UNITED STATES DEPARTMENT OF DEFENSE

DEFENSE HEALTH BOARD

OPEN MEETING

Arlington, Virginia

Wednesday, December 12, 2007

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P R O C E E D I N G S

(8:15 a.m.)

CAPT BLOOM: -- consequences may result from untreated or under treated PID, including four to ten fold increase in the risk for chronic pelvic pain, a six to ten fold increase in the risk for ectopic pregnancy, a six fold increase in the risk for infertility, as well as an increased risk for recurrence and the potential for tubal ovarian abscess, and peri-hepatitis among active cases.

The pathogenesis of this disease is highly complex, with etiology likely to be polymicrobial and CT chlamydia representing one important causative organism. Chlamydia itself is now the most frequently diagnosed bacterial sexually transmitted infection among industrialized nations with approximately three million cases annually diagnosed in the United States.

Of particular note is the large proportion of female chlamydia infections that are

assymptomatic and a high probability of progression to pelvic inflammatory disease among chlamydia infections.

Furthermore, data suggests that chlamydia associated PID is itself often assymptomatic and that a prior chlamydia infection may predispose one to later PID development. Recognized risk factors for PID and chlamydia are generally consistent with one another, primarily age less than 25 years, which comprises both a behavioral component, risk taking behavior, and a biological component associated with the histology of the cervix.

In addition, race/ethnicity, with African- Americans generally being at greater risk than other race ethnic groups in the United States. More recent, new, and a greater number of sexual partners are both associated with increased risk for chlamydia and PID development.

In addition, contraception methods have been associated with PID. Barrier methods are associated with a decreased incidence,

intrauterine devices a temporary increase in PID risk, and oral contraceptives have been associated with a decreased risk of PID development.

Also, low educational achievement, living in the southeastern United States, and other factors such as cigarette smoking have been associated with increased risks for chlamydia and pelvic inflammatory disease.

Due to the high prevalence of assymptomatic infections and severe reproductive consequences of chlamydia and subsequently PID, the United States Preventive Services Task Force recommends that all sexually active women less than 25 years of age receive an annual screening for chlamydia.

In response to this recommendation, this very board, under the prior designation as the Armed Forces Epidemiology Board, recommended chlamydia screening for all female military accessions, as was noted in the introduction.

The U.S. Army instituted a policy of screening during the first year at the annual

required gynecologic exam in fulfillment of this Armed Forces Epidemiology Board recommendation, whereas the U.S. Navy has instituted a policy of screening all women within the first few days of service. So, screening of Army recruits may be delayed up to 12 months compared with the Navy recruits, assuming 100 percent compliance with service specific screening policies.

Our aim for the analysis I'll present today was to consider rates of PID among Army and Navy accessions by service and to describe any differences observed.

For the purposes of this analysis, a case was defined as the first occurrence of an outpatient pelvic inflammatory disease diagnosis on record. This was ascertained as a 614 prefix ICB9 Code.

Now, we restricted this case definition to outpatients only in an effort to first, increase the internal validity of the analysis and that inpatient and outpatient disease may be patho-physiologically different. For example,

chlamydia associated PID generally presents as a more mild condition than that associated with gonorrhea with the later perhaps increasing the likelihood for hospitalization.

In addition, we wanted to increase case capture and generalizability of the analytic results as the majority of U.S. cases are diagnosed and treated in the outpatient setting.

Data for the current analysis were captured using the Defense Medical Surveillance System, the DMSS, which many of you are likely very familiar. Women were included in this analysis if they one, were accessioned into the active component of the Army or Navy between the first of January 2001 and December 31, 2005.

Now, the starting date was chosen in order to allow services time to implement the 1999 Armed Forces Epidemiology Board chlamydia screening recommendation. And the ending date was chosen in order to assure complete data capture at the time of data analysis.

In addition, women had to be less than

25 years of age in order to focus the study on a higher risk group and maximize the number of events captured. And women had to have no missing covariate data. I'll describe these covariates in a moment.

We captured just over 58,000 Army and 33,000 Navy accessions for this analysis. Now, the women included in this study were followed from their date of accession into service until the first diagnosis of PID, their 21st -- 25th, excuse me, birthdate, separation from the active component, or the end of follow up again on December 31, 2005. We captured 1,276 incident outpatient PID cases among Army accessions and 546 cases among Navy accessions.

This figure demonstrates the distribution of follow up time in the current study stratified by service, in which Army is represented by green bars and Navy by blue bars. The median follow up time among Army accessions was 12 months with 57 percent of the cohort followed for a minimum of 12 months. And these

women contributed 588 case diagnoses.

The median follow up time among Navy accessions was 21 months. Sixty-six percent of the cohort was followed for a minimum of one year, and these women contributed two hundred and forty case diagnoses.

Covariates that were identified in the literature as important predictors for pelvic inflammatory disease and were also available in the Defense Medical Surveillance System included race/ethnicity and home of record, which were fixed at the time of accession into service; in addition, age, which we used year of birth as a fixed proxy during analysis and time in service, for which we used year of accession as a fixed proxy.

In addition, education, rank, which was employed as a proxy for socioeconomic status, and marital status, which was employed to represent sexual behavior varied over the duration of follow up.

Now, our analytic strategy during this

study comprised several phases. In the first, a uni-varied analysis was conducted, in which crude PID rates were characterized by service and values for the aforementioned considered covariates. We also conducted a bivariate analysis in which associations between and among service covariates and PID rates were considered.

In the third phase, a multiple Poisson regression analysis was employed to evaluate the effects of covariates on the observed service specific PID rate association. This employed a multinomial approach in which service was entered as a predictor for PID.

And any covariates demonstrating a p value less than.01 during the aforementioned bivariate analysis were entered into a steprise procedure. There were -- retained p value for a coefficient was less than.05, competence interval of 95 percent, excluding unity.

In addition, confounding and employing a changing coefficient criteria for the service PID association as well as interaction employing a

change in log likelihood criteria relaxed to a p less than.01 were subsequently evaluated during their multiple plus zone regression analysis.

A time to event analysis was conducted as well in the fourth phase, and this employed the life table method using four month intervals of follow up to characterize changes in risk for PID over the duration of follow up or time since accession.

This table demonstrates the distribution of fixed covariates at accession. All covariates fixed at the time of accession demonstrated statistically significant differences between service using p less than.05 as the criterion.

Army accessions were more likely to be African- American or Hispanic than Naval accessions and less likely to be Asian or Native American. Furthermore, Army accessions demonstrated a higher probability of reporting a home of record in the southeastern United States than did Navy women.

This table demonstrates the distribution

of time varying covariate values at the time of accession. When considering time varying covariates, values at accession were also significantly different between services. Army accessions demonstrated a higher proportion of postsecondary education at accession as well as a higher probability for being married.

In addition, Army women were accessed at greater rank overall than were Navy women. This table demonstrates crude risk ratios and 95 percent competence intervals for PID by covariate. Only statistically significant risk ratios are presented here in the interest of space. These risk ratios were generated using simple Poisson regression models.

Army presented an incidence rate of 13.6 diagnoses per thousand person years. This was approximately 64 percent greater than the Navy rate of 8.3 diagnoses per thousand person years or follow up.

Among race ethnicity, only Asian, demonstrating a percent decreased risk relative to

the reference category, white and African-American demonstrating a 60 percent increase risk relative to the reference category, whites, were statistically significantly associated with pelvic inflammatory disease diagnosis.

Women who reported a southeastern state as their home of record were at a 22 percent increased risk relative to those women who did not. Each increased level of education demonstrated a 33 percent decrease in PID risk. Education was modeled as an ordinal variable.

Unexpectedly, married women were at a 27 percent increased PID risk compared with unmarried women. However, other data suggests this observation is due to a greater healthcare utilization and case ascertainment among married as compared to unmarried women, rather than due to a causal association between marriage and pelvic inflammatory disease.

We also noted a linear trend of decreased risk with increasing rank as evident by the 48 percent and 75 percent decrease in PID risk

among senior enlisted and officer ranks relative to junior enlisted ranks respectively.

Following consideration of all the aforementioned significant covariate predictors of PID, possible confounding and interaction terms, the final multivariable model comprised service, race/ethnicity, marital status, and rank as predictors for pelvic inflammatory disease.

Please note that the effect estimate for service indicating a statistically significant 62 percent increased risk for Army compared with Navy and adjusted for other conditionally independent predictors of PID is very similar to that which was observed for the crude analysis, which was an approximate 64 percent increased risk.

This suggested that no confounding occurred by the considered covariates. Again, Asian race ethnicity was protective and African-American was a risk factor for PID independent of service.

The increased "risk" associated with marriage was also independent of service, and the

protective effects of rank persisted in the multivariable model as well. Also please note that education and home of record were not retained in the final model, indicating that they were not independent predictors of PID conditional on other covariates in the Poisson regression model.

Whoa, okay. This graph demonstrates the hazard function with what were supposed to be 95 percent competence intervals as a function of time since accession. Hopefully, they are visible on your handouts. These are stratified by service with solid lines representing the army and the broken lines representing Navy.

The hazard function, for those who aren't familiar, describes the instantaneous risks for being diagnosed with PID conditional on having not been previously diagnosed or censored, so conditional on still being at risk at any particular time point T sobye (?).

Please note in particular that during the 8th to 24th month of follow up and you can't

see on the picture here, but in this interval, the 95 percent competence intervals for the instantaneous hazard function do not overlap between services, suggesting a statistically significant difference.

Substantial overlap of these intervals occurs following the 24th month of follow up. Further note that the greater variability appears to occur among the Army accessions, the solid line, with the Naval accessions, the broken line remaining comparatively uniform during the period of follow up.

The ratio of the hazard function over follow up approximates the earlier described crude and adjusted risk ratios, which were 1.64 and 1.62 respectively.

So overall in this analysis, we observed that adjusted PID rates were approximately 62 percent greater among Army compared to Navy accessions. Marital status, race/ethnicity, and rank were independent predictors of pelvic inflammatory disease diagnosis among military

accessions, Army and Navy. And significant differences in the hazard rate were evident in the approximate 8 to 24th month post accession.

There were several limitations for the current analysis, just a few of which I'll summarize. The complex pathology of PID, that is there are several causative organisms associated with pelvic inflammatory disease development. In addition, a small proportion of pelvic inflammatory disease is not even associated with sexually transmitted infection. Furthermore, no incubation period is currently defined for PID.

We also employed a clinical case definition, which may have poor sensitivity as well as specificity. And the later has been demonstrated previously in studies comparing clinical case definition to the gold standard of laproscopy.

Our service comparison, that's Army versus Navy, the exposure assessment in effect assumes differential patterns of CT screening, chlamydia screening. We have no data to confirm

this assumption. Due to the surveillance nature of these data, we had no information regarding sexual habits, use of contraception, or other important covariates that may be substantial confounders of any service pelvic inflammatory disease diagnosis association.

Furthermore, there was a possibility for an ascertainment bias due to the diagnosis of women with PID while at sea among the Naval accessions that may not have been captured by the DMSS, our data source. However, other data we have suggests that this role, if in effect, would likely be limited.

However, the current study offered -- analysis, excuse me, offered several advantages including the employment of a large sample size with a fairly large number of events. Furthermore, the results of this analysis were consistent with those of a clinical trial of chlamydia screening and PID development among high-risk civilian women in Seattle, Washington.

We had complete covariate data with

accommodation for variation in covariates over time, and the effect estimate for service risk was consistent regardless of covariate adjustment.

In conclusion, I believe the results of this analysis suggest a need for the design and conduct of a comprehensive, hypothesis driven study to identify the most probable source of the reported difference in service specific PID rates among female military accessions.

