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Moderator: And we are at the top of the hour now, so I would like to introduce our participants for today’s presentation. Dr. Aasma Shaukat will be presenting the report finding. She is a Core Investigator for the Center for Chronic Disease Outcomes Research and Section Chief for GI Section and Staff Physicians for Gastroenterology Section at the Minneapolis VA Healthcare System. She is also an Associate Professor at the University of Minnesota in the Department of Medicine, in the Division of Gastroenterology and a Staff Physician at the Fairview University of Minnesota Medical Center.

Joining us today, also, is Dr. Mark Helfend. He will be leading our discussion with our operational partners, as well as moderating the Q&A at the end. And he is the Director of HSR&D’s Emphasis Based Synthesis Program Coordinating Center, located at Portland, Oregon VA Medical Center. He is also a Professor of Medicine and General Internal Medicine at the Department of Medical Informatics and Clinical Epidemiology at Oregon Health Sciences University, School of Medicine, also in Portland, Oregon.

Our operational partners today that are going to be joining us as discussions, we have Dr. Jason Dominitz. He is the National Program Director for Gastroenterology for the Department of Veteran’s Affairs, acting GI Section Chief at VA Puget Sound Healthcare System in Washington, and Professor of Medicine in the Division of Gastroenterology at the University of Washington, School of Medicine.

And finally, we have Dr. Art Wallace joining us. He is the Chief of Anesthesiology Service in the San Francisco VA Medical Center and a Professor of Anesthesia and Perioperative Medicine at the University of California in San Francisco.

I appreciate everyone joining us today. And at this time, Dr. Shaukat, are you ready to share your screen?

Dr. Shaukat: I am.

Moderator: Excellent. There we go.

Dr. Shaukat: Alright. Good afternoon or good morning, everyone. And thank you for joining our ESP cyber seminar today. I would like to start by acknowledging our co-authors/collaborators and other individuals that were instrumental in preparing this report. You can see the topic nominators, stakeholders and expert panel, with representation from anesthesia and GI. And these individuals were critical in giving us guidance and feedback in shaping the report and giving us feedback as the report went by. So I would like to thank all these individuals.

Just in ways of disclosure, none of the investigators on the report today have any affiliations or financial involvements that conflict with the material that will be presented in today’s report.

A word on the VA ESP Program – this program is sponsored by the VA Office of Research and Development and Quality Enhancement Research Initiative, or QERI. And this program is established to provide timely and accurate synthesis of reviews of healthcare topics. The idea is these are questions that are important to clinical practice and relevant to veterans. And the topics can be nominated by anybody throughout the VA. And they go through a vetting process. And here is the website that provides more information on topic selection. This site just outlines the process of ESP report synthesis. It goes through a steering committee. There is a technical expert panel, external peer reviewers and other policy partners. And there are reviews and comments on the draft report. And then the final report is posted on the website and disseminated.

So this brings me to our current report and topic for today, which is Colonoscopy Outcomes by Duration of NPO Status Prior to Colonoscopy with Moderate or Deep Sedation. And you can see the full-length report on the ESP website, and the link is provided.

So by way of background, 14-million colonoscopies are performed in the US annually. Colonoscopies require bowel preparation for cleansing and to be able to sufficiently visualize the colonic lining during the exam. To maximize cleansing, bowel preparation is generally split into two sessions, and this is referred to as a split dose, where half the dose is given the evening prior to the colonoscopy and half the does is given the morning of the colonoscopy, several hours prior to the colonoscopy. And then, typically, some level of sedation, which is typically moderate sedation, is used during the colonoscopy.

Now, the goal recently set by the US multi-society task force on colon cancer screening is that 85% or more of colonoscopies should have an adequate preparation. And this is to make clinics and systems evaluate their process for meeting this benchmark.

Monitoring of preparation quality is recommended by the most recent VHA Colon Cancer Screening Directive, which was released in December 2014. And so the VA acknowledges that preparation quality is highly important and should be monitored. And then most recent GI multi-society guidelines recommend using a split preparation, with the last dose of the purgative given two to 2-4 hours prior to the colonoscopy.

Practice guidelines from the American Society of Anesthesiologists Committee on Standards and Practice Parameters for preoperative fasting for healthy patients undergoing elective procedures suggests the following minimum fasting periods with the goal of minimizing anesthesia-related risks (primarily aspiration). They recommend 2 hours of NPO, or clear liquids, such as water, fruit juices; 6 hours for milk and 6 hours of NPO after a light meal, such as toast or clear liquids.

So an optimal bowel preparation and NPO status seeks to balance two things -- Need for optimal colonic preparation, patient convenience, scheduling efficiency (typically a shorter NPO window status), with the safety of the procedure and any anesthesia concerns for elective procedures, which would typically require a longer NPO status.

So that brings us to our study ends, which was to review the evidence on To review the evidence on relationship between timing of NPO and incidence of aspiration, other anesthesia related harms,

and colonoscopy outcomes. These are our key questions, which were developed as part of this report. The first key question was does the incidence of aspiration and other anesthesia related harms for colonoscopy vary by NPO status or bowel prep timing?

