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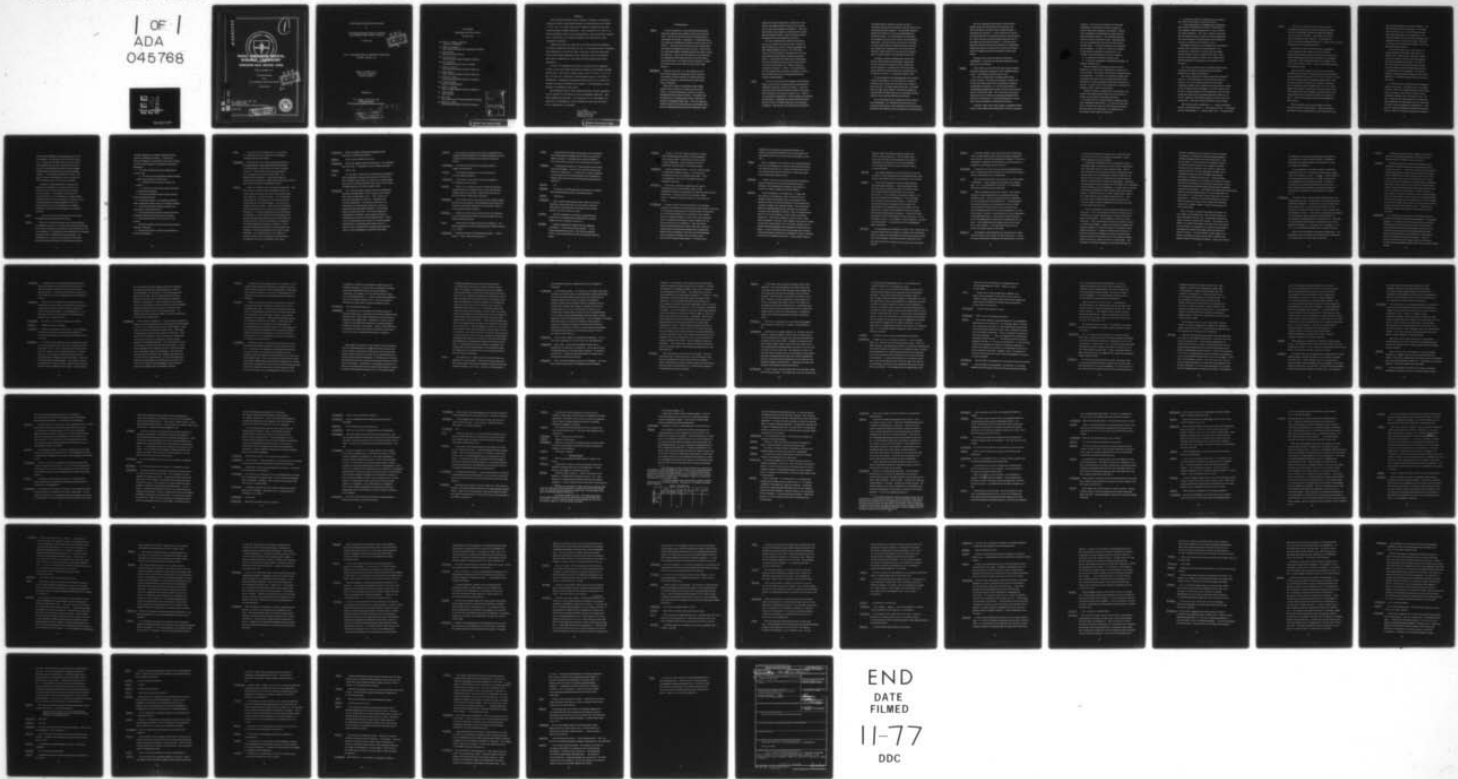
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**NAVAL SUBMARINE MEDICAL
RESEARCH LABORATORY**

SUBMARINE BASE, GROTON, CONN.

SPECIAL REPORT 76-1

Edited Proceedings

from

The Longitudinal Health Study Review

22 April 1975

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R. L. Sphar, CAPT, MC, USN
Commanding Officer
Naval Submarine Medical Research Laboratory

27 July 1976

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LONGITUDINAL HEALTH STUDY REVIEW

at

Naval Submarine Medical Research Laboratory
Naval Submarine Base, Groton, Connecticut

22 April 1975

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✓ NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY
✓ SPECIAL REPORT 76-1

Philip E. Enterline, Ph. D.
University of Pittsburgh
Review Chairman

Released by:

R. L. Sphar, CAPT, MC, USN
Commanding Officer
Naval Submarine Medical Research Laboratory

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ATTENDEES

Longitudinal Health Study Review

22 April 1975

- Dr. Philip E. Enterline, Chairman
University of Pittsburgh
- Dr. Robert C. Bornmann
Naval Medical Research and Development Command
- Dr. David Discher
Stanford Research Institute
- Dr. Charles F. Gell
Naval Submarine Medical Research Laboratory
- Dr. Eric Gunderson
Naval Health Research Center, San Diego
- Dr. Claude A. Harvey
Naval Submarine Medical Research Laboratory
- Dr. Rupert Hester
Naval Submarine Medical Research Laboratory
- Dr. Douglas R. Knight
Naval Submarine Medical Research Laboratory
- Cdr. Stephen McArdle
Bureau of Naval Personnel
- Dr. Robert E. Mitchell
Naval Aerospace Medical Research Laboratory
- Dr. Adrian Ostfeld
Yale University
- Dr. Alan Purdy
National Institute of Occupational Safety and Health
- Dr. Raymond L. Sphar
Naval Submarine Medical Research Laboratory