And in this vein, I'd like to leave you with a favorite quote of mine by Isaac Asimov. I believe it's curiously appropriate. "The most exciting phrase to hear in science, the one that heralds new discoveries is not eureka, but that's funny."

I'd like to acknowledge and thank my collaborators on this project and analysis for their hard work and especially their patience and tolerance. And thank you, the audience, very much for your time. Thank you.

(Applause)

DR. POLAND: Okay. It's open for

questions. I'd like to focus, because there's a lot of methods guys here, a little less on the methodology and more on the substantive issue.

Just as a reminder, you have under tab 8 the considerable number of times the Board has considered this and issued basically the same recommendation in regards to recruit training. And this is data confirmatory of our concerns that this be done at the recruit accession level.

So, Wayne, you want to start?

MR. LEDNAR: Wayne Lednar. A very nice analysis of this issue, so thank you for taking us through this. And without dwelling on the methodological issues, I thought you explained them really quite nicely.

CAPT BLOOM: Thank you.

MR. LEDNAR: What I wonder about the Army's experience, when you describe it's an older groups, it's a higher ranked groups, is whether or not the accessions into Army basic training have a greater proportion of individuals who will go onto the reserves and the National Guard than perhaps

the Navy accession stream, so that they're bringing to basic training really quite a difference experience and of course, coming out of basic training in the follow up period, will be perhaps in a different situation as well, obviously more married.

So, the groups are quite different in a way that may relate to risk that may be important as we think about implementing a standardized set of screening.

What I was listening for but I didn't hear was given the difference in service policy for screening and your analyses, how you come back and tie the two together.

So, would you suggest the Army would be well served by adopting an approach more similar to the Navy given your observations of incidence and follow up?

CAPT BLOOM: Well, in response to your first point, all of these women that were captured in this study went into active duty at least in this case, both Army and Navy. And this was -- we

decided on doing this in order to be able to capture most, if not all, medical encounters among these women who have complete medical coverage through the military, as you're well aware, on active duty.

As far as whether or not the Army policy should be changed to resemble that of the Navy, I can't answer that, sir. All I -- all I believe this analysis says is that something in the Army appears to be going on differently than that in the Navy. And a hypothesis driven study looking at chlamydia screening possibly itself will be merited in order to find out what accounts for this difference.

DR. POLAND: Dr. Halperin and then Dr. Gardner.

DR. HALPERIN: The methods are great. Can't resist and I'm paralyzed by the separation of methodology from policy but I'll try anyway. So, rather than a whole other study, within the Army, you have people who were screened at various times from very soon, like the Navy, to very late,

at the extreme at a year.

So, have you done or considered, for example, a nested case control study within the Army looking at essentially dosing it? That is, women who are screened within the first month, within one to five months, within five to nine, nine to twelve, looking to see whether the impressive differences that you found really have to do with the thing that's staring us in the face, which is the Navy screens early and the Army screens anytime, so it's basically a dose response within the Army.

You already have the data, looking to see whether the earlier looks more like the Navy and the later looks worse than what you've shown for the Army because the Army is obviously a combination of early and late screens.

CAPT BLOOM: That will be an ideal approach, I think, sir, to what we have here. However, at the time of the study -- and I'm not sure if this has changed -- the DMSS did not have laboratory data available, and so, that's an

inherent limitation here is that I have no idea -- or we have no idea, excuse me, who was actually screened and who wasn't and when they were screened.

If we did have these laboratory data, I would be thinking exactly along the lines hopefully of what you just mentioned, because I think that's a very appropriate approach.

DR. POLAND: Dr. Gardner?

DR. GARDNER: Another variable I didn't hear covered was the partner treatment and was that equal in the two services. The Navy screens males the leukocyte esstrays (?) test at recruits and the Army doesn't. So, if you -- if you got rid of -- if you treated the males or more effectively, then you might end up with differences in the (inaudible) in the two services.

CAPT BLOOM: That's an excellent point, sir.

COL GIBSON: I just want to add we've got a series of presentations here which will add

to and synergize with Dr. Bloom's work. This issue of availability of laboratory data, the ability to look at the compliance with policy on periodic reproductive health programs and doing chlamydia screenings at those reproductive health exams will add to the discussion.

I have one real small question. The -- I noticed you used rank and we had some E6s in there and since your cohort was under 25 years of age, what was the -- how many E6s do we have who are under 25 years of age?

That's kind of an unusual group, couldn't have been very many. I'm surprised that it was selected as the covariate rather than length of service, which is -- what I would think would be the one to go in.

CAPT BLOOM: Yes, sir. We examine length of service as well, which actually the slopes even stratified by Army Navy were flat in terms of PID risk for length of service. And with regard to the E6, there were one or two in the entire group that were identified. And I can go

back and check on the exact number --

COL GIBSON: There was -- when we had this cumulative risk ratio, the -- and I agree your methods were pristine, very nice. But you have -- we have quite a bit of difference in the time in service for these two cohorts. The issue is cumulative risk over time. They're -- obviously, they've been in longer. The Army was in longer. And you use the covariate of rank to look at that. I was -- I guess I'm just a little surprised. I would have expected the opposite to go into the -- into the model. But, good work.

CAPT BLOOM: Thank you, sir. We can discuss more after. That's a very interesting point as well.

DR. POLAND: Dr. Shamoo?

DR. SHAMOO: I realize all epidemiologists -- almost all of them use race as one of the parameters. And I'm all the time uncomfortable with that for a variety of reasons. One, I think it's stigmatizing. Second, it's inaccurate, especially in this day in age of

genetic sequence, especially for African-Americans. The genes which controls pigment has very little to do with all the rest of susceptibilities.

And genetic sequence is becoming cheaper and easier and faster. And my thinking is when would the epidemiologists start thinking and moving away from using really the race as one of the parameters. Because what do you consider race, one over thirty-two, one over sixteen, or homozygous, only one out of one. It just makes no sense. It's a terrible average and it's terribly stigmatizing.

CAPT BLOOM: I couldn't agree more on that issue. These were self-reported races.

DR. SHAMOO: I understand.

CAPT BLOOM: And reported in the surveillance data, but I couldn't agree more with you.

DR. POLAND: Dr. Silva, I don't want to go deeper into that issue because it's not one that's going to get fixed her today, so --

DR. SILVA: Oh, I know that. But, I think setting this committee up for future thinking and our preventive officers. I mean the time has come to start using this arbitrary designation.

And I got home last week and I found out our students of the University of California, all 252,000 decided race for Asians was very arbitrary and they want a breakdown now into 16 or 18 different categories.

So, we're not going to solve it here today.

DR. POLAND: Okay. Dr. Parkinson?

DR. PARKINSON: I'm just scratching my head looking at this 62 percent difference just like everybody around here. And what I -- sometimes I just -- just basic blocking and tackling. Are we confident that our coding, the way the Navy codes and the Army codes are both equal here, I mean in terms of the way in which it gets from the doctor's note into your database?

I mean, do we systematically go back and

quality improve that? I'll tell you, my own experience is we take these numbers as gospel and we don't dig behind what actually happened in the clinic, so just to double check.

But, I mean, it's striking the difference and I'm sitting here scratching my head saying why in the world would it be so different. Because screening issues aside, I can tell you there's not 100 percent compliance with any doctrine that comes out of DOD or for that matter, Bumed.

So, I don't -- I'd just ask us to go back and look at the accuracy and the quality of coding practices across the two services and the guts of how it actually works -- just a thought.

DR. POLAND: Dr. Oxman?

DR. OXMAN: Is there any difference between the cultural availability, if you will or the stigma or lack thereof of going for an ob/gyn symptom-driven visit in the Navy and the Army?

CAPT BLOOM: That's an outstanding question. I have no idea. Would you repeat that?

DR. OXMAN: I just wonder --

DR. POLAND: Turn your mike on.

DR. OXMAN: I wonder whether there is some difference in the likelihood that a moderately symptomatic woman would seek care, ob/gyn type care in the Army versus the Navy, whether there's a different stigmatization or some philosophic difference that could account for that.

CAPT BLOOM: That's an incredibly good question. Let me add this on top of that. Most of these -- most services -- the services have a policy for annual reproductive screenings. In most cases, they have some method locally, not generally, but locally to -- to make sure the appointment is kept for they -- for your annual pap smear.

That in itself would tend to lessen the issue of cultural differences, granted they have to -- you know, a woman who is symptomatic has to present so at least annually. Please, go ahead and add to my --

DR. POLAND: Do you have anything pertinent to that? Did you have a comment pertinent --

MS. HITCHCOCK: I do. Good morning. My name is Penny Hitchcock. I'm the former chief of the Sexually Transmitted Disease Branch of the National Institutes of Health, and it was under my tenure that the daily school study was done in Seattle, which showed a 41 percent reduction in PID if you screened women who came in to a clinic with a risk profile and treated for chlamydia as opposed to waiting for women to come in with symptoms that are consistent with PID.

So, let me say that I completely empathize with the discomfort with respect to racial issues. However, it has -- back to Tuskegee, racial issues have been a valid parameter and predictor of sexually transmitted infection.

And I think that one of the questions that was asked here towards the end is really important insight. Both access to care as well as

insurance affect people who are marginalized both socially and economically from seeking care. And time and time again, the manifestation of chronic disease is higher in African-Americans primarily for that reason.

Now, although the military is colorblind with respect to providing care, we're inheriting infections when people enlist. And I think it's really important -- another point that was made is to screen regularly and early on to try to understand this better and to try to develop and effective intervention strategy.

Just a couple of more points if you --

DR. POLAND: Very brief, please.

MS. HITCHCOCK: I think that the issue with mean is extremely important. Recent papers, there are now four of them in literature to suggest that serology for chlamydia trachomatis is a predictor of infertility in a marriage whether or not the woman is sero positive.

And I think as soon as we see mean as a key part to preventing and controlling

infertility, in this case cabbett tests, we are not going to be able to solve this problem.

So, there are new tests coming on board, rapid tests. And with the use of erythromycin, I think we have the tools to deal with this.

The question is -- to use your quote, which I liked a lot, can we use this peculiar set of circumstances to help rethink our strategy here. Thank you.

DR. POLAND: Thank you. Colonel Defraities, you, I think, wanted to make a presentation.

SPEAKER: Yeah. Thanks very much. As Mike mentioned, he was on active duty with the Army medical surveillance activity for the last year and just recently decided to seek his fame and fortune, such as it is, in academics. He's always welcome back. And to that end --

COL GIBSON: They give good haircuts.

SPEAKER: Yeah, really. He has got his hair cut already, so he's able to come back on active duty. We did have an award that we didn't

get an opportunity to present him. And just keep your seats but please tend to the orders.

The Department of the Army, this is to certify that the Secretary of the Army has awarded the Army Commendation Medal to Captain Michael D. Bloom, United States Army Center for Health Promotion and Preventive Medicine for meritary of service while assigned as a senior epidemiologist at the Army Medical Surveillance activity. Captain Bloom's epidemiological expertise, hard work, and outstanding initiative were instrumental in the continued success of EMSA and the Defense Medical Surveillance System at a time of severe resource shortages. His performance reflects great credit upon him, the United States Army Center for Health Promotion, the Army Medical Department, and the U.S. Army from 1 November, 2006 to 31 October, 2007, given under my hand in the city of Washington this 24th day of October, 2007, Michael V. Kates, Brigadier General, Veternary Corps commanding U.S. Army Center for Health Promotion and Preventive Medicine. Thanks

very much.

(Applause)

CAPT BLOOM: All right.

SPEAKER: I won't poke a hole in your nice suit here. Army -- field expedient clip here, so.

CAPT BLOOM: Great. Thank you very much.

COL GIBSON: There's a citation in the orders, very important to get these orders to you too so you can put that on your records.