Our second key question was what is the effect of variable timing of bowel preparation and NPO status on the quality of the bowel prep; the colonoscopy outcome, such as diagnostic yield; and other quality indicators, such as completion rates, adenoma detection rates; total procedure time; cecal intubation time and withdrawal time.

Key question three was what is the effect of NPO status prior to colonoscopy on resource use, such as costs, unused procedure slots, delays in rescheduling, delays in diagnosis, increased volume of procedures, scheduler and nursing time associated with cancelled or delayed procedures?

And key question 4 was what is the effect of bowel preparation and NPO status on patient adherence to bowel prep, such as rescheduled colonoscopies, patient satisfaction with bowel preparation and/or colonoscopy?

So the population we considered was adults undergoing bowel preparation for elective colonoscopy with moderate or deep sedation. Interventions were NPO status of 2-4 hours, and this would either be that liquid or bowel preparation was allowed up to 2-hours prior to the procedure. This was compared to any alternative or longer timing of NPO status. And our outcomes, as mentioned, were aspiration events, rescheduled colonoscopies and secondary events of adverse events and outcomes of colonoscopy, including quality indicators.

We considered quality of bowel prep as an intermediate outcome, as well as a whole host of other intermediate outcomes. And the timing was from start of sedation for colonoscopy to completion of sedation for colonoscopy. We did not include studies where there was an aspiration event while taking the preparation prior to colonoscopy. And the setting was either inpatient or outpatient clinics.

Our researched med line for articles published between 1990 through October 2014 and we included studies of any study design that gave any information on duration of NPO. Studies were limited to human subjects published in English. And we also searched references of guidelines, existing reviews, as well as references received from stakeholders and our expert panel members.

We used objective criteria for assessment of risk of bias, for both randomized control trials and observational studies, and based on this individual study, rated as low, moderate or high risk of bias.

We rated the evidence based on published criteria. Overall strength of evidence was rated as insufficient, low, moderate or high. And separate ratings were provided for randomized control trials and observational studies.

So, here is our literature flowchart. Our initial search yielded 1177 references. About 1000 were excluded at the abstract level. We reviewed 108 full text reviews. Many were excluded for the reasons listed. And then we also, based on our hand search and references provided by experts, were able to add several other references. So in total, we included 40 studies, 28 randomized controlled trials, 2 case control trials and 10 observational studies.

So this just shows the characteristics of the included studies. A total of 22,000 patients were evaluated. And most of these studies were from the US and Canada, mean age was 57. And most of these studies reported on colonoscopies or screening colonoscopies.

And this shows the minimum time of NPO that was reported. And this illustrates that about 27 studies reported NPOs of 4-hours or shorter. And this could either be NPO after intake of preparation or NPO for liquids.

And here are some of our results. So for key question one, risk of aspiration, we found 6 studies that reported on aspiration. The studies ranged from 136 to 1300 individuals. Two were low risk of bias. Four were deemed moderate risk of bias. Five of six reported no aspiration events. One low risk of bias RCT, with 125 participants, reported one aspiration event that required hospitalization during colonoscopy under moderate sedation. And this particular individual was a male, obese patient, who was assigned to consume half of the prep 4-hours before the colonoscopy.

So, in summary, shorter duration of NPO is not associated with higher incident rate of aspiration. We found low strength evidence.

Regarding our co-primary outcome, rescheduled colonoscopies, we found one moderate risk of bias, randomized controlled trial, with 113 participants. And rate of rescheduled colonoscopies was 3% in the group that completed the preparation in the morning before the colonoscopy. And it was three and eight times higher, at about 8% and 24% in the group that completed preparation quality the night before. Based on this, we found insufficient strength of evidence that shorter duration NPO is associated with lower rate of rescheduled colonoscopies.

In terms of other harm, there were seven studies, six with moderate risk of bias, one with low risk of bias, that reported on other harm. Four studies reported no adverse events. Three studies reported adverse events to the magnitude of about 1% of the procedures. And these were varied, but they included things such as low GI bleeding, an MI, episode of pancreatitis and an episode of non-cardiac chest pain. And none of them occurred in the group that received the shorter duration of NPO.

Regarding NPO status and gastric volume, there were two studies that were included, with 141 and 712 participants; one low risk of bias, one moderate risk of bias study, where tandem EGDs were performed on individuals that had prepped for colonoscopy at the time of colonoscopy. And in the one studying, comparing NPO of 1.5-hours prior to colonoscopy versus an overnight NPO, the gastric volume was similar. In the other study, reporting a 2-hour NPO prior to colonoscopy versus day before NPO, also reported similar gastric volume. And this is one of the studies that I just highlighted. And you can see the study had three groups of the control group, which were individuals that underwent endoscopy only. And they were NPO after midnight. The second group had their colonoscopy preparation evening before. And the third group had a split dose preparation, with the last dose preparation, with the last dose given 2-hours before the colonoscopy. And the gastric volumes were very similar.