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FOREWORD

The Longitudinal Health Study of Submarine Personnel, a multiphasic prospective medical surveillance program, was conceived mainly by Charles F. Gell, M.D., D.Sc. (Med), when he was Scientific Director of the Naval Submarine Medical Research Laboratory. This conception of Dr. Gell's was perhaps predictable due to his own experiences in aviation medicine research and, in particular, his intimate knowledge of the 1000 Aviator Study conducted at Pensacola.

Though the project was conceived in 1966 and approved and funded by the Bureau of Medicine and Surgery in 1967, it took several years of planning and development of the protocol before there was a smoothly functioning system which brought submarine sailors from their "boats" and bestowed upon them the advantage of a very sophisticated executive-type health examination.

By 1975, one thousand men had been so examined and the Commanding Officer of the newly-formed Naval Medical Research and Development Command decided that it was time to conduct a peer review of the LHS. On 22 - 23 April of that year a committee of distinguished experts in the fields of epidemiology, occupational medicine and biostatistics met in Groton and reviewed the status and future of the project. The proceedings of those meetings is contained in this report.

The Commanding Officer, Naval Submarine Medical Research Laboratory, is most grateful for the efforts of that distinguished committee. Many useful suggestions were made. It is hoped that all of the members will continue to be interested in the LHS through the years and that there will be opportunity to meet again.

R. L. SPHAR
Captain, Medical Corps,
United States Navy
Commanding Officer

Morning Session

SPHAR: I'd like to welcome you to the Naval Submarine Medical Research Laboratory and to explain what we had in mind for today. Over the last 20 years the Navy has accumulated a vast number of man days - submerged - in FBM submarines. The submarine atmosphere is certainly not pure country air but frankly, those of us in this field are not very worried about what might have happened in the last 20 years. What concerns us is what might happen in lengthened patrols for newer classes of submarines. That is one of the reasons we are conducting the Longitudinal Health Study and that is one of the reasons you are here today to try to help us with 2 questions: 1) where do we go from here ? and 2) have we started in the right direction ?

BORNMANN: Thank you very much. Dr. Gell is going to go into the historical aspects of the project which he started in this Laboratory when he became the Scientific Director, distinctly influenced by the success of the 1,000 aviator study at Pensacola.

There are a number of Longitudinal Health Studies within the Navy of which two of them are here at New London. A study of submariners, which is the focus of the discussion today and one on divers. The aseptic bone necrosis study is a specific project which is also part of the divers' longitudinal health study. One of the things we wanted to make sure was that there was a correlation within the Navy Medical Department of all the longitudinal health

studies and I include therefore the 1,000 aviator study which is still going on and the returned Navy prisoner-of-war study which is going on in Pensacola. There are other studies at San Diego at the Health Research Center directed towards recruits coming in the Navy and their subsequent history and experience in the Navy.

We were concerned about whether this particular study at New London was sized correctly, whether the input of subjects was correct, whether statistically they were being assembled correctly. The other thing is that in a 20-year history we wanted to have a 20-year master plan which will allow a succession of project officers. We wanted to find what was the ultimate goal, what was the payoff in this study and how much would it cost and so with the help of Dr. Lawton, the head of occupational medicine at BuMed, we assembled from the United States what is obviously a collection of some of the best talent in the area of occupational health and medicine and biostatistics.

GELL:

Let me tell you how the study began in this Laboratory. When I first came here I found that several branches were interested in long-term studies for instance - vision was concerned with the close confinement myopia in submarines which incidently is not related to aviation at all. Auditory was interested in hearing loss, and the hearing sonar problems in submariners. Physiology was concerned with pulmonary function relative to relatively high CO₂ in the submarine atmosphere. Biochemistry was concerned with cholesterol

and triglycerides in relation to the open ice box on submarines and the fact that actually by law they cannot serve unsaturated fats like margarine. Our personnel selection people were interested in long-term psychological and psychiatric studies. Our Dental Branch was interested in development of cavities over a long-term period aboard submarines. The net result was that we had a composite of a half a dozen different disciplines desiring to do long-term studies and my suggestion at the time was that we establish a study similar to the one they had at Pensacola which eventually became the Longitudinal Health Study.

We began to become concerned with problems like dysbaric osteonecrosis and interestingly enough about that time the National Research Council Committee on Aviation Medicine in reviewing the 1,000 aviator study recommended that studies of this type be conducted for all 3 branches of the Navy. The study was funded in 1968.

We went through the usual growing pains and concerned ourselves with whether or not we should have controls in association with the study and who would we try and get to be the controls. We thought about surface Navy, we thought about the Coast Guard Academy, Civil Service people and eventually gave the whole thing up as an impossible situation inasmuch as the cost would become astronomical.

We've had frequent visits to Pensacola and have utilized their methodology. Dr. Mitchell has been up here as our consultant and we did have some relationship with NIH (National Institute of Child Health and Adult Development and Aging Branch).

