCNEIL: But things like that always happen, unless we have a much more detailed discussion about how to run the scale and iterate a few times.

DR. MATUSZEWSKI: Rating it from 1 to 105, that's what we would have needed.

DR. MCNEIL: Well, I'm not sure that showing the 25 items done in a short period of time without a lot of background, we would have done too much better, so I think we're probably okay. First of all, I would like to thank everybody. This discussion was just enormously interesting and hopefully very helpful to Barry and to Steve. I think we got a lot done. I'm actually surprised we got as far as we got in an amazingly efficient fashion. So I thank you all, and thank the

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audience, members of the audience who participated and gave us their thoughtful remarks. We have your presentations and are very grateful to you for pinpointing the discussion in a way that was most helpful to the committee, so thank you. Unless there are other things to say, I think we will adjourn the meeting. Thank you, everybody.

(Whereupon, the meeting adjourned at 2:38 p.m.)

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