This slide summarizes hospital or population-based studies on aspiration risk during colonoscopy, as reported in the literature. And there are three large studies here highlighted for you that report on the overall risk of aspiration for elective colonoscopies. The first one is a study in 165,000 Medicare patients. And the other two studies are from Australia and Italy, respectively. And the rate of aspiration for colonoscopy reported in these studies ranges from about 1 in 1000 to 1 in 100,000. As you can see, in two of these studies, the duration of NPO prior to these colonoscopies was not reported. And the third study reported that they allowed clear liquids up to 2-hours before the procedure.

Regarding our key question 2, colonoscopy outcomes – we evaluated 39 studies, 28 RCTs, 2 case control studies and 9 observational studies for some of these outcomes. These studies used a variety of different rating scales to rate the quality of the preparation. Quality of preparation was consistently rated higher for NPO intervals of 6-hours or less, compared to intervals of more than 8-hours. However, our study focus was the secondary outcomes, which is completion rate, diagnostic yield, abnormal detection rate, procedure times and withdrawal times.

So regarding abnormal detection rates, we included seven studies and the results were mixed. Four reported similar ADRs, abnormal detection rates in that 2 NPO group. Two reported higher abnormal detection rates in the group with shorter NPO, 4-hour and 5-9 hour NPO compared to the evening prior, respectively. And one study, where the NPO was 4-hours in both groups, found higher abnormal detection rates in the group that received morning only preparation.

So this slide is a [\_\_\_\_\_00:18:34] that summarizes evidence that we found for completion rates, abnormal detection rates and diagnostic yields from the randomized control trials that met our eligibility criteria. So, the first outcome you can see is completion rates. And you can see that we did not find a difference between duration of NPO and rates of completion. Regarding abnormal detection rates, the one RCT also did not show a difference in abnormal detection rates, between shorter and longer NPOs. And also, for diagnostic yield, we did not find a difference in diagnostic yield between a shorter and a longer NPO.

And these are the same three outcomes, but data from observational studies have been included. And you can see from observational studies, there was a suggestion that the completion rate is higher with a shorter NPO and, also, abnormal detection rate was higher when the NPO was shorter, three studies included in that. And you can see the overall estimate, as represented by the black diamond on the screen.

For our key question three, which is NPO status and resource use – so we found no studies that reported resource use, and we searched pretty broadly for resource use as any study that commented on cost, unused procedural slots, delays in rescheduling, delays in diagnosis, increased volume of procedure, scheduler or nursing time associated with cancelled or delayed procedures. Although some studies reported inadequate bowel preparation quality led to cancelled procedures, they did not report whether the colonoscopy was repeated.

Regarding key question four, which is patient adherence, there were no consistent findings for adherence; four RCTs suggested better adherence to bowel prep with split dose versus the day before; whereas, three RCTs showed similar adherence with split dose versus same day preparation.

Regarding patient satisfaction, this was also key question four, we extracted information on elements of satisfaction that would be impacted by different schedules for bowel preparation. So we included work or school time lost. And there were five RCTs that addressed this question. Three reported fewer hours of work lost with split dose versus day before preparation. Two studies reported that the groups were similar in their reported work or school time lost. So the results were somewhat mixed.

Regarding sleep disturbances, there were 7 randomized control trials and 1 operational study that were included. And again, the results were somewhat mixed. Three found that there were less disturbances in sleep with the split dose preparation; whereas, 5 found that the group was similar in terms of sleep disturbance.

So to summarize, hospital or population-based studies have reported the risk of aspiration requiring hospitalization during colonoscopy is low, 1 in 1000 or lower. Duration of NPO in these studies was unknown. In 3 randomized control trials and 2 observational studies, totaling 2300 patients, comparing shorter NPO status to NPO status of 8-hours or longer, no aspiration events were reported.

It is important to note that bowel preparation was completed at least 2-hours prior in 2 studies and at least 3-hours in one study. Clear liquids were allowed up to 3-hours prior in one of the studies and the final study only reported that bowel preparation was completed in the morning for an afternoon colonoscopy.

Twenty of 24 studies reported that time from completion of the preparation to colonoscopy of 1 to 6 hours is associated with greater quality of bowel preparation than time intervals that were longer than 8-hours. One small randomized control trial reported a significantly lower percentage of rescheduled colonoscopies in the split dose compared to the evening before group. And no studies reported on other resource use outcomes, including unused procedure slots or increased volume of procedures by NPO status.

The results were mixed for diagnostic yield, completion rates and abnormal detection rates, with no consistent findings based on NPO status. And results were also mixed for time lost from work, sleep disruption, with no consistent findings based on NPO status.

And here is a summary of the different outcomes that were studied in our key questions and the strength of evidence behind some of the outcomes.

So, we need systematically performed studies that assess duration of NPO status in relation to timing of colonoscopy and recording serious adverse events, such as aspirations requiring hospitalization, special populations at higher risk of aspiration and other anesthesia harms would be of particular interest, such as elderly patients, those with higher comorbidities, disabilities and other factors that limit their ability to follow instructions and complete the preparation. We need evidence-based multi-society consensus guidelines that bring together patient representatives and members from anesthesia, gastroenterology, and other related medical specialties to really come to a consensus on what constitutes best practice. And some of these things can be done through setting up prospective registries of veterans undergoing colonoscopies. And our future efforts should truly be directed towards developing standard methods to collect this information.

