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EDMUND G. BROWN JR.
Governor

Percutaneous Coronary Intervention Advisory Oversight Committee (PCI-AOC)

August 21, 2014 @ 2 – 4 p.m.

California Department of Public Health (CDPH)
1615 Capitol Mall, 95814
CDPH Building 173, Rooms 665 & 666

Facilitators: Dr. Anthony Way and Dr. William Bommer

Welcome and Introductions – Dr. Anthony Way

Announcement

Dr. George Smith, a PCI-AOC committee member passed away on April 15th from apparent heart complications at his home in Santa Rosa. We are all terribly sorry to hear that and he will be missed.

Roll Call

There are 12 members. There will be 11 with the passing of Dr. George Smith. Dr. Fehrenbacher is out of the country and Dr. Robert Davidson is unavailable today.

Members in attendance:

- Dr. Aditya Jain
- Dr. Sushil Karmarkar
- Dr. Steven Arnold
- Dr. Rohit Sundrani
- Dr. Steven Forman
- Dr. Ralph Brindis
- Dr. William French
- Dr. Dipti Itchhaporia

Members absent:

- Dr. Fehrenbacher
- Dr. Robert Davidson

- Dr. Mahmoud Farsani

There are eight members present. A quorum for 11 members would six. The PCI-AOC can conduct business.

Participant Roll Call – Gladys Glaude (Sacramento State)

The following individuals also participated in the meeting:

- Suresh Ram
- William Bommer
- Robert Forey
- Kevin Spruce
- Dennis Patrick
- Danielle Bennett
- Edith Jonas
- Joanne Easley
- Amie Selda
- Anthony Way
- Tessa Semanski (Sutter Roseville)
- Kathy Robidoux (Los Alamitos)
- Lucina Mallavarapu (St. Rose)

Introduction

The California senate received the legislative report created last November approximately two weeks ago. It has been posted on the California Department of Public Health (CDPH) website and should be posted shortly on the PCI-AOC website. It will not be discussed today because we need to await feedback from the legislature.

Dr. Way turned the meeting over to Dr. William Bommer from the University of California Davis Medical Center to report three-year and four-year study results.

PCI-CAMPOS Data Update (three-year data) – Dr. William Bommer

Extended condolences on the loss of Dr. Smith, “an esteemed leader in California for cardiovascular health care and a valued member of our AOC who contributed greatly.”

The AOC report contained information that was current at that time, basically the two-year data that was submitted and included in the AOC report. The data reviewed today represents those two years, plus one more. It is a three-year cumulative report.

On August 1st (2014) we finished our first four years of the program. Planning to release that data in December after analyses.

Slide Presentation

- Title: The Percutaneous Coronary Intervention California Audit Monitored Pilot with Offsite Surgery (PCI-CAMPOS) Outcomes in 153,950 Patient Procedures in Hospitals with and without Onsite Cardiac Surgery
- Participants have a copy to review.
- This data was also presented at the American College of Cardiology as one of the featured research presentations at the annual meeting of the American College of Cardiology in Washington DC.

Disclosures (slide)

- This study was conducted by the California Department of Public Health and was funded by the pilot hospitals without onsite surgery.

Background (slide)

- The ACCF/AHA/SCAI guidelines listed elective PCI as a class III indication meaning not recommended in 2005. That changed in 2011. This program began between those guideline changes. Therefore, it was initially enacted as a pilot program to study this so we could get more information for California on performing elective percutaneous coronary interventions in hospitals without cardiac surgery.

Aim (slide)

- The aim was to determine and compare the initial safety and efficacy outcomes of PCIs performed at hospitals with (onsite) and without (offsite) cardiac surgery in California.

Method (slide)

- Our design is a prospective parallel cohort multicenter registry controlled trial. The co-primary end points include composite safety, which was death, stroke, or emergency CABG (coronary artery bypass graft), and composite efficacy, which was <20% residual stenosis and post TIMI-3 flow.
- The secondary outcomes include all-cause mortality, stroke, and emergency CABG as individual entities and residual stenosis <20% and post TIMI-3 flow as individual entities.