One of the criticisms made toward our study was the attitude that we were starting from the wrong end, that what we should do is go back into the medical histories of submariners for the past 5 - 10 years and from this source, we could probably get a pretty good estimate of aging problems. Dr. Hester started an ancillary program going back into the past submarine records and histories. It has shown some trends but certainly would not take the place of a Longitudinal Health Study because in the past 10-20 years there has been a period of changing submarine development and operational history.

During the last 3 years the study has accelerated tremendously -- we've set up an excellent examining routine and we have over 900 men.

KNIGHT:

To date there are five Naval Submarine Medical Research Laboratory publications pertaining to the Longitudinal Health Survey. I will briefly summarize them for you:

(1) In 1972, Doctors Sawyer and Baker published the survey's protocol. The reason for initiating the project was to define the health hazards of the environmental exposures of submariners and divers. Dr. Gell was instrumental in encouraging and supporting the project, based on his experience with the 1,000 aviator study. The 1,000 aviator study represented many years of experience gathering sequential health data from naval aviators. Its success indicated that a similar study could be successful in submariners and divers.

Therefore, efforts were made to apply a Longitudinal Health Survey to those officers and enlisted men in the Navy's undersea

programs. The survey was intended to be performed periodically on each subject in order to monitor the health of the worker population; and hopefully, to bring about meaningful recommendations for safer and more pleasant working conditions. The data processing was outlined in detail in the Sawyer report. Biomedical data was to be translated onto Hollerith cards and stored on computer tapes. Two types of programs were developed for the computer. A "print-out" format was developed for the formal presentation of the stored data. An "editing" format was designed to allow the computer:

- a. To protect the study from erroneous data
- b. To alert the investigators of significant pathology, for purposes of patient care.

Whereas computer processing presented technical difficulties to be surmounted, organizational problems were also discussed. One problem was obtaining an adequate sample of the population. The authors recommended changing from a non-random selection process of studying submarine school candidates to a random sampling of submariners and divers in the fleet. Of major concern was the selection of personnel who intended to select a career in the military.

Finally, the authors recognized that a major pitfall to the success of the study would be variations in interest for the project, and variations in investigator personnel.

(2) In May 1974, Dr. Tansey published a progress report of the Longitudinal Health Survey. He stated that there was a lack of a surveillance system for monitoring environmental effects on divers and submariners. He suggested that a surveillance system fulfill two objectives:

1. An immediate objective of identifying the incidence of both subclinical disease and medical risk factors.

2. A long-range objective of identifying the occupational health trends in submariners and divers. Tansey felt that the multiphasic health examination was a means to provide the needed surveillance. Most of Dr. Tansey's report dealt with describing the current content of the health examination. The major categories of biomedical data were presented as they are now entered into the computer, that is:

Demographic information, Psychological/Social information, Mortality date, Anthropometric measurements, x-ray examinations, dental health, pulmonary function studies, hearing function, a doctor's physical examination, visual function, clinical laboratory studies, and a medical history (electrocardiogram is performed, but not entered into the computer.).

Dr. Tansey concluded that the Longitudinal Health Survey was indeed successful in gathering valuable biomedical information for computer assessment.

My closing remarks will be those listing already published reports, in-press publications, and future reports from the LHS data: (a) In 1974, McKay and Ryan found that Navy submariners require more correction for myopia than Navy divers or Navy Submarine School candidates; (b) In 1974, Kinney found that from a subject population of 750 submariners there was more myopia than expected from the general population statistics; (c) In 1975, Tappan et al published an analysis of SMA 12's from 566 submariners. Their data revealed essentially normal findings.

Other studies nearly completed are: a. A study of pulmonary function, and smoking habits; b. Anthropometric data; c. Psychologic and Social descriptions; d. A dental profile and e. A hearing profile.

HARVEY:

I want to say a few words about our data collection techniques so you know how we go about doing this in-house. We have in the MilApps Division four people who dedicate their time totally to the LHS. Two of these are civilians and two of these are Navy corpsmen. We also have the Head of the Submarine Research Branch, Dr. Knight and Mr. Parker who supervises the statistical collection.

The majority of the tests that are done are designed to produce figures of some nature that can be stored into computers and therefore subject to analysis, but, many of the doctors' findings are subjective and, therefore, very difficult to quantitate. Most of the physical (with the exception of the chest x-ray) is done in one day. Chest x-rays usually are done the following morning.

Most of our data is prepared in-house by our own data processing unit and then it is stored on tapes at the Underwater Systems Command for use in the UNIVAC 1108 computer. We have scattered programs within the storage program itself to look for obvious errors for instance if we measure a man with a 500 inch waistline, why the computer says "no" I don't really believe that and kicks it back at us, so it's within some limits. The computer print out is reviewed by us and compared to the original data sheets to make sure we didn't have punch card errors. That is the safeguard that we have for keeping our data accurate.

When the subject comes in to go through the LHS he receives a packet for data collection. Blocks are numbered and coded so that the cardpuncher can work directly from this

sheet to punch the cards to go into the computer. The man carries this with him as he goes. A few things don't fit into this, e. g., the SMA 12 has to be hand coded before submission to the cardpuncher. The electrocardiogram is at the moment not being put into computer form but it is read by our staff. We have not carried out an extensive data analysis yet but have done a preliminary analysis.