And that concludes our ESP report. I am happy to answer any questions. Thank you.

Moderator: Thank you very much, Dr. Shaukat, that was great. At this time, before we get to questions from the audience, I would like to talk, sorry, turn it over to Dr. Helfend and he will be guiding the discussion with our operational partners, Dr. Wallace and Dr. Dominitz. Over to you, mark.

Dr. Helfend: Hello.

Moderator: Yep, you are coming through.

Dr. Helfend: Okay. I just want to check to see who wants to go first? I suppose we could start with Dr. Wallace or Dr. Dominitz. Jason, are you there?

Dr. Dominitz: Yes, I am here. Can you hear me?

Dr. Helfend: Yeah, sure. Do you want to give us a – do you want to say a few words first on the context for this and any other observations you want to make?

Dr. Dominitz: Sure. I’ll try to be brief. So, this is a really important topic. There are about 14-million colonoscopies performed every year in the United States, about 300,000 done among VA patients. About 200,000 of those are done in the VA and about 100,000 done through fee basis. And we need to be very pragmatic about this issue. Split dose prep is the standard of care and is being used worldwide. There are FDA approved regimens for split dose bowel prep. And the risk of inadequate bowel prep is something that is of considerable consequence. Dr. Shaukat reviewed some of the information. Unfortunately, the evidence around some of these issues is limited. The randomized controlled trials of abnormal detection rates based on short versus longer NPO status was on very, very small studies. And the abnormal detection rate is an incomplete measure of colonoscopy quality. All you have to do is find one adenoma to determine the abnormal detection rate. There are other quality measures that have been proposed, like the ADR plus, look at the total number of adenomas.

We know that we have about 140,000 colon cancers diagnosed each year. And about 5% of the colon cancers that are diagnosed are what are called interval cancers, meaning they occur after a colonoscopy. And so it is thought that about half of the colon cancers that are interval cancers are lesions that were missed during colonoscopies. How many of those were missed due to an in adequate bowel prep, we have no idea at this time. but when you have a bad bowel prep, you repeat the procedure, which exposes the patient to another round of sedation, another pushing of the scope through the colon, so the risk goes up and the risk of serious complications with colonoscopy from a metaanalysis are 2.8 per thousand. That is a pretty big number, so we want to minimize the number of time we put people through colonoscopy.

The studies of gastric volume are very reassuring. Gastric emptying of liquids is quite effective. And aspiration events occur despite long NPO status. We really don’t know if the risk of aspiration events increases with a 2-hour NPO set. But at this point, we have no evidence that it does. So we need to be thoughtful doctors, who make medical decisions, and counsel our patients. And for me, I think that the use of split dose prep and short NPO status is important.

And one of the really challenging things, I don’t think – I missed the very beginning of the presentation, I think, but if you look at the survey, an informal survey that is reported in the full ESP report, there is wide variability across anesthesiologists on how they handle this NPO status. And what does that mean for us? Well, practically, what it means is that we go to the least common denominator. If there is one anesthesiologist who says you need 6-hours of NPO and then other 10 anesthesiologists say 2-hours if fine, we have to go with the 6-hour, because we don’t know who is going to be the anesthesiologist on the case. And so everybody gets treated at the least common denominator; otherwise, cases get cancelled. And I know I have, you know, we know that cases are being cancelled, which means patients are being exposed to bowel prep for no reason, you know, no good reason because those cases get cancelled and all the inconvenience that goes with that, and the wasted resources. So although there are no studies on wasted resources, I am sure we all have anecdotal experience that there is considerable waste of resources for this kind of issue.

Dr. Helfend: Okay. Thank you. And Dr. Wallace, do you have some general observations before we get to sort of specific questions for all of you?

Moderator: Dr. Wallace, you’re on the phone with us, correct? Give me just one second. We need to get him his audio pin. So, Dr. Wallace, if you could –

Dr. Wallace: Can you hear me?

Moderator: There you go. Yeah.

Dr. Wallace: Thank you very much for allowing me to talk on this subject. One of the things I found about this subject was that there were an enormous number of people who wanted to send in e-mails, to talk about it. And there is a controversy back and forth. And one of the things that the anesthesiologists are very concerned about is the risk of aspiration. And we had a long discussion about the risk of aspiration. And when we started this evaluation, I decided to do a survey to see what the views were in the VA of what the NPO status should be. And what you found was that about a quarter of people thought that you should have a 2-hour NPO status, and a quarter thought it should be somewhere in between, and a quarter didn’t have an opinion. And some people thought that 6-8 hours was reasonable. And it has gone around, and around, and around, and I have had a number of people say to me, you know, when you look at the FDA status or criteria for this drug, the NPO is overnight. And I talked to someone this morning, who said, you know, this drug isn’t even approved by the manufacturer for use in the split dose preparation. So there is a lot of controversy that has gone around. And I have had people this morning call me to tell me that it’s not approved for split dose preparation. So there is a lot controversy.