CAPT BLOOM: Yes, sir. Thank you very much.

DR. POLAND: Congratulations.

(Applause)

DR. POLAND: Our second speakers this morning are Dr. Ben Diniega -- Welcome back, Ben -- Dr. Kelley and Colonel Kugler. They'll provide a briefing on chlamydia screening compliance and again, their information is under tab 8.

DR. DINIEGA: Dr. Poland, members of the board, service liaisons, and members of the

audience, it's my pleasure to be here to address the ward. As a former executive secretary for the AFEB, this is the first opportunity I've had to address the transformed Defense Health Board since I retired in 2003.

Many of the things that I'm going to show on the slides have already been eluded to or mentioned. So, I'm basically introducing some of the issues and then -- the meat of the matter will be a presentation of a study done by the national quality management program for the military healthcare system.

These are the prior U.S. Preventive Service Task Force and CDC recommendations. These have been updated and you'll see the updates not much different in a later slide.

In May 25, 1999, a recommendation was made by the AFEB and there are some of the older members -- elder members of the board still sitting here.

DR. POLAND: Long standing members.

DR. DINIEGA: Senior members. But as we

all know, it was to screen all female recruits as early as possible and recommended to do it during the recruit training. But also it was acceptable at that time, the recommendation said, to do it within the first year of accession and then for -- in following the U.S. Preventive Health Services Task Force to do an annual screen at the time of the pap smear.

This slide just shows numerous communications from the AFEB to Health Affairs mainly asking for updates of implementation of the policy and additional information about chlamydia monitoring, which is very difficult as you'll hear later on at this stage.

The allusion that was made -- the mentioning of the laboratory data is called -- is contained in what's called in the information management, information technology world for DOD, block 3 and that's to a database and data system to collect all of the laboratory data. That piece is under discussion right now to being funded and moving forward to be implemented. So, we still

don't have that database and data collection system.

The communications between the AFEB and Health Affairs focused on monitoring compliance due to policies as we all should do and also, taking a look at whether or not it was worth the squeeze to do screenings early.

These are the current U.S. Preventive Services Task Force and the CDC recommendations. Both years, they were A recommendations and highly recommended.

These are the current service policies. The information was provided by the service liaisons. Pay close attention to the implementation dates. You'll see that some of them have been rather recent. The Navy recruits all go to great lengths and they've been doing chlamydia screening with cultures since 1994 until this past midyear, and then they started using the urine application tests.

The Marines use cultures. They train at Paris Island. And they've been doing this since

1997. The Air Force did -- implemented urine testing of female recruits since 2005, Coast Guard since 2004. And the Army does theirs in conjunction with the pap smear at their first duty assignment.

This means that the female recruits will go through basic training and advance individual training, and then when they get assigned after their training is complete, then they'll get it as part of the female wellness check up.

This just lists the letters that Health Affairs -- the ASD Health Affairs responded back to some of the communications from the AFEB. The most recent communication talks about the services have complied with the recommendations as was stated in 1999, but it also mentions some of the current initiatives which are to take a look at DOD metrics for chlamydia screening and to do a study under the National Quality Management Program looking not only at compliance but a little bit at some of the potential complications of STIs.

I'll be followed here by Dr. John Kugler from the Office of the Chief Medical Officer who also chairs the Scientific Advisory Panel to the National Quality Management Program, which conducted a study of chlamydia screening among active duty women looking at screening compliance at recruit training and with the service policies for accessions and also the annual screening.

Dr. Kugler?

COL KUGLER: And I'll be brief. My job is really to review for you the role of the National Quality Management Program -- uh-oh.

SPEAKER: That's okay.

COL KUGLER: To describe briefly the role of the National Quality Management Program and the quality program within the military health system and its overarching approach and then where the special studies fit into that and how we came about to commission the study on your behalf.

The NQMP has a history that actually predates 1996 in one form or another, but the NQMP program itself was formally a result of a DOD

directive in 1996, which was to support the independent and impartial evaluation of selected aspect of healthcare performance and it's managed out of our office at -- the TMA Office, the Chief Medical Officer.

There are four major functions of the program, monitoring Orix measures in our inpatient facilities, selected balanced scorecard measures, other, both a combination of HEDIS and Orix measures or non-core Orix measures, education derived from learning from those performance measures as well as the special studies and the special studies themselves which are administered -- a part of the scientific advisory panel, which is a tri-service panel that commissions the quality studies.

This is just a mishmash of the various components of the MHS clinical management program and relevant for us is over in the clinical quality measures division, the special studies, which is a key component of the feedback loop for quality management within the MHS.

And this is just a diagram of information flow so that the -- it's clear how performance improvement and quality information such as this, readiness for flow within the MHS. Scientific Advisory Panel is underneath the Tricare quality clinical forum, and that -- it feeds the results directly into that forum.

The forum is composed of, again, members of the three services, quality representatives and representatives from Health Affairs and TMA and HBA and E. They basically review the products of the Scientific Advisory Panel and the special studies and will make recommendations.

It requires recommendations for further senior leadership is made directly to the clinical proponency steering committee, which is a committee composed of the deputy surgeon generals and the chief medical officer. And they will either endorse or add feedback to our recommendations. From there, it goes to most senior MHS leadership, Dr. Cascells and the surgeon general. And it has Ds at the smack

level.

They also make recommendations downwards and in the quality forum there are the senior most quality reps representing the three services, so they will -- they may have recommendations that come up from the services or we will make recommendations that will go out through those reps through the services.

Many of the members of the Scientific Advisory Panel also known as the Clinical Quality Forum or they're not directly communicating with them.

Also, just a illustration of the other components of quality, one form or another, patient safety, risk management, and the operational aspect of execution of our plan, which is carried out by the medical directors. Quality issues come up from those folks as well, and they are funneled into this -- into the program.

Any questions about the NQMP program before I turn it over to our study?

Okay. It's my pleasure to introduce Dr.

Joe Kelley, who is retired Army, who on behalf of Ben Diniega and of this board, we asked our partner to commission a study to look at chlamydia screening and part of that is the direct policy implication and the differences in the three services.

So, Joe?

DR. KELLEY: Okay. Thank you Colonel Kugler. Thank you for the opportunity to present some of the results of the study that we --

DR. POLAND: Joe, you'll need to speak up.

DR. KELLEY: Okay. Can you hear me now? Is that better? Holy smokes, okay.

I'd like to thank you for the opportunity to speak about the study that we have completed. We've completed the work. We have not completed the final written report for submission to Colonel Kugler's office. And I'm telling you that because when that's done, any of you will be able to obtain a copy of the report.

So, if you find this information

interesting, compelling, probably in a month or so, we expect that that full report will be available.

COL KUGLER: I would also add that the feedback today is important to this report as well.

DR. KELLEY: We conducted a study on chlamydia screening in active duty women primarily to examine the compliance of the chlamydia screening with policy and the different services. And we also wanted to look at the relationship between adverse outcomes from chlamydia infections and the screening patterns that we observed in the women.

Okay. This is simply an information briefing for the board. As a little background, Dr. Bloom has --

(Interruption)

DR. KELLEY: -- and it does have a high prevalence rate in the military. Also, there are DOD policies in place that Dr. Diniega has already spoken about, but they're also listed on this

slide.

And the final point of information and background is, and you all know this very well, the Defense Health Board has had recommendations a couple of times relating to screening of active duty women on chlamydia.

What I'd like to do is run through a series of slides to present the findings of the study. And what this slide displays is just the areas that we're going to try to hit. Primarily what I'm going to be talking about is the findings related to policy, to prevalence, and to PID, to make it to three P's.

But it wasn't just PID. We looked at PID, we looked at ectopic pregnancies, and also at infertility. The data sources that we used for this study were the -- were number one, data from the defensemen power data center. We used them to identify the women who were in the fiscal year 2005 accession cohort. That's all women who came into the military for the first time during that year.

We also acquired data on chlamydia screening from the population health support division, which I believe has changed its name. And Colonel Bonnema will be speaking a little bit later. He can correct me on that.

Also, we had -- we obtained data from the MHS data repository. And that data was the data that we acquired on PID and the other adverse outcomes.

The final piece of -- the final area that we went to, and it was a little bit odd, was the health clinic at Great Lakes. And we found that we had to go to them for data because the data that were provided to us by Dr. Bonnema's office, we thought were complete in terms of having laboratory screening data for all of these women for all services.

When we analyzed it, we found that there was a large hole in the data related to the accession screenings -- or the recruit screenings that were done on Navy women. So, we had to send out a special request to get data from them.

Now, as I said, the study population contained all of the female accessions for fiscal year 2005 that were 25 years or less. And for this group, we also only looked at women who were on -- who came into active duty. We did not look at Guard and Reserve for the same reasons that Dr. Bloom has already mentioned.

We followed these women through March of 2007. And we picked that as an endpoint for convenience. We wanted to go as long as we could, get as long a time frame as we could and still collect complete data from the MDR.

And lastly, there's a breakdown of the slides -- or breakdown of the population. We identified 22,283 women. And as you can see, the Army had the largest group. That's about 43 percent of the accessioned cohort. The Navy -- the Marine Corps had the smallest group. That's about 10 percent of the accessioned cohort.

In terms of screening, the first bit of analysis that we did was to identify women who were ever screened during the period of time that

we looked at them. So, this could be a period as short as about 18 months or as long as about 30 months, depending on when the women came into the military.

And what we found is that approximately 79 percent of all women who entered the service during that year had a chlamydia screening at anytime that we could find, one or more screening, which means that about 21 percent of the women we could find no record of them having any screening whatsoever.

When we looked at those that were screened versus not screened based on the usual demographic variables, we found no differences there. The difference that we found was based on the service that the woman had entered.

And you can see from this slide that for the Army only about 70 percent of the women had a screening in that roughly two and a half year period. And on the high end, the Navy -- for the Navy, we could find screenings for about 91 percent of the women.

To go a little bit more into the screening of these women, we tried to characterize them -- their screenings as either an initial -- as to whether they were screened initially or whether they were screened annually. When we looked at the group, and this a group of approximately 17,000 women who had any kind of screening, we found that about 14,000 of them had an initial screening.

And that initial screening is described as either for the Marine Corps and for the Navy, that would have been a screening during the first 60 days. They normally get screened when they come into the service, during the first week or two, during the first couple of weeks. We gave -- we gave them the luxury of getting screened the first 60 days.

For the Army and the Air Force, the period that we gave them for initial screening was one year. And the data that we used for this study were collected before the Air Force made their change to screen women in basic training.

And as you can see from the results, when we look at initial screening, based on service policy, the Navy still did not screen approximately 20 percent of the women or looking at it the positive side, they screened approximately 80 percent of the women in basic training and the Marine Corps wasn't far behind.

The Army and the Air Force screened between 50 and 60 percent of their women within the first year. And when we looked at that and spread it out and when we looked at it on a monthly basis, we found that there were a number of women in the Army who were screened during the first two months of service, which means that they were screened sometime in basic training.

We didn't do any further analysis on that, but I thought that that was interesting information. They were -- we assume that they were probably screened for cause, that they were screened during basic training. There was something that made them go for healthcare.

When you look at the annual screening

rate, I think that that was a little bit more disappointing. Overall, annual screening wasn't accomplished on 50 percent of the women. And for annual screening, we were -- I thought we were fairly generous. We looked at the accession date and we gave them not 12 months for an annual screening, but we gave them a 14-month window for every annual screening figuring that sometimes you don't quite make it in 12 months. So, but 14 months was enough.

And for the annual screening -- so, for some of these women who received the annual screening, if their accession date was early and in -- in fiscal year 2005, they could have potentially been screened three times during the study period, during 30 months. If they were -- and if they came in on the late end, it wouldn't have been that many.