We'll hit the 3-year mark, on the first of our subjects that has a total profile, some time in the spring of 1975. Since we have not started "recalls", most of our efforts so far have been collecting data that would characterize the profile, if you will, of what our submarine and diving populations are like. Our initial report on the first thousand people will be a characterization of our population. We obviously will have to implement some comparisons and do some updating of our computer analysis when we get into the first recall.

Dr. Hester has been working with the retrospective aspect of this project. He's been looking at the figures for 1969 to 1971 from the BuMed data tapes which record all of the diagnoses that have been labeled to every submariner and diver here in that period of time. He also is collecting from BuPers figures on everyone who had a designator as a submariner or diver to make sure we haven't missed the people in the BuMed tapes. From this he is using the international nomenclature system to find out if there is an abnormal prevalence of disease of

some kinds for diagnosis in this population group in that 3-year period. He has been at this a little over 2 years now. It seems like an awfully long time but we ran into some problems that we had not anticipated such as the fact that the international nomenclature system changed during that period and therefore the storage techniques changed, -- he is making good progress, however. We expect to have an initial report out some time about the end of this fiscal year on the retrospective aspects.

Although the Longitudinal Health techniques were designed to be applied over a long period of time, we believe that a lot of these techniques could be used for subacute problems. For example, one could look at a single FBM patrol or you could look at a single isolation experiment similar to the Trident patrols. Because we have a good examination technique established we have considered putting this type of an approach into a different application and that is one of the things we are examining currently.

SPHAR: Let's move on now to the discussion of the related hypotheses and their application to the study.

KNIGHT: There are two important reference sources for objectives and hypotheses of the LHS: The most recent research summaries, and a listing of questions formulated at a recent review of the LHS by key personnel. The objectives of the study stated in the research summaries outline immediate and long-range goals. The immediate goal is to determine the incidence of subclinical disease and medical risk factors in submariners and divers.

The long-range goal is to identify occupational health trends in submariners and divers. A more recent review of questions to be answered by this Survey resulted in several broad categories of hypotheses and practical applications:

1. The study could provide bases for application in several areas:
 - a. The use of accumulated data for legal settlement of health claims against the government.
 - b. Opening up of new research interests and pathways.
 - c. Future use of a data bank of health information on submariners and divers.
2. Document relationships between health disorders and environmental stresses.
3. Recommend changes in the working environment likely to bring about improvement in the working conditions.
4. Document the subjects' adaptive changes to the environmental conditions with time.
5. Define physical and psychiatric measurements that will predict future work performance by the subject.
6. Study both populations for the incidence of bone necrosis.
7. Correlate morbidity with those health characteristics reflecting risk factors.
8. Describe the subjects' psychosocial adjustments to the work environments.

SPHAR: Let me now turn the meeting over to our Chairman, Dr. Philip Enterline of the University of Pittsburgh's Graduate School of Public Health.

ENTERLINE: I think before I start, I have a few questions based on the discussion that I think will help clarify some things -- I just became aware of the fact that you haven't done any re-exam -- I didn't realize that you have just done the first go-around and you're up to about 1,000. The problem is one of selection. A great deal of what you said had to do with getting a profile of the submariners and divers and yet do you know what the population is like?

HARVEY: I think, Dr. Enterline, that I can answer that question. If one were to devote a whole section on population selection, we consider that quite frankly one of our most important vague areas right now -- we have 2 sources -- we have inexperienced people who are starting out at the Submarine School and therefore have not been available -- we have not been tapping that source recently. Instead we have been drawing from the boats primarily from one of our two categories of submarines -- we have the big ballistic missile subs that go out and make 90 - 60 day patrols actually submerged and we have the fast attacks that make runs for variable lengths for various activities. Most of our population is coming from the missile submarines and they are volunteers. We do not know the exact characteristics of the people who do not volunteer. We may be missing some of the most stressed individuals. It is a population that is very difficult to describe in detail and more important we don't know what the population that is not volunteering is like exactly.

ENTERLINE: What is the BuMed requirement regarding periodic examination of submarine personnel ?

HARVEY: They all have a physical once a year.

ENTERLINE: So the Navy requires submarine personnel to have a physical once every year -- the physical you do is separate from that ?

HARVEY: That is true.

GELL: Dr. Enterline, I think when you talk about the age incidence and the distribution of age you get the picture of the Navy as a rule, especially aboard ship, of a large crew of younger people and several of a greater age farther above them but it's actually a youthful group as you'll find the peak at age 24.

ENTERLINE: OK, I think that helps, because when we are talking about hypotheses and applications I think it's good to have a better idea of what the population is like. -- Well, why don't we just open the discussion on just that -- Hypotheses and Practical Applications. One thing that strikes me in the discussion of this retrospective study that it would be a great hypothesis-generating mechanism - if you had gone back even further than 1969. I don't know enough about the problems for example, nobody mentioned radiation -- I would assume that there is some radiation hazard - I notice that in the questionnaire that you give to the persons getting physicals there is something about radiation history. I wasn't clear as to whether that's something they themselves knew or it that's something you could add to this thing.

HARVEY: Every man who is exposed to the nuclear submarines has a radiation monitoring badge and the radiation exposure he has had during his time in submarines is recorded in his medical record.

ENTERLINE: Are these radiation histories interesting enough to suggest any hypotheses ?