And it is interesting that in this review what you find is that we don’t really have definitive evidence that the split dose is dramatically better. And we don’t have definitive evidence that you have a risk of aspiration. But I know that there is an enormous amount of emotion about this topic because aspiration is a very serious problem.

The other thing is when you look at an aspiration rate of 1 in 1000, to a gastroenterologist that is a low number. To an anesthesiologist that is a high number. The risk of aspiration for normal cases is something 1 in 20,000, so 1 in 1000 is a number that is concerning to an anesthesiologist. And so, I was disappointed that the ESP was not able to find definitive evidence that this was better. And I was also disappointed to find that it wasn’t – that there wasn’t clarity at the end of it. But I think what you are finding is that evidence-based medicine is difficult to do. And there is going to be controversy after this report because we didn’t end up with a definitive answer, and I will yield to the next person.

Dr. Helfend: Well, the next person is me for a second here, to ask another question of you, Dr. Wallace. You know, there was also a survey that was published in the *Journal of Gastroenterology Research and Practice*, and this is a paper by Deepak Agrawal and colleagues. And they just surveyed anesthesiologists and gastroenterologists, about 100 each. And, of course, there were big differences in how long people should wait until sedation, as far as fluids. But what I found, but what I want to pull out of this is that the main reason anesthesiologists in that survey objected to shorter waiting times was that they didn’t consider polyethylene glycol a clear liquid. And this seems to be, and I should say this is the very first question that an audience member for this cyber seminar just posed. So, it is a, I think, a very representative thing. Could you comment on the concerns about sort of aspiration of polyethylene glycol versus a general liquid period for prior to a procedure?

Dr. Wallace: This is a very important issue, in that the clear liquid rules are for clear liquids, which are water, maybe juice that is clear. And the volumes are considered small volumes. You know, they are 8-ounces or less. Now, the prep that you are using for a colonoscopy is at least a liter, and it has ethylene glycol in it. And ethylene glycol, when you aspirate it, causes pneumonitis and a very severe ARDS type reaction. So, this is not a clear liquid to an anesthesiologist. It may be clear, in that you can see through it, but it is not a benign fluid that if you aspirate it, it would cause no injury. And so, there is a lot of concern about drinking a liter of fluid 2-hours before, and that fluid, if you actually aspirated it, would cause pneumonitis and death.

Now, let’s think about another comparison to this. When you say what is the 1 in 1000 event rate? The event rate for general anesthesia for obstetrical cases is considered a big issue, and people really worry about aspiration in obstetrical cases, because the women have a full stomach, and they have a high incidence of nausea. And the event rate for mask anesthesia for an obstetrical case is about 1 in 200. Now, no one would ever provide mask anesthesia for, general anesthesia for a woman at term, because the 1 at 200 event rate is considered a catastrophic event and too high a rate. So 1 in 1000 to an anesthesiologist is a very high event rate. And I think that is the problem you are seeing, that you are giving someone a liter of fluid that can cause aspiration pneumonitis and the event rate is a number you can measure, like 1 in 1000. And to us, that is a big deal.

Dr. Dominitz: This is Jason Dominitz from GI. Can I comment? I don’t think we know what the event rate is with this. The 1 in 1000 is coming from the Medicare population, from a database study, where we don’t know the NPO status. We don’t know if these aspiration events are truly related to these procedures or not.

You know, there are tremendous volumes of split dose preparations being done. And we are not hearing about this. It doesn’t mean that it is not happening, and so further research is certainly welcome. But, you know, I am a VA right now, in the middle of the country, that is using in-house bowel prep, where they administer the bowel prep before the colonoscopy, in the procedure room, and finish 2-hours before. And they have had no known aspiration events, but they are going to go look at it now because we are talking about this. And they have been doing this for 20-years. So they were quite surprised the number of 1 in 1000 because they do 3000 or 4000 procedures a year at this institution, 3000 or 4000 colonoscopies.

So we really don’t know. I mean, we must be careful about using this 1 in 1000 number. Also, the bowel prep is being completed at least 2-hours beforehand, not being drunk at 2-hours, so it is typically in the 3-4 hour range that they are starting to drink that additional bowel prep.

And if you look at gastric emptying, the stomach is very effective at emptying liquids, you know, and that is why we are only seeing 20 mls of fluid in the stomach. And it may not be anything – it may not be any of the Colyte that is in those 20 mls. It may be purely gastric secretions and saliva.

So, you know, I think there are a lot of unknowns here, and so we have to be very careful about making assumptions about this. And the FDA approval, how many bowel preps are FDA approved for split dose? And as we all know, once a company gets FDA approved for a certain regimen, they are not going to go back and spend the money on getting FDA approval for a different regimen. So we have to be honest about this, and so let’s be honest about this. FDA approval does exist for split dose prep. We can’t keep spouting this lack of FDA approval.

Dr. Wallace: As someone who has done a number of trials, what I have learned about event rates is that people are really lousy at writing down events. And we did a number of studies in strokes, in cardiac surgery, and people would say this never, ever, ever occurs. And then you will say, well, here is the event rate. We did the NeuroCog test before and after. We did stroke scales before and after. And unless people are looking for events, they are really terrible at identifying them, recording them, publishing them. They occur, and I think you have to be careful that someone says well, we’ve never seen this happen. My reaction to that is, well, did you look? And frequently, people haven’t really looked.