Hospital and Operator Requirements (slide)

- Offsite hospitals required approval from the California Department of Public Health; a formal PCI development program; participation in the elective PCI pilot program and NCDR® Registry; signed emergency transfer agreements and 24/7 backup for transfer; and the capacity to perform 200 PCIs/year and 36 Primary PCIs.
- Offsite operators had to perform at least 100 PCIs/year, 18 Primary PCIs; with lifetime experience ≥ 500 PCIs; have ABIM Interventional Cardiology and Cardiovascular Disease certification; and be active participants in a CQI program.
- Onsite hospitals also had to participate in NCDR® Registry and onsite operators needed to be approved by hospital credentialing.

Method (slide)

- Includes all California patients admitted for primary and non-primary PCI from July 2010 to 2013.
- There were six offsite hospitals and 120 onsite hospitals with surgery included.
- The exclusion criteria included individuals that were deemed to be high patient risk and high lesion risk. Offsite hospitals were recommended not to include patients that were both high patient risk and high lesion risk.

Method – Audits (slide)

- For offsite it includes 100% central auditing of the case and review of all Cath/PCI fields. The hospital site received a 20% audit onsite, 10% random and 10% PCI complication selections. Interventionalists at the central office reviewed 20% of all angiograms.
- Onsite programs had NCDR® 100% review of certain fields and selected hospital sites received an audit. Twenty-five national sites were identified each year for random NCDR® hospital review audit.

Statistical Methods (slide)

- We developed a multivariate PCI risk model and risk adjusted the primary outcomes for the six pilot and 120 non-pilot hospitals that performed procedures.
- Initially bivariate analysis was used to create complete, parsimonious, and refined multivariable logistic risk models.
- All models were evaluated with a Hosmer-Lemeshow goodness-of-fit statistics and deciles calibration testing.
- C-statistics were reported as measures of predictive power.
- A general linear model for analysis variance was used to compare observed, expected, and risk-adjusted composite event rates. The Poisson exact probability method was used to calculate and compare provider risk-adjusted composite rates.

Baseline Characteristics (slides)

- On each of these slides you will notice that on the left we address All PCIs, the middle columns contain information on Primary PCIs, those patients who came in with STEMIs, and the right-hand columns refer to the Non-primary PCIs, that is non-ST-elevated myocardial infarction which could include elective or ENSTEMIs as well.
- Age range across all these groups is fairly similar, approximately 65 years of age.
- Two-thirds of these individuals are male.
- The ethnicity is mostly white with smaller proportions of black, Asian, Hawaiian, Indian and Hispanic ethnicities.
- Offsite hospitals represented 32% of patients with STEMIs versus only 17% in the onsite. Right away we see that the pilot hospitals have a higher prevalence of STEMI patients coming in.
- If we look at PCI status, there are obviously more emergent PCIs and salvage done at the offsite hospitals, again reflecting many of those emergent cases are STEMIs for admission at 34% versus 19% for the onsite hospitals. And the corollary to that is

seen for Non-primary PCIs. The onsite hospitals had a higher prevalence of elective PCI cases at 47% versus 41% in the offsite hospitals.

- Most of these changes in patient population were statistically significant. Realizing that we enrolled 150,000 patients at the onsite hospitals and 3,773 at the offsite, the large numbers in these populations means that small differences are clearly statistically significant in almost all of these fields shown.

Lesion and Procedural Characteristics (slide)

- We cover the type of lesions: the location in the coronary artery, the presence of bypass graft lesions and the length of lesion, and lesion stenosis.
- The lesion length is somewhat shorter for all cases, but for Primary PCIs it is also somewhat shorter for offsite compared to the onsite hospitals. There is a two- or three-millimeter difference that is shorter mean length of lesion in the offsite hospitals compared to the onsite hospitals. This may reflect the fact that all or many of these patients at the offsite hospitals were audited with angiographic review and corrections or changes were made in many of these cases to shorten the length of the lesion. That angiographic review was not present at the onsite hospitals and there was a tendency for those to be somewhat longer despite looking at similar populations in California.