So, looking at it, about half of them got screened. And if you look at it as well by service, the Marine Corps seems to have done, compared to the other services, reasonably well.

Now, I don't know if that -- if 68 percent makes policymakers happy, but it's clearly -- clearly better than any of the other three services.

Okay. This slide presents the prevalence data and what I should tell you is that there are -- there is a study period prevalence. That's on the top row, 2005 through 2007, where we asked did -- if the woman was -- had a positive screening at anytime during the -- during our study period. And for that, 15 percent of the women in the cohort had at least one positive screening at anytime.

We received a question and reanalyzed. Based on a request from the staff, they wanted us to look at annual prevalence, and so that's what you find below in 2005, 2006, and 2007 annual rates. So, a woman could have been represented in one or more years in the fiscal year numbers.

The only thing I'd point out on this slide is that the rate seemed to rise in 2000 in the second year for all services. And of course, when you look at slide again, the Army has the

highest rate of prevalence. The Marine Corps is also high. The Air Force is -- has the lowest rate, has the lowest prevalence.

And I think that the pattern of Army being the highest, Air Force being the lowest, and then the Navy -- or the Marine Corps and the Navy being in there, that's -- throughout these slides you will see that repeated for all of the other slides as well as a pattern.

Then we looked at the adverse outcomes that we thought were associated with chlamydia. And again, we looked at adverse outcomes. They could have been caused by another sort of bacterial infection, gonorrhea or something else, but we identified the conditions based on ICD9 codes. We looked at PID, ectopic pregnancy, and infertility. And this slide displays the distribution of infections.

Overall, 1,146 infections were noted. PID accounted for 90 percent of all the infections. What I found surprising was that we found any infertility, realizing that infertility

-- an infertility workup takes a little bit of time, and we're only dealing with a two and a half year period maximum. But we still had women who were diagnosed with infertility.

Here again, when you look at -- when you look at the different adverse outcomes. The Army appears to have the highest rate of adverse outcomes, and the Air Force has the lowest rate of adverse outcomes in all categories.

I think this is the last piece of information that I'll present. And I -- what I decided to do for this one was show you -- focus on PID and on PID rates. If you look at the headings across the top, we have categories that say initial plus annual, annual only, initial, and no testing.

The initial plus annual is a category of women for whom we found an initial test that met their service policy, so for the Marine Corps and Navy women, that would have been -- they would have been tested during basic training. And we found records for them as being annually tested.

They met the criteria for being annually tested.

The second group, annual only, we could find no record of those women having been tested within the service policy at the beginning of service, but we found chlamydia testing done annually.

The third group, initial only, they had the first test, but we didn't find any annual tests. And the fourth category, I call it no testing to save space here. That's not technically correct. The women in that category could -- some of them had no test. And we know that approximately 5,000, 5500 had no test we could find. But there's also a small group in there that could have been tested, but it didn't meet the criteria for either annual testing or initial testing.

And when we look at this, what we find -- and this is also -- the display is done and the data is presented a little bit differently for this, we present it as cases of the condition per 1,000 population.

And so, what we find is that overall if you combine all three types of -- I'm sorry. This is just -- if you're looking at PID, what we find is that approximately -- you have 51 cases per 1,000 overall, across all services.

We found that most of the cases, though, were in the group that were tested initially according to policy and also had an annual test. What we think this really represents is that the women who had a health issue would come in and they were tested, but the testing was not done as a screening test.

A lot of these women qualified on an annual test because they were -- they were tested for diagnostic confirmation when they had a health condition. We haven't been able to confirm that but we suspect that that is probably what happened. And you can see that the women who had no testing done at all had the lowest rate of PID. And here again, Army has a much higher rate than the Navy, Marine Corps, or the Air Force.

Okay. In summary, the overall screening

rate for the services for everyone was 65 percent. The Navy screened -- did most initial screening. The overall annual screening, which was somewhat disappointing was only about 49 percent. The Marine Corps did the best there. Overall at some point during service, about 80 percent of all women had at least one test.

In terms of infections, if you look across the entire study period, about 15 percent of the women had a -- had an infection at anytime. And the annual rates varied with the Army being the highest up around 13 percent. And additionally, Army appeared always to have the highest rates and the Navy -- the Air Force, the lowest.

As far as the adverse outcomes are concerned, I've already said that 90 percent of those were in chlamydia. And again, adverse outcome rates were the highest for the Army and lowest for the Navy.

What we took away from this is that we think that somehow emphasis needs to be placed on

screening in the services. Clearly, we have service policies and service policies for whatever reason aren't -- the goals aren't being met. So, that would be one obvious recommendation.

Another is we think that based on this that we probably do need to start testing women in the Army during basic training simply based on the amount of disease going on. And I think that's it.

Are there any questions? Yes?

DR. POLAND: Yes, Dr. Walker?

DR. WALKER: Do we know anything about whether the positive screening is followed up and what the -- the proportion of those that are followed up or treated and what the outcome is of the treatment.

DR. KELLEY: We do not know that. Our assumption or hypothesis going in was that for women who are identified as being positive that they will be treated.

DR. POLAND: Dr. Gardner?

DR. GARDNER: Yeah. Just to follow that

same line and to follow the recommendation that you made in your letter, Greg, in the December '05, you know, the last action item is assessing the effectiveness of male chlamydia screening options, it seems to me, in STD guidelines, clearly once a woman is identified as having chlamydia, male partners are identified as to be notified and treated. And we have no idea as far as I can tell whether that's being done.

I've not heard a single word about male -- notification of partners, and there might be significant differences in the different services as to how actively that's pursued.

So, I think that clearly needs to be one of our recommendations --

DR. KELLEY: Yes, okay.

DR. GARDNER: -- that at least we follow established guidelines for notification treatment of partners.

The other thing that I'd like to hear a little bit more about in the screening -- and the table here tells that -- says that there had been

male screening, the leukocyte esstrays. I'd like to hear somebody refresh me as to what the sensitivity and specificity of that is a test, but it's an easy test to do.

And since this is entirely a heterosexually spread disease, it always bothers me when we just treat one of the genders and don't pay any attention to the other. So, it seems to me that like -- it's just putting urine in bottle, that's not much of a problem of getting a specimen.

DR. POLAND: Does anybody know the answer to that question, sensitivity and specificity?

DR. GARDNER: Yeah, please.

SPEAKER: It's high.

SPEAKER: A number of years ago Dr. Julie Schachter at University of California San Francisco, who was really one of our best (inaudible) --

DR. KELLEY: Uh-huh.

SPEAKER: -- did this evaluation and it

is 50 percent sensitive and 50 percent specific. In other words, you can flip a coin, and you're just as likely to have an answer with respect to male infection. It's just not very good.

DR. GARDNER: Not so good, so ineffective as a screen. Would it identify people for follow up? Could you use that as a screen test for a follow up test and if so, what would you do?

SPEAKER: Well, I guess the question is if you're going to meet half the people who have some white cells in their urine with this test, perhaps you might get a better result with say a urine based PCR assay afterwards, but I think you're still talking about the limitations of your initial screening tests.

Again, I think urine based screening for men and vaginal swabs for women are with PCR, it's clearly the best. And there are some rapid tests that I think are going to give us more cost effectively to get at that.

DR. POLAND: Okay. Dr. Lednar?

DR. LEDNAR: Wayne Lednar. I have a question about the data that were available to you for urinalysis. You mentioned one of the early slides in your deck the data sources. And I'm -- I'm just not able to tell from this information.

Did you have access to clinical encounters that would have occurred outside the military that perhaps would have come in via Tricare? Was that part of your data capture?

DR. KELLEY: We would not -- no, that was not part of data capture.

DR. LEDNAR: So, to the extent that any of the women either were not at a military facility where this was possible to screen and they needed to rely on out of military care, you just wouldn't have access to that experience.

COL GIBSON: Let me add to that. These are active duty females, so they are at a military installation or deployed or on a ship.

DR. LEDNAR: With the capability to --

COL GIBSON: With the capability to do that. We know that it's -- we know that some of

our enlisted force believe that -- and certainly our officer force believe that a diagnosis of a sexually transmitted disease in a medial record may impact their career. That's the perception. Don't know how much reality there is to that; I don't think any.

It is likely that some of these folks, particularly if they were symptomatic, would go downtown for care so that it wouldn't show up in their medical record. That's possible.

DR. LEDNAR: So, there's a potential for ascertainment by --

COL GIBSON: Exactly.

DR. POLAND: Yes, Dr. Halperin?

DR. HALPERIN: Is this like Dr. Bloom's study ecologic? That is, did you have data on the individual participants, whether they had PID, when they were screened?

DR. KELLEY: Yes.

DR. HALPERIN: You did. So, you could do the nested case control study looking at --

DR. KELLEY: Yes. We've not -- we've

not done that analysis. And typically, what we do on our contract is when the study is turned over to TMA and they're satisfied with it, we also turn over the data set with that. So, there would be a data set available for secondary data analysis.

DR. HALPERIN: That would be done by DOD? Is that --

DR. KELLEY: That could be done by whomever. Probably, yeah, I would think that maybe AMSA would be the most logical organization.

DR. POLAND: Colonel Gibson?

DR. HALPERIN: I really encourage going in that direction because it will answer some of these questions about when the screening should be done or at least what the association is when it's done versus the outcome. It will also answer the question of whether after adjusting for that, whether there really are differences between the services, which --

DR. KELLEY: It's, you know, possible. That's an issue that -- that -- I know that we discussed it and discussed doing that, but in

point of fact, we didn't receive data from the Navy at Great Lakes to even fill this out until October, so --

DR. POLAND: Colonel Gibson and then Dr. Parkinson.

DR. KELLEY: -- it's relatively new.

COL GIBSON: Go to slide 12 just in your books, if you -- you notice there's a -- I lost it. There it is. The rates of screening run from about 68 percent to 41. Keep this in context with the data that you were provided back in 2005 when we were dealing with this issue that showed that that chlamydia screening rate was 30 off the chart audits.

So, at least -- we either have a more accurate method of ascertainment than chart audits or we've in fact improved our screening rates over that period of time.

DR. KELLEY: And the HEDIS measure hasn't changed that much in that time.

DR. POLAND: Mike?

DR. PARKINSON: Yes. I just -- first of

all, I wanted to commend the work. I think this is the essence of quality improvement. And while it's obvious to this group we don't do it enough, which is look at policy, its implementation, its impact, and then convene the stakeholders to model a best practice or continue to get better. And I stay the course because oftentimes what happens is we know -- we do the study and it dribbles away and we lost the exclamation point, which is the point of quality improvement.

So, I do hope -- and again, Colonel Stanek and I had the opportunity to provide some high level, you know, input to the study early on, which we appreciate. So, good job on the whole thing.

DR. KELLEY: Thank you.

DR. PARKINSON: But in the implementation of quality improvement, I would urge us to look at the two arms of this, which are recruit health and the policies and practices in the recruit training bases and the core military health system.

And I'm concerned that with the atrophy, what I understand or perhaps the lack of attention to the recruit health forum, where we basically can model best practices across all the service and say why does the Marine Corps have 81 percent, you know, let's really dig down and do that. And is it something we wanted to look at in the Air Force or the other services.

Likewise, what is going on with annual screening in the direct care services in Army MTF versus, you know, a Navy facility? We really need to hone down on those to continue to drive improvement because -- because of our population, because we take all these young men and women and it's so highly prevalent.

So, good job. Let's not drop the ball on the recruit health or on the mainstream healthcare. And let's continue to move it forward. And we should do it -- I mean, these numbers -- yeah, we can always say the glass is half empty. I think it's more than half full.

It's great. We're moving forward.