Dr. Dominitz: Well, and that’s why I said they are going to go back and look at it now. And that is important. You are absolutely right.

Dr. Helfend: Let me, yeah, I think everyone, certainly the two speakers, three speakers, including Dr. Shaukat, you know, I think everyone agrees that a lot of this discussion is about sort of the evidence not being where we would like it to be. And, sort of, in a way, we are formulating or thinking about the ideal study, or the study, even if it is not ideal, that would answer some of these questions. And I wanted to summarize where we are, just so far, in the conversation.

The, first of all, everybody has focused a bit on this issue of aspiration as an outcome. One thing that I noticed in the report is that it is talking about aspiration requiring hospitalization. If you were designing the next study, though, an outcome defined as something like aspiration requiring hospitalization can be hard to ascertain; that is, somebody could have a procedure, not aspirate dramatically at the moment enough to be hospitalized, be hospitalized later. And then there is some doubt, because of other illnesses or other things going on, about the cause of the aspiration, or what to say about it.

And so, the other aspect that has come up in the conversation so far is the consequence or severity of the aspiration. This gets at the issue of whether aspiration of a clear liquid and aspiration of polyethylene glycol is any different.

So, I guess, what I am trying to get at is that when we say or, Jason, when you say they are going to look at their data. There have only been a few thousand patients in the studies to date that the review talked about. There are hundreds, as you mentioned, hundreds of thousands of colonoscopies. How feasible is it to quickly get a handle on the actual rate of hospitalizations after colonoscopy, and maybe how many are attributable and how severe they are?

Dr. Dominitz: I think it is quite doable. In fact, you know, I don’t know if there is anybody on this call who wants to do that study, but I have been thinking about doing a study doing the corporate data warehouse, where you have to identify outpatient colonoscopies and then see how many of them end up being admitted and for what reason. And with 200,000 procedures pure year, it is relatively easy. What is not easy is determining –

Dr. Wallace: We have already started doing that in San Francisco, because we think it is important to get a real number. And so we are starting to do the analysis.

Dr. Dominitz: Right, but what is not easy is determining the NPO status of the individual patients. That information is not recorded in a systematic fashion, so it would require chart review and even that may not document the actual duration of NPO status. So, as a surrogate, you could potentially identify facilities that, by protocol, use split dose versus those that don’t and see if there are differences.

Dr. Wallace: Our plan is to survey the facilities to get the NPO status and then see if we can see an association between their stated NPO guidelines and the event rate.

Dr. Dominitz: Right. That will be very interesting information.

Dr. Helfend: So, Dr. Wallace, I want to turn this last issue – I don’t want to leave this issue of polyethylene glycol because, as I said, it seems to be so much of a concern. Does that mean, conversely that, you know, and I am not trying to get ahead of ourselves here, as a sort of a system. But does that mean there would be much less concern with the 2-day split dose regimens for the low volume preps, you know, the things like sodium picosulfate, magnesium citrate, those kinds of preps? Does that mean that a lot of this concern would go away?

Dr. Wallace: It depends what is in the material. I mean, if – the way people try this out is they take an animal and they squirt it into the lungs of an animal and they say does this cause pneumonitis or ARDS. And I haven’t looked at the literature for these other preps, but that is the standard approach is to squirt it into the lung of a test animal and see what happens. And anesthesiologists think about what the PH is, the volume is, what is in the material. And you would need to look at these other agents to see if they are safer.

Dr. Dominitz: And if I can speak, on behalf of GI, obviously, nobody in GI wants a patient to have an aspiration. We have – this doesn’t make our lives any better to have patients have aspiration. And the NPO duration doesn’t directly make our lives easier or harder. What it makes a difference in is the quality of the bowel preparation. There is high quality evidence that bowel preparation is better with shorter duration.

Dr. Wallace: Well, I – before you push that on, I mean, the ESP didn’t really conclude that, which is kind of shocking to me, because everyone says it is much better. But the evidence from the ESP was that it was hard to show it was a lot better.

Dr. Dominitz: It was better, in terms of bowel prep quality rating. But the study is looking at other outcomes, like abnormal detection rate or cancer rate. There was very limited evidence on that. There were only very, very small randomized control trials. Observational studies showed it a benefit in ADRs, but randomized control trials were very small. Aasma, correct me if I am wrong.

Dr. Shaukat: That is right.

Dr. Dominitz: So bowel quality using [\_\_\_\_\_00:45:32] shows a dramatic difference. But further outcomes have not been well studied. Is that a fair assessment, Aasma?

Dr. Shaukat: Yes, that is a fair assessment. There were very few studies that looked at hard outcomes. A large body of evidence suggesting that shorter duration of NPOs associated with higher quality of bowel preparation; however, the studies had not done the next step, which is look at outcomes of colonoscopies, such as completion rates, diagnostic yields, abnormal detection rates.