Multivariate Logistic Regression Model for Composite Event (slide)

- This represents the model where we identified 24 significant variables to include in the model. When those were included the C-statistic on the right is shown as 0.892, which represents a relatively significant amount of the variation could be explained by this model and represented a relatively high C-statistic for this analysis.
- The Hosmer-Lemeshow showed a p-value <0.0001, which represented some difference between the actual predicted model and the observed model that was shown. Calibration analysis, however, showed that there were no systemic underestimates or overestimates of events when we defined all of the individuals into calibration of risk status.
- The left side of the slide shows the individual variation that was present in the multivariate analysis. For some of the parameters, as an example the presence of intra-aortic balloon pump or cardiogenic shock significantly increased the odds ratio of an event, which was the composite event (death, stroke, or the need for emergency CABG). The risk for those risk factors was very significant in this analysis.
- Other parameters of borderline significance are also included in the multivariate analysis with their relative risks shown based on the slide by their distance from unity on the line through the center.

Safety Endpoints (slide)

- This is perhaps the real meat of the trial: Can PCIs be done safely in hospitals without surgery on site, the so-called offsite hospitals?
- For All PCIs, the observed composite outcome event rates were 2.86% (offsite) and 2.33% (onsite) ($p < 0.033$).

- However, the predicted endpoints based on the risk assessment of each individual, were 3.58% (offsite) versus 2.31% (onsite). Each of these composite endpoints was risk adjusted in the model and the offsite risk-adjusted composite event rate was 1.87%. The onsite composite adjusted risk outcome was 2.36%. Thus there is a significant difference with the onsite hospitals with cardiac surgery having a risk-adjusted higher composite outcome (death, stroke, and need for emergency CABG). This was statistically significant for All PCIs.
- There indeed was still a higher risk-adjusted mortality and stroke and CABG rate for individuals even if they had primary PCI. This was statistically significant.
- Under non-primary PCI, there is a slight difference between offsite and onsite risk-adjusted elective cases but it is not statistically significant. There was a lower event rate for All PCIs and Primary PCIs that was statistically significant. There was a slightly lower event rate for Non-primary PCIs that did not meet statistical significance.

Question from participant (Dr. French via phone)

- How can there be risk stratification if by definition all high-risk patients were not supposed to be done offsite but were supposed to be transferred to onsite? They can't be the exact same patients.

Response from Dr. Bommer

- We talk about that in limitations. Some elective high patient risk and lesion risk patients were excluded from the trial. Now, your question is, "How are we seeing such a high-risk population here?" The reason in the offsite hospitals is largely because offsite hospitals take twice the incidence or prevalence of STEMIs that the other hospitals do have and obviously STEMIs come in with more chance of cardiogenic shock, more chance of having or requiring balloon pump and having other high-risk features. The high patient risk and lesion risk applied only to elective cases in that situation. As we look at more elective cases, which are the Non-primary PCIs, there is a slight difference there but the predicted rate for the Non-primary PCIs was still higher in the offsite hospitals than in the onsite hospitals. This relates to lesion length, complexity of the lesion, all of those features. What we have is at least evidence here that even though the offsite hospitals were avoiding the very highest risk patients, that is, high lesion risk and high patient risk, their overall mix of risk was still as high or higher, even in the elective cases, than the onsite hospitals. The onsite hospitals performed a larger number of low risk patients and that may relate to the referrals patterns that they are encountering.

Return to Safety Endpoints (slide)

- Moving down to secondary endpoints which are listed as death, again these are only observed endpoints because we did not risk adjust for the individual endpoints and we show for example here, the observed endpoints for death (cardiac cause, non-

cardiac cause), emergency CABG and stroke. You can see here that other than observed death, none of these numbers are statistically significant. They are listed for observed but I caution against those because those observed endpoints are not risk adjusted as the upper composite events were.

- The most important aspect is listed in the third row down, the patient risk-adjusted endpoint rate, which again showed significant differences that is lower risk-adjusted rate for All PCIs and for Primary PCIs. There was no significant difference for Non-primary PCIs. This data suggests that the safety endpoint was as good or better for All PCIs, Primary PCIs and Non-primary PCIs at the offsite hospitals compared to the onsite hospitals.