Let's keep it going. So, don't misconstrue our comments here today to be anything but --

DR. POLAND: I'll have a different take on that in just a moment.

Colonel Defraities?

COL DEFRAITES: A question and a comment. Will you -- you mentioned that you were concerned about the level of ascertainment of the data for the Navy, so you went directly to the source. They have one basic training installation, and you got the data directly from them.

Were you concerned about the ascertainment or completeness of data from the other services? What led you to believe that the others were complete? That's a question.

The comment was just in testing the partners -- I know you know this already, but just to remind ourselves that the recruit population -- this is not a closed population. They sort of come in trailing clouds of glory as they come from all over the United States.

And so, the contact tracing, which I'm sure the Navy -- I mean, the Navy Great Lakes, they could probably tell you exactly how they do it, but again, it would involve calling the home station or at least that contact tracing. It's not just looking at other recruits that happen to be at Fort Leonard. The contacts would be somewhere else, so just to keep that in mind.

After -- when you get on active duty and assigned to an installation, then it tends to be more local. You still have, you know, interfaces with the local county and health department, but it tends to be more of a local phenomenon. That's all.

DR. POLAND: Okay.

DR. KELLEY: An answer to the question, the data source that we have gone to in the past most often is Colonel Bonnema's shop down in San Antonio. And we know that their data are -- have in the past -- we've never questioned their reliability and completeness because they get feeds from CHCS out of the different platforms.

For some reason, they did not get a feed from Great Lakes because we -- there was an issue with it because we found no data at Great Lakes. It wasn't as if we found a couple of women. There was simply -- there were simply no test results for anyone that we could tag to the Great Lakes facility. So, something had to be wrong.

We went back to Great Lakes and we worked a data use agreement with them to provide their laboratory data. And I'm assuming because of our longstanding relationship and the work we've done with PHSD, all the other data were good. And maybe Colonel Bonnema and talk about that.

DR. POLAND: We're running a little late, so I want to keep the comments very tight and focused, please.

Dr. Stanek?

COL STANEK: This is Colonel Stanek. I just wanted to first thank the group for doing the studies and all the information on chlamydia. This is an ongoing issue that continues, will

probably continue for quite a while also.

I wanted to point out one issue that's changing in the future for the Army. The policy as it was described is correct. We do have -- our policy is that the test be done during their first year. Most often, it's the first duty station.

However, I wanted to point out that there's an initiative now that will probably take effect in -- this coming April, April of '08. In Colonel Diniega's slide, he said that screening for the Army would start in the recruit training in spring of '08. That's not quite correct.

In the spring of '08, there's an initiative that's going to be started which will have a women's health initiative encounter, if you will, at the advanced individual training site. Now, they go to basic training for 9, 10 weeks, and then they go get their specialized training, and then they go to their first duty station.

And part of the thing that the Army has discovered in -- is that soldiers need to be ready to deploy once they get to their first duty

station after they complete their advanced individual training and part of that is having a current pap smear in their record that's completed and resulted and all that sort of thing.

You know, so there will be an initiative to be done at all of the advanced individual training sites where we have female soldiers, and that will include the -- having the pelvic exam and the pap smear done at that particular point and during that encounter also they will receive a chlamydia screening as well as any preventive services or recommendations that need to be done.

So, that should start April -- spring of '08 and then go on from there.

DR. POLAND: Tom?

LT CDR LUKE: Yes, sir. My name is Lieutenant Commander Luke. In 2005, I presented to the board on data about chlamydia prevalence rates at Navy and Marine Corps recruit stations. And the rate was five to nine percent point prevalence.

And the discussions that we had right

there is -- as I recall, is the real lack of any type of screening program in our male population, such that some of the data I presented then is that our women's health branch had done a survey of unmarried, pregnant naval service members and it indicated that about 80 percent of their partners were other active duty members.

And I think that we can increase certainly the screening and the efficacy of our screening programs in women. But without a policy for our young men, I think ultimately we're not going to be very successful.

And I'll relate a couple issues here, former enlisted and in the fist five years of my active duty time, I moved seven times. It is a very mobile population that are coming together and moving out. And I think that the board should really take a look at what we're doing with our young men, the 80 or 90 percent of our population that are frankly the root cause of the infection in women.

We just cannot succeed with only going

by U.S. Task Force recommendations for screening of women. We have to look and consider the men if we want to resolve and solve this epidemic. Thank you.

DR. POLAND: Okay. We're going to need to move on here. Let me ask now our third speaker, Lieutenant Colonel Albert Bonnema, chief of the Clinical and Phermatics Branch at the Population Health Support Division, Brook City Base, Texas, who will give us a briefing on DOD population health metrics for chlamydia. And his slides are under tab 9.

LT COL BONNEMA: All right, good morning. And Colonel Gibson, thank you for the opportunity and the invitation to present before the board this morning.

The topic that I'd like to talk about this morning is about the quality improvement portion for Dr. Parkinson. The -- we are going to begin doing chlamydia metric ascertainment, measurement on a monthly basis beginning this coming month. And so, what I'd like to do is show

you a little bit about what we've done here and explain this in terms of the HEDIS methodology.

HEDIS is the health employer data information set. It's from the National Committee of Quality Assurance. This is the group that uses secondary or administrative data primarily for quality outcomes.

It's -- we use it to benefit in some other studies, you know, maybe a little bit of epidemiology and other quality studies within the office. But this is purely within their particular methods. And they have very specific technical specifications for which we've adhered to very closely.

The group that we're talking about here in this case is going to be the women 16 to 25 years old who've been continuously enrolled to an MTF. So, these folks have got -- before we first measure them because we're now holding people accountable, they've got to be within the control of the group for about a year. So, we're only going to hold people accountable for the group

after they've been there within the system for a year.

And then we're looking for women with at least one chlamydia test, and then we're looking for the sexually active women, which is different than many of the other methods. And in the intersection there, we have the numerator and the denominator.

To put that in terms here, the numerator makes up the 16 to 25 year old women who've been continuously enrolled with at least one screening test for chlamydia in the past 12 months per the U.S. Preventive Services Task Force guideline. And the denominator is all sexually active women who are 16 to 25 years old and are continuously enrolled during the preceding 12 months.

We have a couple of exclusions for this, and it does take out a few women. Number one, it's those that have had pregnancy tests, because that is an inclusion criteria for sexual activity. But if the pregnancy test is only done within the guise of an x-ray, so radiology exam or

prescription for Accutane, which is now the mandated guidelines and there's no other inclusion criteria, we exclude this group from the measurement.

The determination of sexual activity is the challenging part from administrative data. And now that we've got 60,000 health risk assessments done within the last year for active duty, I'm looking forward to doing it from self reported data instead.

But what we're looking for is for people who are on contraceptive, IUD, diaphragm prescriptions, some kind of contraceptive, infertility or pregnancy or post-partum codes and then some kind of lab test for pap smear, pregnancy, sexually transmitted infection. This actually brings in the majority of women in the 16 to 25 age group.

The -- I'm not going to go over this in detail. This is the method in which we take and build this particular metric and we've got seven years worth of experience in doing this.

We're taking this from a vast majority of administrative and clinical data sets, radiology, pharmacy, clinical chemistry, encounters that are done in the network and also in the direct care system and including lab and radiology. And then we use the enrollment file for the Department of Defense.

The -- the results -- and this is up to date as of a week ago, we did this. This is for looking November 2007. This is the current rate using the HEDIS guideline for all active duty. And this is regardless of sexual activity. We took out, because of the interest of the board, that particular exclusion of sexual activity.

And we took all women to see where we currently are, which is going to be a little bit different than Dr. Kelley's study where they looked at 2005. This is the snapshot of this particular moment in time. And these are the -- these are the rates for the Air Force, Army, Navy and then all the branches combined. And we're currently at 71.8 percent.

Now, this has been a rumor for a little while that we were going to do this. And as I've seen in the past, what usually happens is the rumor starts, people start practicing because they know accountability is about to come.

Another thing that will be of note and Dr. Kelley unfortunately had to deal with this was the gaps in the lab data. The other beauty of starting to do this on a regular basis and putting this out for everybody to see and I imagine soon to be publicly, is that the data quality is the number one part that's improved in the first year of practice.

There will be a very steep improvement in the data quality. And as we saw with the Great Lakes, it was really just a classification of where the lab results were and they have now since fixed that. And so, the Navy was looking much better as you can see.

The percent of women -- if you look at all DOD beneficiaries, I think we do very well definitely considering our civilian benchmarks

that we use from the National Committee of Quality Assurance. For all sexually active women, it's 77.4 percent in active duty and all beneficiaries. And this is specifically looking at just the sexually active component with that in there.

Now, one of the things we're looking at is how to make sure that we get this into the system, so thinking about the process. We really would like the screening to occur, not as a separate event from the women's health exam but to be included with the pap smear.

And so, we were looking at some congruents between whether a pap smear and a chlamydia screen were done at the same time. And in fact, we found that 90 percent of the time, that the pap smear and the chlamydia test were done together. And for the -- all beneficiaries, it was 83.7 percent.

So, that means our margin of improvement in process is not going to be very high. It's about 10 to 15 percent that we haven't processed. The rest of the delta will have to come from

people who, for one reason or another, haven't been screened at all.

So, that's the essence of what we're looking at. And we will begin doing this -- the Army and the Navy will have their way of presenting this to their particular services. We usually present this in a once a month meeting to the general officers from which it will disseminate down to all the managed coms and the military treatment facilities.

A few limitations to take into account with this, number one, the methodology will identify women who are not sexually active. There are women who are on oral contraceptives and that have pap smears who are not sexually active.

Pregnancy tests, many times, are done by protocol. You go to the emergency room with abdominal pain, you're going to get a pregnancy test regardless of sexual activity as being one example, preoperative studies and things like that.

And the other is that methodology may

not capture all screening. As you know, some people will go to other sources for their women's healthcare other than where they're enrolled at and have ample opportunity, especially with the college aged group that we're dealing with to do that, for example, planned parenthood, college clinics, or other non-network facilities.

If they bill it, we collect it generally speaking in terms of the data. But if they do not bill us and it remains anonymous or as self pay or done as another part, we won't have any record of that particular activity.

Are there any questions?

DR. POLAND: Mr. Parkinson?

DR. PARKINSON: Just to clarify. Great presentation again. This does include purchase care data?

LT COL BONNEMA: It does, uh-huh.

DR. PARKINSON: It does, okay. Well, let me just say as someone who has spent a lot of time with employers and quality and data and relative to the VA, the DOD has not been very

public in publishing quality information. And I would encourage you to, you know, assume it's sound or the methodology is good to get this into the public forum.

I mean, what it essenti8ally shows is that we are double even a 90 percentile plan. So, the leading top five percent or two percent of plans in the country, DOD exceeds in terms of meeting the standard metric for chlamydia screening, now everything else equal in terms of how we treat it and sexual partners aside, but your general comments about defining the metric using a nationalized standard, publishing the information for inner service, inner MTF quality improvement is a great model. And it's the reason that the whole program was set up in the mid-nineties and we never quite followed through, I don't think.

So, maybe this is a great entrée into doing that, so again, good job, get it out, use it for quality improvement across the system, and you know, we can talk about the margins, but I mean,

the 90 percentile plans are performing -- if you really saw that line, they're performing at 45 percent. DOD is performing at best I can tell at 85 to 86 percent around a nationally accepted standard for chlamydia screening.

So, again, well done.

LT COL BONNEMA: I think that the advantage that we have over many of the plans is that we -- our office collects the clinical chemistries by name, by date, by person, by lab result. And I think that gives us a significant advantage in terms of data collection compared to if you were doing it purely on administrative data.

DR. POLAND: Colonel Gibson?