HARVEY: Our submarine population as a whole really has a very low radiation exposure.

ENTERLINE: Lower than or at the level of the general population - or something in excess of that ?

HARVEY: They may have slightly more than the general population because they get more regular chest x-rays but the amount of radiation they get on the subs is usually well below what you get from routine roentgenologic examination.

BORNMANN: If you consider that they are spared cosmic radiation during the time they are undersea, some hypothesize that they get less radiation in submarines than they do in normal life, except for a few selected classes of workers.

MITCHELL: Probably one other area too where they have less exposure, is in the microwave area which of course is coming under very intensive study at this time.

GELL: I would feel that it might be worth the investigation -- this group is exposed to all sorts of electromagnetic radiation devices, e. g., sonar.

ENTERLINE: Somebody mentioned in the opening discussion -- a cancer hazard -- I didn't really follow up on that --

SPHAR: I mentioned that the organic contaminants of the atmosphere may include some carcinogens that we really don't know much about at this point. I mentioned this in terms of whether or not we might wish to consider those contaminants in this study.

DISCHER: I would like to ask about Dr. Hester's study from the standpoint of three things -- two have to do with the numerator and one with the denominator -- the first one is "does an individual on the tape who has an annual examination and the diagnosis of disease made at that time have his examination data go into the numerator?"

HARVEY: No.

DISCHER: If he goes to a private physician for treatment of a condition would that ultimately get back to that official record?

HARVEY: Probably not.

MITCHELL: May I interject something here which I think is true in the submarine community as well as in the aviation community -- these people occasionally don't want things in their records because it may well "shoot them down".

HARVEY: This also undoubtedly is selecting our population from people that have problems from smoking heavily and other things may not be motivated to come to us.

DISCHER: I think you answered the question that the individuals are followed -- how are they exactly followed -- he's no longer associated with the Navy. Why would he cooperate with Dr. Hester and provide him with any information about his health?

HARVEY: He won't. All of Dr. Hester's information is taken from the BuMed tapes where they've been categorized with a disease either at, during time of active service, or time of discharge. When he became a veteran he would have no further data as to the military tapes.

BORNMANN: These are separate studies -- what Dr. Hester is doing is working with available records. If the records are incomplete his study is complicated at that point -- there is an opportunity in the LHS to ask people if they will cooperate in the future.

MITCHELL: We've had a tremendous cooperation with those individuals who are out of the service, many of these individuals coming even great distances at their own expense for the examination -- because we don't have the funds to bring them in -- hardly a week goes by that I don't see at least one or two.

ENTERLINE: It seems to be that even if you had 750 out of a thousand come back, I would be very worried about the 250 that didn't come back. If I were going to spend money on a study like this I'd concentrate on a fairly small sample but very intensely so that I wouldn't have a non-response problem; or have some way of examining the non-respondents (that is, take a random sample of say the 250 if you had 750 out of 1,000 back). There are reasons people come back and there are reasons they don't come back. I would think for example that somebody who is symptomatic might be more encouraged to come back more than somebody who's asymptomatic thinking it was a good way to get a physical and/or getting things resolved. You know, we're

supposed to be talking about generating hypotheses, but I think you can't generate hypotheses until you understand what the potentials are for study and what kind of population you will have.

SPHAR: We try to impress on our subjects at their initial examination, that this is the equivalent of an executive type examination which they might have received in a preventive medicine clinic and we try to impress them with the importance of a follow up as part of good preventive medicine practice.

DISCHER: I'd like to look at the environmental stresses as perhaps a source of what sort of environmental stresses have been identified. Does everybody get exposed in this situation or do you have cohorts of exposure to specific agents?

HARVEY: I think the question is an excellent one. To begin with, the stresses on the submarine, there are some trace contaminants within the atmosphere due to the operations of the machines and due to the natural production of contaminants such as carbon monoxide from cigarette smoking. We can quantitate these from ongoing studies that have been held in recent years. Circadian cycle undoubtedly is affected. Most of the submariners work on a 6 on 12 off schedule, so they in effect are living an 18-hour day. They may be working 12 on and 12 off for a while while they qualify, so that their work schedule varies rather markedly. Certain watch stations require a lot more direct attention and concentration and psychological stress on gauges and instruments than others. I do not at the moment have any way within the LHS study to break them down in stresses for an individual in order to correlate it with what we're finding out about him. We can break it down by

officers, chiefs and enlisted personnel, things of this nature in terms of their rank. We can break it down by age; we can break it down somewhat by time spent on submarines, but basically we can't take an individual at the moment and trace him in terms of exactly where his stress has been.

DISCHER: I am wondering whether or not the plans for the LHS are to improve at least information from the worker himself, about what he's been doing in terms of the preceding 3-year interval.

HARVEY: We have been thinking of sub-acute studies using the LHS examination techniques -- actually checking the crew just before patrol, putting some observers aboard to take 24-hour automatically recorded EKG's and then check post control. I'm not answering your question directly, but that is one approach we have thought of. The second thing we have done is review our patrol reports. We have gone to San Diego and from the group out there (thanks to Dr. Gunderson) we have arranged to get patrol reports from the destroyers to compare their incidence and sick bay incidence with our own submarine patrol incidence. We have not tackled the question of what's been going on the last three years. One of the things we want to ask the people is "what's happened to you since your first physical"? We have put that off 'til the longitudinal aspect downstream.