Efficacy Endpoints (slide)

- For efficacy in this trial we included successful treatment of the lesion. Successful treatment of the lesion was defined as the composite of <20% residual post-PCI stenosis and the presence of TIMI-3 post-PCI flow. Adequate flow in the vessel and no significant residual lesion.
- If we look at All PCIs we can see offsite at 88.4% and onsite at 91%. This small difference was statistically significant showing that onsite hospitals had a somewhat better success rate for the composite efficacy for All PCIs.
- If we look at Primary PCIs, we see a small 2% to 3% improvement for onsite hospitals for the composite efficacy rate; statistically significant.
- If we look at Non-primary procedures there is again a slight increase of about half a percent improvement for onsite hospitals over onsite. This was not statistically significant.
- Overall, there appears to be a small, in two situations, significant increase or greater success rate for the composite in onsite hospitals compared to offsite.
- The secondary observed endpoints outline the stenosis post procedure by itself and the TIMI-3 flow by itself. As you would expect there is a somewhat better efficacy with higher rates of low stenosis in the patients that were onsite compared to offsite as well as a slightly higher TIMI-3 flow for patients who were All PCIs as well as in individuals that had Primary PCIs. The significance disappeared when we got to the more elective, Non-primary PCIs.

Dr. Karmarker comment

- “The lower success rate at the offsite hospitals was by design perhaps. In our practice if there is any impediment to delivering wire or balloon we’re supposed to terminate the procedure and not go to more and more aggressive wires which you can do at onsite. So the lower success rate is almost by design of the study. Does that make sense?”

Dr. Bommer response

- “Yes. I mean I understand what you’re saying. The question will be, “That success rate which was perhaps almost audit biased, which means we went and did quantitative angiography on the angiograms we received, and we, because of

quantitative angiography downgraded initial estimates of post-PCI stenosis rates in many cases of the offsite hospitals. This was not performed for the onsite hospitals. There was no angiographic review of the onsite hospitals.”

Hospital Safety Ratings (slide)

- For the offsite, five hospitals performed as expected with a 2.0% risk-adjusted event rate in the first three years. One hospital performed better than expected with a 1.25% composite event rate. There were no hospitals that were worse than expected.
- For onsite hospitals, we found 106 performing as expected with a 2.48% risk-adjusted composite event rate. Eight hospitals performed better than predicted at a 1.23% composite risk-adjusted event rate. We identified six hospitals performing worse than expected with a 3.8% composite risk-adjusted event rate, which was statistically significant. These were outliers in the onsite hospital population comprising initially of 120 hospitals of which six were outliers and worse.

Summary (slide)

- California Pilot Offsite hospitals perform proportionately more Primary PCIs (32%) versus onsite hospitals (17.9%).
- The risk-adjusted composite safety endpoint (in-hospital death, stroke, emergency CABG) was significantly lower in offsite (1.87%) versus onsite (2.36%) hospitals.
- The composite efficacy endpoint of stenosis <20% and TIMI-3 flow was significantly lower in offsite (88.4%) versus onsite (91%) hospitals.
- No significant differences were seen in stroke, emergency CABG or Non-primary composite safety and success endpoints.
- No significant hospital volume/outcome relationship was seen.

Limitations (slide)

- These were similar cohorts in many ways but they were different. There was a much higher prevalence of STEMI patients or Primary PCIs in this group. They were not randomized. In other words, individuals coming into this program arrived at one hospital or another and were not randomly assigned to an onsite or offsite hospital.
- There was a higher level of audit in offsite PCI procedures that may have had some influence on the results.
- The exclusion criteria are individuals who were deemed to be or met the criteria of high lesion risk and high patient risk were encountered in 0.4% to 0.64% of offsite hospitals. In other words, some of the supposed patients who should have been excluded did get included at some point, but it was a small number (between 0.4% and 0.64%) of offsite candidates. This number was also evaluated for individuals who met the exclusion criteria who were performed at onsite hospitals and there is a higher prevalence of these very high-risk patients encountered at the onsite hospitals, between 1.68% and 2.97% of the onsite patients who met the criteria for high lesion risk and high patient risk. However, the individuals in both groups who met the high lesion risk and the high patient risk and met the exclusion criteria did not experience worse outcomes at either of the sites.