COL GIBSON: A couple points. First of all, Dr. Parkinson, totally agree with what you said. It goes back to why we have HEDIS, et cetera, if we measure it, there's accountability.

Correct me where I'm wrong on my statement here. What we mean by metrics is through the system with population host support,

we can drill down to the hospital, to the provider, and monitor these issues. So, if Colonel Bonnema had Brooks Air Force Base's rates of chlamydia screening for this population is outside of the norm, the hospital commander is going to know that, the magcom is going to know that, et cetera. So, there is an accountability.

I totally agree with what Al said. This rumor that we're going to do this has been going on for what, 18 months, 14 months? It has already made a difference. Think back to what I just told you a little while ago. The last real chart audit of this showed 30 percent. This is remarkable.

And part of this whole issue of if we do -- if we do a really good job of reproductive health in our annual program, we can then measure the attributable benefit from recruit screening.

DR. LOCKEY: Just one question. Of the percent of women that are in the Armed Forces, what percentage is it that this under 25 -- 25 or under age group represent?

LT COL BONNEMA: I don't know that

number. I don't know what percentage that 16 to 25 is. It is -- none of them are 16, but it's hard to know right off hand. Yeah, we have some 17 year old accessions, but.

DR. POLAND: Dr. Walker?

DR. WALKER: If I could comment that with the movement of these people from base to base, I'm not convinced that they're all being treating if they get a positive test coming back.

DR. POLAND: Brief comment.

MS. HITCHCOCK: Yeah. Thank you. First of all, let me commend the DOD for really setting the standard and getting the country off its duff with this problem. Compared to the public sector, you're quite a ways ahead.

I think the question is the national standards, are they appropriate? Is it process versus results? And how are we going to tackle this?

There's a very disturbing but enlightening study that was done in reproductive physiology several decades ago. A number of women

both never pregnant and pregnant at least once volunteered for a study. They used latex particles with a little radio tag on each one. They put the women in stirrups on the table and took a syringe and gently lavaged her cervix putting these particles that are (inaudible). They waited two hours, they wheeled her into the X-ray room, and they took pictures. Within two hours, every single one of those women had radiotonic particles in up in her fallopian tubes. Okay. So, the point is that good pathogens take advantage of Mother Nature's selective forces. Sperm are supposed to get up there and get up there quickly, and so therefore, these organisms get up there quickly.

So, I think the risk of getting upper tract infection with initial infection is high. I think if you look at the data, 14 year old boys are sexually active, 15 year old girls are sexually active, and by the time they're 19, 85 percent of them have had 3 to 5 partners. I would say that you have a 30 to 50 percent chance of

everybody that enters the service already being infected.

So, is the program good enough to beat this pathogen at its own game? And do you have to look at something much more intensive than what you already have? Now, I don't know whether it's worth it in terms of cost benefit, but if you're results are not where they need to be, the question is are you wasting your money.

And this -- I'll close with an example. Let's supposed we lived in Bangladesh where every summer, summer diarrhea, which is the surrogate for cholera, occurs. What would you recommend? Wash your hands once a day, once a week, once a month, every six months to reduce your risk. Well, I would say you'd figure out what the likelihood is of infection every time you went into a situation where you're likely to have feces on your hands, somebody else's. And you'd fashion your prevention message around that.

And I think that work has not been done and I think it's not available to you. I think

you have an opportunity to do it if you can start with a screening program that actually puts you back to baseline with chlamydial infection in these men and women. Thank you.

DR. POLAND: I have a couple of comments on that. I'm frustrated with this. We have made recommendations for going on 10 years for a health problem that's measurable, for which there are validated things that we can do, it's treatable, treatment is cost-effective.

And we can't continue to say people are our most important asset and then let loose with something as relatively simple as this in a population where we have the wherewithal to do it. And some metrics, as Mike has pointed out, we do well. And others, as you've heard this morning, we don't do well.

I haven't heard about a male screening program, though we directed that one be developed three years ago. I haven't heard about movement toward a universal at basic -- at accession screening program, though we've asked that that be

done for years now.

This, to me, is a leadership issue. Someone doesn't think this is important enough to do. There's no getting around this. This is clear to me, unless I am seeing it in some biased or unclear way. This is an important thing to do. It's the right thing to do.

There -- we can argue and nitpick and some of the methods, but the data here are reasonably clear. We don't do what we said in our own policies we should do, and this needs to be fixed. I'm not sure what else to do in this regard.

We have written memos to the ASD for Health Affairs, who in turn, have leaned on some of the services. Evidently, we have to do something more. We've made incremental progress, but I'm not happy where we are even after 10 years of dealing with this.

So, I will confer in executive session with our board members, but this needs to be taken care of, enough with this. We need to do this

right, and we need to do it in a high fidelity manner.

With that, I'll stop the discussion unless there are any other comments, and we'll move on.

CDR SCHWARTZ: Just to add some diversity of opinion on this, in the Canadian Forces, we would not made testing -- chlamydia testing on enrollment accession an obligatory act. We would recommend and guide and say this is good. And we probably wouldn't have the compliance numbers that you have. And again, I'm -- Canada is a fair bit behind in having data to look at on our rates of -- on our prevalence.

So, I just put that subtle point of difference of how we influence behavior for a life and maybe we influence a better result on personal choice by the woman or the man by essentially insisting that this is a right and good act as is done, and maybe that shapes better choices later on in life.

But I just think that there's some

element of the personal choice element --

DR. POLAND: Sure.

CDR SCHWARTZ: -- that I'd bring to the table.

DR. POLAND: And in part this relates to our request three years ago, that an education program be developed, disseminated, and deployed.

Okay. We're going to move on to a question on vaccine use in military recruits. Captain Neil Nato will provide this.

MR. NATO: I'd like to thank the board for taking on this question. And it'll be a brief presentation, so it'll get us back on track here.

The question is actually broken up in two parts. And the genesis of the question came from our recently inaugural public -- Navy Public Health Advisory Board, which received this question from our recruit training centers.

And the first one in regards to immunizations is like some recommendations from the board whether recruits who are younger than 18 years old develop less immunity when receiving a

mixed series of pediatric and adult doses of a particular vaccine, as opposed to having only the adult dose.

So, as the board is aware of the cutoff on a lot of the vaccines is 18 years old, and a fair number of our recruits are under 18 years of age and so they receive a pediatric dose and then especially on the series of hepatitis vaccines that I'll discuss in a little bit more detail, then they get -- go on and get the adult dose. So, the concern is whether that's appropriate.

The second question is in regards to influenza vaccination and if it were made available during the summer period, should we be doing it in our recruit training centers.

So, in regards to question number one, hepatitis vaccination is the one that has the most interest, in regards that there is a nice combination product, Twinrix for 18 years of age and over, but there's not a similar dosing schedule for under 18. So, consequently then you have to use the single does vaccinations of Havrix

or I think -- believe it's Energix for hepatitis B.

And so, as you can see from this slide, the dosages are about half when using the pediatric dosing schedule versus the adult dosing schedule.

In regards to question number two in regards to the flu vaccination question, we do see some influenza activity during the summer, albeit it's not huge. And this data comes from the Febrar Respiratory Illness Surveillance Network that NHRC maintains.

So, in July -- in August of 2007 of this year, there were several cases of influenza A H3 occurred in the basic training population of Fort Benning, and MCRD was approximately a dozen cases. And then there was some influenza noted out among the fleet also during the summertime. But again, the numbers aren't huge.

So, the -- so again, the question in regards to both of these is are we -- our vaccination programs in our recruit training

centers, can they be further optimized by again looking at trying to go to adult dosing for our 17 year old recruits?

And also, in regards to the influenza, actually there is a product available in limited quantities with an expiration date through August of 2008 called Flulivol. However, it does suffer the same limitations in regards that it's only for the 18 year old and above population.

I did contact the manufacturers and there is European data on these issues in regards to the under 18 population, that in Europe there were trials involving 17 year olds receiving adult doses. And it looks like, you know, in regards to the side -- you know, concern about any side effects, nothing out of the ordinary.

Questions?

DR. POLAND: Neil, this is Greg Poland. Is your concern with the -- with question number two one of decrement of protective antibody levels?

MR. NATO: In regards to the flu?

DR. POLAND: You're talking about northern hemisphere vaccine; right?

MR. NATO: Right, correct.

DR. POLAND: And if it were to be available, you're asking, could it be given.

MR. NATO: Or should it be given to our recruits because, again, I don't -- didn't have the time to collect any data, but again, from our -- the recruit population, probably the vast majority of them did not receive the flu vaccine during the previous year.

So, again, would there be an advantage to go ahead and give them the flu vaccine? These would be the summertime accessions.

DR. POLAND: Ah. So, you're referring, for example, this summer --

MR. NATO: Right.

DR. POLAND: -- giving people this season's vaccine?

MR. NATO: This season's, right.

DR. POLAND: Mike?

DR. OXMAN: I'd like -- I'd like to

address these. I talked with Neil yesterday a little bit, so I've thought about it, the question of whether to use the standard adult dose of hepatitis A and B vaccine in 17 year olds that you're using in 18 year olds.

From a scientific point of view, a 17 year old has an equivalent adult immune system and has a body habitus that is much closer to that of an 18 year old than of a nine or a ten year old. So, I think there is every scientific reason to use the Twinrix, the ordinary vaccine in the 17 year old in the military, and it's only an issue of licensure or what have you.

DR. POLAND: Yes.

DR. OXMAN: And I think that it certainly -- there is no rationale for using a pediatric dose of the vaccine in a 17 year old that I can see. So, I think the answer to the hepatitis one from a scientific point of view is very straightforward and is --

DR. POLAND: I would agree. And often, these time -- these age limits are a function of

the company not studying adequate numbers in that age group to be able to alter their BLA.

DR. OXMAN: And it's informed consent. I mean, there are practical reasons why they start at 18.

DR. POLAND: Yeah. So -- right. So, I mean, the real issue is there's no scientific reason not to use the adult dose, but are you stuck in this issue of not being able to --

MR. NATO: Right, the off label considerations.

DR. POLAND: Yeah. But with a board recommendation, could you do that?

COL GIBSON: Let me add -- this is Colonel Gibson. Let me add to that. We're really not asking y'all to engage in our issue with FDA as far as trying to get an exemption here.

We really want to stick to this question with respect to the biological issues, scientific issues, two parts, giving adult dose to 17 year olds. And the other is starting with a pediatric dose and then ending with an adult dose for these

individuals, what's the science -- what are the biologic implications of doing that?

We'll take our discussion to FDA anyway. Would your opinion help, maybe, but probably not. The issue is we just have to -- we really would like some expert opinion on the biology of this issue.

DR. POLAND: Well, from a biologic point of view, I know of no data that would lead to an adverse immunologic or side effect profile. In fact, the immunogenicity is such that you would have enhanced immune responses, at least in these cases of these vaccines.

Pierce and then Joel.

DR. GARDNER: I totally agree. I think all of us would say it's better to give the adult formulation, but I think you're trumped by the idea -- unless you do it on label, you're not going get there.

Now, the only thing that would be on label, actually, you can give the influenza year round, and that's been recommended. So, the

answer to that one is clear. You can go ahead and -- there's not a different formulation for 17 and for 18 year olds; is there?

DR. POLAND: No, not for flu.

DR. GARDNER: It's just the question of timing. So, the answer to that is yes. But as you said, the rest is the company didn't submit the right data, and biologically we would all say it's fine, but -- and hepatitis A, we over immunize already. We give two shots when you really only need one. So, let's leave it there.

DR. POLAND: Okay. Dr. Silva?

DR. SILVA: Ditto. I was going to make the same comments. Now, you could turn the coin around and say maybe this lower dose is doing a disjustice to someone physiologically whose -- as Mike has described.

DR. POLAND: Mike?