DISCHER: If I understand the environmental stresses, many of these that you mentioned might have some objective correlates to go along with it. Have you considered the possibility of obtaining monitoring records from watch schedules, information about job performance from personnel and this sort of thing to back up what the guy says about himself?

HARVEY: It would be possible to get at least some of this information from our patrol reports where they list atmosphere ranges that have occurred. Some of this information is available. We have not made plans to utilize this and incorporate it at the moment but it sounds like a good thing to think in terms of.

BORNMANN: I would like to go back to the fact that we are talking about a LHS in submariners and I would like you to identify those stresses that are characteristic only to submariners.

GELL: We are faced with the fact that there are a lot of small insults to individuals -- such as living in an atmosphere that contains about .75 to .1 CO₂ practically all the time. As I said before, they have an open ice box on the submarine.

HARVEY: There are certain other peculiar stresses. They need do *submarine escape training which is a pressurization escape* through the water. The sonar exposure they have undoubtedly is a bit different than the submarine per se. The psychological stress from isolation and communications are more marked on the FBM patrols because they do not communicate back -- they get messages aboard but do not send messages out as in the service ships. Overall, I'd say the people do not get a high degree of any identifiable stress. I think those have been eliminated as we have engineered and worked with the submarines over the years. I think perhaps one of the biggest effects of this study isn't to find problems. I really think that's going to be one of the most valuable aspects of this study.

OSTFELD: The problem of what hypotheses you could test are all bound up with the nature of the sample, and with the size of it. It seems to me that there really six problems all intertwined and I just want

to mention this because we're going to have to talk about them one at a time or else we'll really get disorganized. I think sample selection is the first problem.

The problem of finding out how your participants and non-participants differ to what extent you will be able to characterize that, I think will come out in your discussion later. Then we have the problem of cycle duration which for 1,000 men has been 30 years and if you are considering a sample of 2,000 men, the problem of cycle duration is complicated and is tied up with the adequacy of funding and the problem of changing staff. Then there are the problems of follow up, both navy and civilian, and of hypotheses. The Navy believes it has two obligations -- the first one is to monitor as precisely as possible the health of people under these circumstances. I think that the Navy is a better judge of what it wants to do in these regards than any civilian consultant can be. I think if the Navy were to establish specific goals and areas of monitoring we might be helpful in suggesting certain ways that might be more useful than other ways.

In terms of hypotheses, they're obviously related to what you want to do -- if you are interested in looking at the precursors or risk factors, for major chronic diseases, 1,000 men will be adequate in some respects. Other hypotheses I think that could be stated are -- first of all, the high concentration of carbon monoxide in submarine atmosphere - might be associated with a higher than expected incidence of cardiac arrhythmias and, therefore, with a higher than anticipated incidence of sudden demise (because it's believed that cigarette smoking has its effect in coronary heart disease primarily by increasing blood CO and therefore leading to cardiac arrhythmias, which in turn lead to sudden death). Will inhalation in submarine atmosphere be associated with either an

increase in respiratory tract carcinoma, chronic bronchitis, or emphysema? Because these men have reduced physical activity and because they have the kind of diet that Dr. Gell has described, it would certainly be a reasonable hypothesis to assume that they are going to be somewhat more obese than usual and that, therefore, they will have a higher than expected prevalence rate and subsequently incidence rate of elevated blood pressures and more higher than expected prevalence of carbohydrate intolerance. (I think the fundus photographs are going to be very useful as an entirely new assessment of the natural history of small blood vessel disease in diving and in hypertension and with the kind of environmental atmosphere in which they are present.) I don't believe that triglyceride measurements which are being contemplated ought to be continued because you really need a 12 - 14 hour fast in order to make much out of your triglycerides. I do believe that the skinfold thickness measurements are going to be useful as they correlate with subsequent coronary heart disease, diabetes, elevated blood pressure and very possibly stroke.

Then, of course, it would be interesting to know what the water supply of the submarines is, what the water supply is in terms of hardness, calcium, zinc concentrations because that might be related to cardiovascular disease. The inclusion of the MMPI is very useful here because it has been used to some extent by us and others in a prospective way. Behavior scales might be correlated with accident rates because these are measures of impulsive behavior. The blood chemical studies might be very useful in monitoring the health of these men in looking for subsequent incidence of cardiovascular disease. Rosen, who invented

the audiometer, has shown that high frequency hearing loss is a predictor of cerebral vascular disease. Hemoglobins and hematocrits might be looked at as predictors for stroke or coronary heart disease.

If it were feasible, I think there would be a remarkable opportunity to look at the correlates and determinants of aging. There is an article by Comfort in Lancet in 1969 in which he lists measurements which have a very high correlation with chronological age and interestingly enough, 12 of these 16 correlates have already been incorporated into this study. I think an aging study will remain a tantalizing possibility but we'll need more information to know whether it is feasible or not.

ENTERLINE: As I listen to this, I can see some dichotomies here of the hypotheses-testing side - the dichotomy is that you can generate a hypothesis empirically. If you don't have any fixed idea of what you're going to find, you just look and you observe that submariners are different in some respects in terms of illness from other people in the Navy. That's one way of generating a hypothesis. It's just looking at data and maybe not understanding it, but observing that something is high and something is low. The other way of generating hypotheses we've talked more about is from a theoretical standpoint, -- if you know a man is exposed to CO₂ or CO, you can theoretically decide what you ought to look for.