- Confirmed operator feedback was available to offsite operators. If we encountered individuals who were or had excesses or adverse outcomes, we called the primary investigator and we talked to the individual and possibly changes were made at the hospital as a result.
- High-risk compassionate use criteria were not included in this risk adjustment. They were available for the pilot program but not for the onsite hospitals because the NCDR® Registry currently does not include high-risk compassionate use criteria.

Conclusions (slide)

- The pilot offsite hospitals showed slightly better PCI composite safety and worse PCI composite efficacy endpoints than onsite hospitals.
- Emergency CABG rates are low in both offsite and onsite hospitals reducing the need for onsite cardiac surgery.
- Offsite hospitals perform more Primary and fewer elective PCIs than onsite hospitals.
- A significant composite safety variation with outliers remains for onsite hospitals.

Acknowledgements (slide)

- Lists the individuals that work on this.
- This is obviously a team approach and it's a very large team. This is just a small number of the large team that is working on the pilot program.

That concludes the slides from the preliminary presentation of three-year data and results of the PCI-CAMPOS program that was initially presented at the ACC annual meeting.

Open Comment on Three-year Data

Dr. Sundrani

- The investigators that you had to so-call police because of the audit in the pilot PCI protocols, were there a lot of people like that? I'm not aware in my hospital, you don't have to go into details, but did you have to do this quite often with people at the offsites that were policed so to speak because the outcomes were bad?

Dr. Bommer

- No, it was a very limited number of individuals.

Dr. Jain

- I know we said Primary PCIs versus Non-primary and we clumped non-STEMI with elective. Wouldn't it be better for people to see this with non-STEMI with STEMI because the pathophysiology is the same with STEMI and non-STEMI versus elective?

Dr. Bommer:

- The grouping that we used was precisely the grouping that was reported in the CPORT-E trial and the MASS COM trial. Those are the large randomized trials related to offsite PCI. We tried to pattern ourselves after those so we could at least examine

the information in relationship to what has previously been reported in randomized trials.

Dr. Jain

- Sure, but I was just wondering, would it be interesting to see. What we've seen in the past few years is that PCI really has a STEMI and non-STEMI population for sure and elective poses a little bit of a different disease and the pathophysiology is different. So I think a stronger case would come if we were to do non-STEMI and STEMI without surgical stand by compared to elective. That's just what we have seen in the past few years from our experience here locally. I was just wondering if you have any comments.

Dr. Bommer

- We do actually report, it's not in these slides, the NSTEMI and STEMI individual cases. The problem with that is we have to have a large enough group together to do our risk-adjusted composite endpoint. We can individually report out the observed both NSTEMI and STEMI situations. Pretty much when we look at Primary PCIs, those are all STEMIs. All the Non-primary PCIs constitute the individuals who had NSTEMI or elective procedures.

Dr. French

- You've done a great job with the data as you usually do, Bill, and I think the data is the data and there's not much you can change. There are obviously some differences; all hospitals are not the same. My concern is extrapolating this data to 40 other hospitals. I'm just totally concerned that this is not the way to go. If the read on the data is that everyone's equal no matter what the criteria, I'm very concerned about that.

Dr. Bommer

- Okay.

PCI-CAMPOS Data Update (four-year data) – Dr. William Bommer

On August 1st we completed our fourth year of the program. I have preliminary numbers available because all of the patients may have not yet been entered into the data system. We will continue to analyze them and anticipate presenting complete four-year data as soon as that is available. I appreciate that you did not get a copy of these slides. These will be sent to you.

Currently, the four-year enrollment of the PCI-CAMPOS program stands at 5,047 patients. The observed mortalities for years one through four are: first year, 2.2%; second year, 2.1%; third year, 2.65%; fourth year, 2.43%. We do see a slightly higher mortality in years three and four versus years one and two.

The volume numbers for each hospital in year four are: pilot hospital one, 403 patients and the largest enrollment; pilot two, 304 patients; pilot three, 100 patients; pilot four, 130 patients; pilot five, 139; pilot six, 198. The enrollment range in year four was a high of 403 and a low of 100.