DR. PARKINSON: Yeah, Neil, just a clarification on question two. Are you saying that your summer accessions you would give what would essentially be a soon lapsed formulation of

that previous season's flu vaccination?

MR. NATO: Current season.

DR. PARKINSON: Right. But I mean, so -- but what happens -- I mean, those accessions who then go to their first duty station, they would have access to the usual influenza program, which is mandatory across DOD anyway; right?

MR. NATO: Yes.

DR. PARKINSON: So, why wouldn't you just wait for them to do that?

MR. NATO: Well again, to cover that period during, you know, the basic training camp for flu activity, albeit it's small. And so, that's kind of the question is should we continue it year round --

DR. PARKINSON: Yeah.

MR. NATO: -- realizing that again, they'll probably end up with two vaccinations in --

DR. PARKINSON: Yeah, right.

MR. NATO: But, and then talking with Dr. Oxman, he had some perspective on that.

DR. POLAND: That actually may be a little bit of an issue because in some studies where one or more of the components don't change from one season's vaccine to another, and those injections are given close together, you can have a -- almost a serum sickness like picture occur or at least large local reactions. It tends to be more common with polysaccharide vaccines than a protein-based vaccine, but it can happen.

So, if you gave, you know, let's say A. Sydney, which was in the vaccine for three years running or so, if you happened to give a dose in August and then you gave another dose when the new vaccine, which also had A. Sydney became available in September or October, you could well see enhanced local side effects and perhaps some spillover into self resolving systemic side effects. You have to take that into account.

Mike?

DR. OXMAN: I would doubt that with the influenza vaccine. And the other advantage in doing it is the next year's vaccine -- some of the

elements will have drifted and so, you have an element of animnestic response, which is an advantage in terms of efficacy.

So, I -- I certainly would have no problem doing that. And it also means that you have a standard routine of immunizing at accession, which I think is a good idea.

DR. GARDNER: Greg, I thought the CDC has been fairly clear that out of season immunization is a recommendation if you didn't -- you can immunize throughout the year. Certainly there are enough extraneous cases that happen that probably justify it.

And I hadn't been -- I was always under the impression, unless you have data otherwise, that the toxicity issues were fairly minimal.

DR. POLAND: I think as long as you probably separate them by a month or so. And the data I'm referring to was a study done in elderly people where they were trying to boost immunity by giving two does. And this is where they saw the enhanced local side effects.

And I'm reasoning that with an even more vigorous immune response, you might see more of that in young people. But I suspect --

DR. GARDNER: Well, that's an issue -- if that's truly an important issue, then we'd have to modify. But otherwise, I'd go ahead and give it.

DR. POLAND: The farther you separate them, the less likely that would be.

Yes?

MS. BETZEL: Yes, Tanis Betzel from BUMED. I see two separate issues here with our recruit population and our fleet going to the southern Pacific. I wonder if we should be looking at acquiring the southern hemisphere formulation for the second group.

DR. POLAND: The board did consider that an issue to recommendation at our last meeting actually, which was to not at this point.

MS. BETZEL: Not do it, thank you.

DR. POLAND: Colonel Hatchet?

COL HATCHET: As far as -- you said that

pediatric vaccine -- we have been in some discussions with the FDA, and their position is DOD would not be in a position of asking for an exemption. It would be through the manufacturer.

DR. POLAND: Manufacturer.

COL HATCHET: And Health Affairs in coordination with Milbax, actually more Milbax, which is kind of pushing it along, they're discussing that option with the manufacturers. However, the reality is that unless they have the data already packaged --

DR. POLAND: No.

COL HATCHET: -- it's not a big financial incentive for them to do that seeing that they also make vaccines that could be easily complied with and provide the same level of protection.

So, chances are if we want to do this, it will represent off label use.

DR. POLAND: It will be a moot issue, yeah. Jim?

DR. LOCKEY: This question is for you,

Greg. Could you go to the question one, the second slide? Would you look at this? I'm not sure I'm clear as to what you recommended. Because the Twinrix, if I read this right, the hepatitis A dose is a pediatric dose?

DR. POLAND: Is what?

DR. LOCKEY: Is a pediatric dose. When you said you're recommending this for 17 year olds, would you -- the pediatric dose for hepatitis A is okay?

DR. POLAND: Well, I think the question that they're asking is could they give an adult dose to a 17 year old.

DR. LOCKEY: Okay. So, when you look at this slide, what would you be recommending? It just wasn't clear to me what you --

DR. POLAND: So, I would not have any problem with them using an adult dose. It's a higher dose.

MR. NATO: Right. That was for the hepatitis B, so again, we want to -- the question that came up is, you know, why do we have to --

from our recruit centers was why do we have to give the 17 year olds the separate dosing of Havrix and then Energix for hep B? Why can't we just keep using Twinrix? But you're right.

DR. LOCKEY: But Twinrix has a pediatric dose for hepatitis A. That was my question.

DR. POLAND: Right. You could -- one could do that, and they're stuck in doing that with the few people who are not yet 18.

DR. LOCKEY: So, would you recommend not using that then, because it has a pediatric -- that's what I'm -- it's not clear to me.

DR. POLAND: So, you're asking me to say in public what they always tell us not to do. From a point of view of a vaccinologist, I would not have any problem giving an adult dose to a 17 year old.

DR. LOCKEY: Adult dose, okay. That's what I'm saying.

COL GIBSON: And that was our -- the real basis of the question is the biology, not -- whether -- we're not asking you to endorse off

label use of a vaccine.

DR. POLAND: But scientifically --

COL GIBSON: We just wanted to have this group give us some insight into the biology underneath this issue and your opinion.

DR. POLAND: Okay.

COL GIBSON: Clear it for the record. We're not asking you to endorse off label use.

DR. POLAND: Okay. Because it's related to influenza, I'm going to move ahead here to -- is Commander Luke here? Yeah, Tom, you're still here, who is going to discuss DOD convalescent plasma treatment guideline development.

I want to commend Commander Luke for raising this issue. He had a very insightful, I thought, thought that he then went and looked into the literature and published a paper. I'm not sure if you have it in your books, but it has previously been circulated to the board. And it has -- I guess it is under tab 11.

And it has engendered a number of sideline discussions regarding the use of

convalescent serum particularly in areas where we may not have a vaccine or may not have any other acute therapy that could be lifesaving. So, I do want the board to hear this brief presentation and it's something that the Infectious Disease Subcommittee will have further discussion on.

So, Commander Luke?

CDR LUKE: So, they're setting this up, so I've had the opportunity to talk to board members and I'm hoping you've had the opportunity to see some of the articles and so forth that were forwarded through Colonel Gibson and Dr. Poland.

The -- as you know, your last set of recommendations to the ASDHA, the board recommended that the DOD formulate guidelines, H5N1 and other virulent pathogens should this therapy be needed.

The real question we're asking today is how do we get there. Now, Dr. Cassell has endorsed those, but there's a mechanism that needs to be considered about how we will proceed.

So today, I'd like to talk about

convalescent plasma therapy. Briefly, we'll talk about the background, some of the implications of -- with H51 and other pathogens and highlight some recent publications not only by myself and colleagues but Dr. Zhou in China and then also talk about Argentine hemorrhagic fever, which is the best known and best studied use for convalescent plasma, briefly about the need for guidelines, and the way ahead, and a potential role for this body.

For background, there's a long history of convalescent plasma in serum. It's been used in the prophylaxis and treatment of multiple pathogens not only in humans, but also in animal models.

There have been two cases of convalescent plasma for H5N1 victims. One was a 57-year-old Chinese female with chronic obstructive pulmonary disease. She survived. And there's also been, by Dr. Zhou, a more recent letter that he sent to The New England Journal of Medicine.

And we've had an opportunity to talk to some of his colleagues and so forth. And something very interesting occurred there, and we'll review that.

Colleagues and I did a meta analysis on some studies that were published in 1918 and 1919, where this was actually fairly well, you know, by the standards of the day, studied but also used internationally, not only within the United States, primarily the United States Navy and with some studies in the U.S. Military, but also in Sweden, in England, in Romania, and other locations.

And I think that at their corollary for other virulent strains of influenza, there may be something that can be brought forward from that study. Certainly used with SARS very extensively during that outbreak. A recent meta analysis of that was -- could not find -- was an inconclusive result, but that was mostly because there was no standardization of therapy. There was no guideline.

So, what -- many of the reports that came out were not comparable. But, if you actually take a look at those studies, it's pretty convincing evidence that convalescent plasma was therapeutic and helpful in patients with SARS.

Measles, through the 1920s and 1930s, this was the standard of care, very effective. And that's also been replicated. As we know, the maternal antibodies protect infants and also protect you against vaccinations, one of the reasons why we have to have multiple measles vaccines. It's very effective.

Hepatitis A, again, in the 1920s and 30s and of course, with South American hemorrhagic fevers, the Arenaviruses, which is a category -- a CDC category bio- warfare pathogen, this is the standard of care. And we'll talk about that.

Obviously known for diphtheria, for orthropox, and it was used -- convalescent plasma and serum was used fairly extensively in India as a prophylactic and treatment regiment, but also is used VIG for adverse reactions for vaccinia and

many others, including anthrax and other diseases which the DOD has particular concern.

The fact here is, in my opinion, that this will be used in desperate situations, like clinicians during outbreaks and epidemics and pandemics. So, I think that to avoid some of the problems that we've had with all of this, particularly with our recent history with SARS, that a well developed guideline and reporting mechanism would go a long way to resolving questions of efficacy and suitability within the DOD and perhaps in other organizations.

I think it is true that DOD personnel are at high risk for epidemics of infectious disease, not only from natural causes but also from the result of purposeful bio- terrorism.

Another fact that I think is very important is that the DOD can collect, produce, and transfuse large volumes of convalescent plasma from military volunteers who have either recovered from a disease or have been vaccinated.

And one aspect of DOD, of course with

our small pox and anthrax vaccine policies is that we essentially have the highest population of individuals that have received those very specialized vaccines, and we may be the only source of convalescent plasma, not only for ourselves but also for our civilian population.

The convalescent plasma or an IBIG product can be used within the Department of Defense and in the civilian population. So, I think that those have ramifications, not only within the Department of Defense but also in other areas that may be having a natural epidemic or be subject to bio-terrorism.

And it is my opinion and an expert opinion guideline and data collection format can reduce morbidity and mortality in the DOD by standardizing the therapeutic approach and collection of clinical data and outcomes so that very firm -- determinations of efficacy can be made.

Briefly, we'd like to talk about plasma. It's routinely required and transfused for the

treatment of very serious diseases, such as coagulopathies. And this is typical done by JACO standards and others and the American Association of Blood Banks after patient consent.

So, even if you were getting a routine plasma transfusion, what we would consider to be routine, patient consent is typically obtained.

Plasmapheresis donors can safely donate 1,000 to 1200 milliliters of plasma per week. This is a very significant amount, particularly if you take a look at the older data and the more recent data about how much is necessary where you have an efficacious indication for convalescent plasma, that a single individual could probably supply enough plasma to treat multiple patients.

Convalescent plasma collected at the local level; that is, at the MTF, could have an immediate impact during the next pandemic influenza or other disease for which no good treatment exists.

That means that we're not reliant totally on supply lines from distant stock piles

or manufacturers is that clinicians have something to offer patients in the event that something very terrible occurs. And certainly that is something that we are looking at with H5N1 and pandemic influenza preparations.

The last point I'd like to make is that donor motivation during emergencies is rather high either from mass casualty events within the Department of Defense or after, you know, a major national tragedy, such as 9/11. I will say that following 9/11, within hours, hundreds of people were lining up at the National Naval Medical Center to donate blood.