Some of us are interested in occupational epidemiology. The dimensions of the study bother me a bit because as I understand it, we're talking about a 20-year study of 2,000 men.

HARVEY: Actually there has never been a definitive decision as to when we'd be closed and the number 2,000 came out of our discussion with Dr. Ostfeld on his last visit here.

OSTFELD: I think that obviously the sample size is going to be determined by a number of things and what questions you want to ask of the cohort -- if the major concern or the sole concern is protecting the health of the men and obtaining data to protect the Navy against serious claims causing illness, then it seems to me a sample could very well be somewhere what it is now. If you're interested in looking at the natural history of conditions about which we don't know very much and if you're interested in looking at this kind of environment and the characteristics of the man - his precursors or predictors -- illnesses in the 40's -- then it seems to me that you're going to need a couple of thousand. If the Navy were really to say that money is very short and therefore we want to support only the things which are more immediate and of practical need to the men and to the Navy in terms of this exposure, then I think 1,000 is what you want. If think if you're interested in longer term problems, 2,000 would be the least you'd need.

BORNMANN: Mr. Chairman, I would hope that this meeting today would help solve this problem and make recommendations. For planning purposes, if we knew the size of the sample then we could make funding estimates and if then your committee could make the recommendation about what would be gained from study sizes of certain limits and how much more would be gained by larger groups and how much less would be gained by a smaller group, then we could make an estimate for the future. I think the important thing is that if we're going to have a 20-year study, we agree from the beginning how big it will be and not shave it halfway through.

ENTERLINE: I would think for your submarine population (the mean age of 26 what with 20 years they'll be 46), there are a lot of diseases I would be interested in that they may not have shown up by then. I would maybe wait 30 years so that some of the things you can think of hypotheses would be expected to develop.

MITCHELL: You don't want to get halfway downstream and all of a sudden find you've got to shave your population and I can just foresee that if you come up with too large a group, that's exactly what's going to happen. It has happened to us. So I think that you've got to more realistically decide what this population size is going to be now.

ENTERLINE: One answer is, how large a sample can you afford.

OSTFELD: Samples are never big enough.

ENTERLINE: Would it be reasonable to think of this -- is it reasonable to suppose you could do a 20-year study for 2,000 men? Can we think of hypotheses that might be tested with that kind of a study?

BORNMANN: If you want to have 2,000 men, then the first thing to ask is do you need to examine them every year or could you examine them every 3 years, if you're just concerned with costs than what is the payoff in terms of experimental data. The other aspect is, can you make a determination about the size of the sample without looking at the size of the group? There are 25,000 submariners, approximately - and it seems to me that you should break it down into attack, missile, shore, and staff. Would that make a difference in the sample? The next thing is

that I would like some time during the day for the Committee to comment on the fact that all these people are voluntary -- is that desirable? Is it necessary? Is it working against the purpose of the study? The last thing I would like to bring in once more is the fact that an annual physical is required by BuMed of all submariners -- would a proper way to proceed be to go not to the research side but to executive's side in the BuMed and then tell them they need to prop up the "executive rules" (because the research side of it isn't doing physicals -- it's making certain that the physical brings out certain measurements, stores them and analyzes them)!

ENTERLINE: On this matter of sample size -- the way I think you should do it ideally is classify the population into risk groups based on everything you know. Some of these may be relatively small groups; in such case you would need to examine the entire group -- some might be large groups in which case you could do a subsample. If you want to make comparisons across risk groups, you should have about the same number (for efficiency) in each of the risk groups in the examination program. That's the ideal way to do it. The frequency of exams might vary with the hypotheses -- some groups you might want to examine every year, some every three years, depending on what you're looking for. One could easily think of an ideal study and put that up against reality and see if you could execute a study like that. If you say the sample size obviously has something to do with what you are trying to learn and if you're trying to find something that occurs very infrequently you're going to need a big sample to find that.

HARVEY: I'll toss out one very realistic barrier we face now. It took us three years to generate 1,000 people, regardless of what the factors were that did it and if we go through another 1,000 people, that's a full time evolution. If we start recalling people at the same time it's quite physically impossible for us to handle that workload.

DISCHER: I'd like to comment on what was just said by Dr. Enterline because that does get to the hard fact of how much can be accomplished here today. It seems to me that unless you can put before us the information as to how the 25,000 would break down into risk groups, I don't think that an answer to your question is possible at the moment. I take an entirely different approach to the design and study than Dr. Ostfeld. I would look at what the risk groups are and also look to the existing studies for contrasting incidence predictions, find out if we could piggy-back on rates occurring among groups with either similar exposures, different combinations of exposures, or perhaps no exposures, and therefore a lot more information would have to be presented to us than we have received so far.