Open Comment on Four-year Data

[No public comment]

Items for Discussion

Senate Bill 357

SB 357, which was our extension, extended SB 891 until December 31, 2014. We are operating under SB 357 right now and will continue enrollment, data entry, and auditing until the end of this calendar year. We will continue hospital CQI, and audit reviews until December 31, 2014, in conjunction with that legislation.

We will also analyze the four-year pilot and California data as soon as that data is available. We anticipate submitting the four-year cumulative data when we have the final four-year results for the PCI program. We will be presenting four-year data with approximately 5,000+ pilot program enrollees and approximately 200,000 California onsite enrollees.

We will submit a final written report of data analysis, comparison, and risk adjustment modeling to the California Department of Public Health by January 1, 2015.

Senate Bill 906

Senator Correa introduced SB 906 on January 21, 2014. It passed the initial committees in the senate and was passed by the senate. It went to the committees in the assembly and passed the assembly health committee and the appropriations committee last week. This week it cleared the assembly with an amendment. It now goes back to the senate because of the amendment. If the senate approves that amendment then it will have passed both houses of the California legislature and will go to the governor. The governor has to sign the bill, veto the bill, or ask further questions.

Public Comment on Senate Bills

Dr. Sundrani

- To plan for the hospitals, what happens January 1, 2015? Do we have a plan for those patients? Any suggestion or feeling? It requires a lot of infrastructure and commitment to get this program to run on our side and on everybody's side including yours. I don't know what to do on January 1st, 2015. Are we prepared for it?

Dr. Bommer

- Under SB 357 the program ends December 31, 2014 and currently there is no signed legislation that takes the place of that. However, if SB 906 passes that bill allows the current pilot hospitals to continue operation for one more year they then would have to apply to the CDPH for ongoing certification to allow them to continue their program. I cannot comment other than if that bill is not signed, then we don't have anything whereby the offsite hospitals could continue to operate at this time. I think

we will have an answer to your administrator within three weeks as to whether it is signed by the governor's office.

Dr. Sundrani

- This question is for Dr. Way. Is there any parts from the state with the good work all the hospitals are doing and I guess serving the community. We are serving the community here. Is there any suggestion or, there is that cost associated with it. Hospitals have been paying for and we'll continue to pay it. Is there any part in that process that the state would be able to let us do that?

Dr. Way:

- Speaking for the state I can't make any comments about pending legislation. It's against the rules, against the law. As an entity that works for the state we can't make comments on legislation at any time.

Dr. Jain

- Let's say if this bill was not to pass, and hopefully it will pass, come January 1st, we are allowed to do STEMIs, would we be able to do non-STEMIs in emergency cases or would it be only STEMIs?

Dr. Way

- The STEMIs are only allowed to be done because of the unwritten rule that you have a life safety event, you have the possibility of death if you don't intercede, but there's nothing written in the regulations that allows a STEMI. It's done strictly off the books because you're saving a life.

Dr. Jain

- So any lifesaving procedure can be done whether its STEMI or non-STEMI if it's saving a life.

Dr. Way

- That's true. Yes. That's allowed, not under the CDPH, but under the Medical Board of California. A physician is allowed to do whatever he needs to do to save a life, even if it's not a purview or normal course of action.

Review Dates for Future Meetings

Dr. Bommer

- We anticipate that the NCDR California data will be released to us approximately October 20th of this year. It will take us three to four weeks to process that data representing over 200,000 patients and a huge number of fields before having a risk-adjusted model to process. So we anticipate that we would need until last week of November or first week of December before we would have data to present to you on risk-adjusted four-year data for the program. We suggest having our next meeting when that new data on the four-year is available and audited and analyzed. That would be the last week of November or the first week in December. We could also go to the second week in December as well. I would hesitate to go beyond that because people will be involved in holiday planning.

Discussion

- The last week of November is the week of Thanksgiving so a vote for first week of December.
- All commenters agreed
- Wednesdays are not good for the Clovis team
- How about December 11th?
- Good for board members on the line
- 2-4 p.m. on December 11th @ HQ
- Calling in is acceptable
- Dr. Way will send a reminder as it gets closer

Adjourn - 3:19 p.m.

Thank you and have a great afternoon.