I think that that kind of motivation will be necessary. And I think that we can expect that kind of motivation during an emergency where we're calling upon military members and others to donate their plasma to save or help their fellow man.

This is what we're looking at here. This is probably the best single graph that I've seen that explains exactly what we're talking

about in the situation of a pandemic of virulent influenza.

This is the Surgeon General's report to the Secretary of War for 1918. It shows that it has a baseline rate of essentially infectious disease mortality on an annualized rate of 5 to 10 per 1,000 per week, which would now be considered a true emergency. It goes up to about 100 per 1,000 per week. And we need to have as many solutions to this problem as we can.

I think that it is likely in the future of influenza epidemics that we could certainly, you know, see similar type of situations. And the ability to rapidly institute convalescent plasma could be lifesaving for many, many individuals.

So data, again, I hope you've had a chance to see this. For the Spanish influenza, this was a meta analysis that we produced in the annual list of internal medicine. It certainly is not the last word on this, but certainly we think that it was an interesting study.

And then of most concern, and you'll see

some data from this, Dr. Zhou with treatment of convalescent plasma that he published in The New England Journal of Medicine.

In the case of the most widely studied and most -- and most -- considered to be the best use of convalescent plasma is Argentine hemorrhagic fever. And there's two examples here, Dr. Ruggerio and Dr. Matzaggui. And I provided those so that you can see those after the presentation has ended and you're back at home.

So, in the study that we did, there were 27 reports that were found; 8 relevant studies involving 1,703 patients met our rather extensive inclusion criteria. Treated patients were often selected because of more severe illness. This was a selection bias in which a convalescent plasma was given a pretty rigorous trial.

The most common laboratory finding was leukopenia. The most common clinical finding was cyanosis and dyspnea. Convalescent whole blood, plasma or serum is obtained from donors one to six weeks after recovery from influenza. Patients

typically receive one or two treatments. And the average amount of plasma in the treatment product was about 100 to 150 milliliters or 2 milliliters per kilogram.

All 8 studies reported a survival benefit. You've seen this in the article that was presented to you, but essentially for all comers, that is no differentiation about when the plasma was applied, the overall crude case fatality rate was 16 percent in those that were treated versus 37 percent among controls. The range of absolute risk difference is in depth with 8 to 26 with a pooled risk differential of 21 percent between the groups.

If this was stratified by early and late therapy, the overall crude case fatality rate was 19 percent for patients treated within 4 days of pneumonia complications and 59 percent of patients treated 4 days or later. The range of absolute risk difference in death was 26 to 50 percent with a pooled risk difference of 41 percent.

This is the recent graph that Dr. Zhou

presented in his article in The New England Journal of Medicine. And I think we can see that something rather amazing occurred here. A 31-year-old male presented to a Chinese hospital with a 4-day history of influenza like influenza.

He was in the hospital for four days, as you see with the green line with the triangles above. He was diagnosed with oceltamivir by RTPCR and immediately started upon oceltamivir 150 milligrams BID, which is twice the recommended dose.

This individual had a series of RTPCRs to determine viral copies per milliliter and continued from the 13th to the 14th. And on the 15th of June, he received 200 milliliters of 1 and 80 neutralizing antibody titer plasma. And within 24 hours, the number of viral particles per milliliter went from 180,000 per milliliter to essentially zero. And there is a more detailed clinical report provided in that article.

This indicates that this works for H5N1. I mean, we can argue that maybe oceltamivir had a

role, but clearly, there seems to be something going on. I will mention that there have been a series of animal studies with the use of convalescent serum in mice, which essentially replicate not only the findings that my colleagues and I found with Spanish influenza but also with the results that Dr. Zhou has reported for the two patients in China.

For plasma therapy for Argentine hemorrhagic fever, which I mentioned is a CDC bio-terrorism category A pathogen, the use of convalescent plasma within 8 days of becoming symptomatic is associated with a 90 percent reduction in mortality. It is the standard of care.

And this is something that I think that we need to be concerned with and something that if we have a situation where an individual is using this or another agent multiple times, it is likely that we're going to have survivors and that we can use that plasma without doing IVIG to go to fact if we're prepared and ready to institute that

policy.

There are some key issues and questions. I think that I would like the board to consider the implications of convalescent plasma therapy to the Department of Defense, not only from a national security situation but also the advisability and need for multiple agency involvement, you know, should the board decide to proceed in this manner.

My concept is I would like the board to bring together experts and other entities to create consensus, that is expert opinion convalescent plasma therapy guidelines to treat H5N1 or other novel pathogens for which effective and plentiful therapeutics do not or may not exist.

Certainly there are some technical, logistical, and clinical issues that need to be addressed, not necessarily resolved with those guidelines, but they should, you know, try to incorporate those specific issues.

And the real question is the DHB role.

As I've said, you have previously endorsed the need for guidelines and that recommendation was accepted by Dr. Cassell's ASDHA. And the question for the board is what is our next step. Thank you.

DR. POLAND: Thank you, Commander Luke. Questions or comments?

(No response)

DR. POLAND: I can say that I think the board would be very supportive perhaps using a mechanism of temporary task force or something, attach the Infectious Disease Control Subcommittee would be a nice way to keep moving this thing forward.

CDR LUKE: Yes, sir. Some of the -- we have had an opportunity and I won't mention them, but we've had an opportunity to talk to, you know, some of the world leaders and experts as well as some individuals represent, you know, some interagency groups and other entities that are willing to participate, you know, should a modicum of funding, you know, be provided to, you know,

bring them. They would be happy. They recognize the need for it, and they would be willing to participate.

COL GIBSON: Tom, this is Colonel Gibson. Just for the record and to be clear, we're talking about a group of maybe like 20 people or so, right, rather than a consortium of hundreds coming to some sort of a conference on this.

CDR LUKE: Sure. So, there aren't a whole lot of convalescent plasma therapy experts, right, so it's a relatively small group of individuals that could help us with this --

COL GIBSON: Thank you.

DR. POLAND: -- sort of a fluid group. Dr. Walker?

DR. WALKER: There is a growing body of evidence for many agents, including agents that people don't pay a lot of attention to that are difficult to treat sometimes that antibodies and of course, viruses, we call them neutralizing antibodies are very effective when they hadn't

been thought to be previously.

For some of these diseases, the antibodies appear late, very late. Like for example, in lesser fever, neutralizing antibodies don't appear sometimes until a year after the patient has gotten well. And so the issue is that it's not the plasma that's therapeutic; it's the antibodies that's therapeutic.

DR. POLAND: Sure.

DR. WALKER: And that perhaps using convalescent plasma isn't the best approach, that maybe we should be looking at engineered antibodies or humanized monoclonal antibodies and pick the targets and make the products.

DR. POLAND: I think a group like this could explore all those issues.

DR. WALKER: Explore that, yeah.

DR. POLAND: Pierce, did you have a comment?

DR. GARDNER: Yeah. I think this has moved from the far back burner onto a viable significant possibility that we should be

supporting. And it clearly is something that Pharma will never take on. And so, the real question is what possible -- this sounds like something that the military should champion. And if we're going to go anyplace, it will probably have to be done somewhere in government.

I don't believe NIH does anything at all with immune therapy in terms -- it's all involving vaccines --

DR. POLAND: In terms of passive immunization, yeah. I think you're right.

DR. GARDNER: I think it's very interesting. Commander Luke deserves credit for keeping our attention on this. And it's something that deserves some increasingly high level of thought with certainly some questions as to who would actually do this because it's not going to be a moneymaker for anybody.

COL GIBSON: As Commander Luke pointed out, there is a national implication to this, so it's important that the other agencies be engaged and perhaps consider ownership of the issue as a

whole.

DR. POLAND: Joe and then Mike.

DR. SILVA: Yeah. I liked the presentation, Tom. Thank you. And I think it's time for us to take this one on as a set of what's being reflected. I think can think back briefly again on my days at Wilford Hall circa 1970 when we had a bad group B.

We actually had recruits come up, give blood. We gave it to -- I can't remember now, 4 to 6 recruits. I don't know if it made any difference. They were on respirators, and we lost about 10 or 12 guys in those days.

But the data was reviewed at that time. And we felt impressed with it, that we wanted to try it as a last ditch effort. So, I think some refinement and even looking at where the science is now, as David had hinted at, could start providing a matrix that we could get serious about this problem.

DR. POLAND: Dr. Oxman?

DR. OXMAN: And actually, we're really

talking about at the first level some general guidelines because it's for the unexpected, and we're not going to stockpile something. You know, with leukemic children before we had VZIG, on Friday night, when a leukemic child was exposed to varicella, we'd call the dermatologists around town and try to locate a few volunteers who would give plasma two or three weeks after their zoster. And so, I mean, this is something that has been done --

DR. POLAND: Good point.

DR. OXMAN: -- you know, in that kind of setting. And I think we should take on -- the Infectious Disease Subcommittee should take this on in terms of getting some additional help and trying to formulate guidelines.

DR. POLAND: Good.

DR. OXMAN: And I also would like to commend Commander Luke.

CDR LUKE: Thank you, sir.

DR. POLAND: Dr. Parkinson?

DR. PARKINSON: I just can't help but

reflect and I don't know the answers to this, but as you fly home today, you think about the discussion we had yesterday, which at its highest level was about the transfusion of whole blood and blood products to today's discussion, which is transfusion of components of blood. And the flow of this discussion is very different than the flow of yesterday's discussion at the end point.

Leave it for your cocktail tonight. What are the aspects of this that makes us comfortable that were absent yesterday or vice versa? And are they even comparable issues at all? So, I mean, that's just for cocktails later. But it's interesting as I sit here, not as an immunologist and not as a primary person, but there are (inaudible)-- versus something -- you know, obviously there's very big differences, but --

DR. POLAND: I think what might be different is the presumption of screening first --

DR. PARKINSON: Yes, yeah.

DR. POLAND: -- and then the presumption

of it being studied under protocol.

COMMANDER LUKE: Yes, sir. If I could just jump in that the -- you could put guidelines out, but without data, you can never truly say whether or not we're helping, we're hurting, it's neutral. So, I think it's essential that the guidelines come with a reporting mechanism, so that we can quickly assess what's being done, who's getting it, what groups, how much, and then pretty quickly we can make a determination for further recommendations to either continue or to stop. I think that's important.

DR. POLAND: I thought I saw one other. Dr. Shamoo?

DR. SHAMOO: I just want to associate my comments with David is that this is a scarce resource and it's a potentially cause of problems rather than solutions if you don't couple it with scale up, that is, genetic engineering otherwise. Just using the plasma as a source and who in the world are you going to give it to?

CAPTAIN JOHNSTON: If I might, this is

Richard Johnston speaking, go for something more philosophical line. I think that what Tom Luke referred to is that these are things that only -- we only use in emergencies. And as a result, they're often not studied as thoroughly as they might be because there isn't the time to get these studies prepared and underway before the emergency is over. And I think one of the things this board could quite usefully do is to recommend not perhaps in just this area but in other areas where similar things might apply. And one example I came across recently was chlorine gas exposure that actually -- an organization like the (inaudible) could well prepare study protocols in advance for things like this. So, there is a study ready and waiting to be performed when an emergency arises so that we actually can collect the hard data that we need to use in these sort of situations.

DR. POLAND: That's a good point. Okay. Thank you very much, Tom.

COMMANDER LUKE: Thank you, sir.

DR. POLAND: I appreciate it and again, our commendation for raising the issue. I think what we'll do now is we'll take about a 15 minute break or so and then we're going to have -- what? Correction. We're ready to adjourn because the remainder of the meeting will be just for board members.

So, thank you everybody. This board will reconvene in April of the 8th year of the 21st century. Happy holidays to everybody.

(Whereupon, the PROCEEDINGS were adjourned.)

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