Dr. Dominitz: And it is important –

Dr. Helfend: I am going to, oh, sorry, I think I am going to ask the thing you were maybe about to answer, Jason, or Aasma, you can answer as well. It is a little surprising. I don’t want to put this question in confrontational way, but the GI guidelines that you cited early on, in one of the early slides, they seem to feel – they seem to come, you know, they gave the impression, I read them a couple of days ago. And, you know, they gave the impression that the evidence about diagnostic lead and yield, and completion rates and so on, was stronger than it came out in your report. I guess what I would think about this and, Jason, this may be what you should comment on. If something is that obvious, that is, if something is, you know, there is only sort of thin or anecdotal evidence, seems self-evident, almost, that procedures are being cancelled, that completion rates are not what they should be, that a number of people are being subjected to more than one procedure, or are being delayed more than we think is safe in order to get their second procedure. If all those things are really at the level that we can see them with our own eyes, without a study, it should be quite easy to find out in a study how big they are. And so, I guess, my question is, how did that happen? Why is it that the studies haven’t been able to demonstrate this, and what is the next step up?

Dr. Dominitz: So, I don’t know that I can give the definitive answer. I will give you my opinion, which is that there are a lot of studies on bowel prep, dozens, and dozens, and dozens of them. And they typically have about 100 or 200 patients per treatment arm. And they are designed by drug companies that are trying to show that their regimen is better than another one. And they want to do the smallest study possible to show a difference in their bowel prep regimen versus another one, and they use an outcome that they can measure that on, which is these bowel prep quality scores. And so they don’t do it on abnormal detection rate, or cancer detection, or diagnostic yield, because that has a lot of variability and if it is harder to measure they would have to have a bigger study design. So I think it is really an issue of who is paying for the study that defines it. But that is my opinion. I don’t have any evidence, other than my experience to base that on.

Dr. Shaukat: Absolutely. I would like to add that so, Mark, we found, as I mentioned, a large number of studies with the outcome of having a higher quality bowel preparation. At the same time, there are a large number of studies that suggested that high quality of bowel preparation led to higher abnormal detection rate, diagnostic yield, completion rates. But we were not able to include any of those studies because they didn’t have information on timing of NPO. So the GI community has taken that as indirect evidence that the outcomes of studies are kind of broken up into two different sets. And taken together, it suggests that shorter NPO improved these outcomes. But there were very few studies that looked at the direct association of the two.

Dr. Dominitz: Yeah, I think it is the transcendent property of mathematics, you know, if A is better than B, and B is better than C, then A is better than C, I think that is what we are doing in GI.

Dr. Shaukat: Right.

Dr. Wallace: The problem with that, in evidence-based medicine, is that it is not sufficient. And that there are a lot of studies where the logic makes complete sense, and I love logic, and logic is great. And then you do the study and then you find that it doesn’t work. So the transcendent property of logic is a wonderful thing, it is just not sufficient in evidence-based medicine.

Dr. Dominitz: Yeah, there are a number of studies that have looked at interval cancers, and interval cancers are what we are worried about. And, so as I said, about 5% of all cancers are interval cancers. And one of the strongest predictors of interval cancers is suboptimal bowel prep. And we know that suboptimal bowel preps are associated with longer NPO status. So, as I was saying earlier, the GI community does not want aspiration events, we really don’t. And so, you know, if there is evidence that the shorter NPO status was increasing the risk of aspiration, then I think you would see the GI community endorsing longer NPO status time. But, right now, without that evidence and with the evidence that we do have, we are worried about missing cancers. We are worried about making patients go through a second procedure. And that is why I am passionate about this issue. I completely understand the anesthesia perspective on this. And, you know, we don’t want patients to be harmed. But they can be harmed by a longer NPO status and it is important to balance these issues together.

Dr. Helfend: I think people listening this, who want to know, you know, how can this be resolved. I was actually struck by your comment earlier, Jason, that just on a practical level, if you are trying to be, if you are trying to schedule people and there are several different practice styles of anesthesiologists, some of who want a longer period of NPO and others who don’t, you have to schedule to, you know, you can’t really – you could end up with a cancelled case if you don’t know who is going to be assigned. So that it could be difficult, really, to assume that the policy of some places, what is really being done, as long as somebody disagrees with the policy. And so, as far as giving our folks listening an idea of what could be next, in addition to more studies. The report suggested, you know, working on guidance. I think, indirectly or directly, you two may also be suggesting some kind of guidance process, with the evidence we have, while we are trying to collect more. And so, I’ll start with you, Dr. Wallace, what do you see as a way forward on this issue?

Dr. Wallace: Well, the first thing you find is that guidance documents are supposed to be based on Level I evidence, and you don’t really have that. And then you turn around and you say, well, okay, we are going to have to somehow go from the current state, which is a giant hodge-podge of different rules, and different people having different rules, to something more consistent. And my opinion about the way you do that is you change the culture slowly, and you prove that what you are suggesting is safe. And so, what I suggest we do is we do some epidemiology to look at what the real event rate of aspiration is in the VA, and we look at whether there is an association with NPO time. And then we say, okay, let’s shift the NPO time from the 6-hours that many, many, many people think it is now, down to 4-hours and see if anything happens. And then if nothing happens, shift it to 3 and then shift it to 2. And I suggested this to our gastroenterologists a couple of years ago, and they didn’t want to do that. And because they didn’t want to do that, we have now gone through three or four more years of having this variable GI NPO rate. And so I think that the way you change a culture is you provide good evidence for what is safe. You provide legal protection to people who are changing what you are doing. And then you shift the culture by doing it slowly. And you say, okay, let’s try 4 and then let’s try 2. And what you will find, if you do this for a couple of years, is that you will quickly be down to 2-hours and people will be comfortable doing it. But if you don’t do that, four or five years from now we will still have this hodge-podge with variable timing for NPO status.

Dr. Dominitz: I mean, it is a tough situation, Mark. And top line, I can tell you where the site is that has been using 2-hours for 20-years now, and maybe you can look at their data and maybe that will help you. But, you know, if we go to 4-hours, what would happen to the sites that are using 2 now? It is quite variable across the VA. And this is not just a VA issue. There are some private sector facilities that are going through the exact same thing.

Dr. Wallace: But more than 80% of the VA thinks that it has a 6-hour NPO status right now, because I polled to find out what it is. And if you want to shift it over, you’ve got to provide people the legal cover to do it, and you’ve got to provide the structure to do it, and you’ve got to reassure them that it’s safe, and you’ve got to show the event rates. And it is very easy to show event rates now. We could do the epidemiology and show that. But you do have to put in the effort to do it to reassure people that what they are doing is safe.

Dr. Dominitz: Yeah, we would have to carefully craft policy that allows, you know, that might maybe goes to 4-hours, but doesn’t disallow a 2-hour NPO status. If we disallowed it, of course, that would be problematic.

Dr. Wallace: Well, no, I am saying move the curve slowly.

Dr. Helfend: Right, and so I am going to amplify on move the curve slowly. I think that moving the curve in the manner that you suggest, or moving it in another manner, like something more quicker, either way, it seems to be the key ingredient is the data driven environment; that is, not doing something for years and years and still not know what its effects are. And so, in addition to the will to try, as an organization, to test the waters on different strategies, you know, the situation we apparently have had, where we are not measuring the things that people really care about, as far as the impact of different policies, that seems to have to change; that is, we have to, right now, and I have sort of heard a couple of instances where people say, yeah, we are going to look at our data. But in a continuous data environment, you know, signals pop out at you if anything happens. That is the environment that permits that kind of change.

Dr. Wallace: So, we are supposed to be a learning organization. And we are supposed to be using our informatic system to improve the quality of care. And the VA Anesthesia Service would very much like, and is working to set up a nationwide VA quality improvement program to be able to give you data like this, to improve systems over time, know what the real event rates are. And make the VA really into a learning organization. And I think this is important. We applied for a grant this year to support this, and it wasn’t funded. But I think the VA really needs to do this if you want to improve care, improve access, and improve quality. I mean, that is how people do it in the modern age. They analyze their data. They make intelligent decisions. They watch what is happening. And you improve the system over time.

Dr. Dominitz: And I fully support that and we are trying to get better data systems for endoscopy. We don’t have a data system for endoscopy in the VA right now. We have a hodge-podge of ways people complete endoscopy reports. And I have been pushing for something along the lines of Cart, which is using cardiology people may be aware of, so that we can get higher quality coloscopy data and other endoscopy data. And, of course, if we did that, it would be possible to have a feel for how long somebody was NPO, and then we would be able to link that information with outcomes data.

Dr. Helfend: And so, we are about out of time, is that correct? We have one minute left?

Moderator: Yes.

Dr. Helfend: I did want to, I did get – I did want to expand a little bit, before we conclude, and say in this data system, or ask, I should say, in this data system. Again, Dr. Wallace, if you could address this. What is the role of the type of the depth and the type of sedation in this? Is this an issue? I noticed that the report had sort of focused on moderate, mostly the studies focused on moderate sedation. But is there anything from the anesthesia side where there might be practices that vary, that could also be important to look at in this, in monitoring how we are doing here?

Dr. Wallace: Much to my surprise, there are places that do colonoscopy without sedation. You know, if you do it without sedation, then aspiration is a lower probability event. There also are different approaches, depending on whether you are using SEDASYS or you are using narcotics. You know, how long people are asleep for. So the type of sedation matters, the depth of sedation matters. How long people are rendered so they are not good at protecting their airway matters. And that is a difficult thing to capture in an epidemiologic study. But all of those things matter in how long people are at risk of aspiration.

Dr. Helfend: Thank you. And so, we are concluding. I want to thank all of the speakers, and all the listeners, and those who submitted questions. And is there a final word that you need to give us, Moderator?

Moderator: Yes. Thank you so much to all of our panelists and presenters for joining us, and for our audience members. And I am going to shut down the meeting in just a second, and there is going to be a feedback survey that pops up on your screen. So please take just a moment to fill out those few questions. We look very closely at your responses and it helps us improve sessions already given, as well as ideas for new sessions to support. So thank you once again to everyone. And this does conclude today’s HSR&D cyber seminar presentation. Have a great day.

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