GUNDERSON: I would like to make a few comments about the relative risk of illness in the submarine population compared with the surface navy. I think there's no doubt that the submarine population has a very low risk and is a very healthy group perhaps one of the healthiest groups in the world short of astronauts or some other very highly selected group. We have compiled very good data with respect to psychiatric illness aboard surface ships and submarines for several years in fact throughout the Vietnam war in July 1965 through December 1971 and the relative incidence rates of polaris submarines with relation to the surface navy is something on the order of 1 to 3 or

even greater in relation to certain types of surface ships, for example, destroyers. In other words, the psychiatric incidence rates aboard polaris submarines are 344 per 100,000 in comparison, for example, with 1,323 aboard aircraft carriers, and 1,115 aboard destroyers -- so there's an enormous difference. This is per hundred thousand per year. This is an enormous difference and I think reflects largely the selective factors.

ENTERLINE: You interpret that as selection.

GUNDERSON: I interpret that as a combination of selection and also the excellent medical care, perhaps greater preventive medicine aboard submarine than surface ships and perhaps safer environments in submarines than surface ships. Furthermore, I think it's partly a reflection of the differential experience in training submarine personnel as opposed to surface ships. There is a large difference in the general morbidity rate between inexperienced young men of say age 19 or 20 vs. experienced sailors age 21 through 25.

With respect to just general minor illnesses, we have compiled some data comparing polaris subs **again** with destroyers, destroyer escorts, frigates, which tends to show that the rate of illness which results in some type of loss of the duty time is about 50% greater on surface ships than polaris submarines. So I think there is a tentative conclusion here that I have reached that the polaris submarine environment is very healthy. Furthermore, we have gone into quite a bit of analysis of the environmental factors aboard surface ships that seem to be related to these general incidence rates. We do find very large

variations depending on the particular job and particular environment under which the man works aboard the surface ships. For example, comparing men who work in navigation-communication type tasks where the communication work group works in an air-conditioned environment relatively quiet (quieter than some other environments aboard ship, and generally having quite good habitability conditions as opposed to the engineering division) to the men who work in the boiler rooms, there is a differential there of almost 2 to 1 in just general illness rates. These are mostly minor infections, bruises, injury, but overall, the men in the engine room have about twice the rate of dispensary visits compared to some of the other white collar or technical groups of more of the same ships. I think aboard the submarines there is less differentiation in respect to the specific environmental stresses that exist. I think with respect to noise, it's a very great factor aboard surface ships, particularly aboard aircraft carriers. A noise level is such that it is over 85 - 90 decibels and hearing loss is a serious problem and also other psychological and physiological responses to this noise level so, there are within the surface ships large differences in environmental stresses that affect the illness factor. Aboard submarines I have virtually no knowledge of the specific types of work and differences in environmental stresses that might exist and I presume they are less diverse and probably have less effect on health also.

GELL:

The submarine is a closed environment and what affects one affects all to a certain degree. There are cul-de-sacs here and there where a person may get electromagnetic radiation and another probably radiologic, I don't know. In general, the atmosphere in

the environment is pretty cosmopolitan as far as the people are concerned.

GUNDERSON: Just one final comment. Our laboratory in San Diego is primarily concerned with surface ships and health problems aboard surface ships. We have undertaken studies using the same types of tapes that are mentioned earlier by Dr. Hester attempting to establish the general incidence rates for disease and injury throughout the Navy. Analysis can be done by type of ship, by specific job in the Navy, by age groups, etc, so that we should have the rates for more serious types of illness (these records are only for hospitalizations). So, we do have a general epidemiological data with respect to health problems in the Navy including submarines. Now our intention is to analyze these with respect to the relative incidences of these diseases and we have selected certain types of diseases which we feel are perhaps more prevalent in relation to certain types of environmental and organizational stresses, but we have the capacity to look for any disease or type of injury.

ENTERLINE: But you haven't looked at the submariners separately. You can look at them separately as you look at the navy-wide experience?

GUNDERSON: That's right. We do have the capability I think to have a parallel type of study that we can follow up. We can see what types of hospitalizations occur and what types of diseases. We also have the death data. We also have data with respect to medical board and physical evaluation board actions.

ENTERLINE: Well, we've almost burned up an hour on hypotheses. For every given objective there seems to be different sets of worthwhile

hypotheses. For example, you're interested or concerned about legal action against the Navy at some time in the future. One kind of thing that is very popular nowadays, is that you are responsible for increasing the risk of cancer. The problem here is that the latent period for most of these cancers might be 20 - 30 years. Looking downstream, this is the kind of legal action that might be taken against you. Is there anything that might be likely to get into the literature in the next 20 years that would trace it back to the Navy and lead to some kind of a court suit? This is certainly a big problem in industry. I just sat yesterday at a meeting on fiber glass particles and saw the number of court suits that came to light as a result of a little article in the New York Times - remarkable. All these fiber glass companies that are now being charged with causing cancer because there were three lines in the New York Times about microfibers in cancer. The point simply being that if you look at the Navy as an industry and as an object of court battles and suits fully in the future, some of the ways industry can protect itself and the Navy could protect itself is by having long-term studies to see whether or not you are responsible or in any way involved with the creation of diseases like cancer. That just suggest a package of hypotheses. Dave Discher and I would start with the environment and try to classify people by the environmental exposures and move ahead from that.

OSTFELD: That would make sense to me too if it's feasible. The only other point I want to make here is that I think the duration of this study is as important as the size of the cohort we're testing. I think it would be better to follow a smaller group for 30 years than it would be to follow a big group for 20. I think 30 years is going to be worth 5 times as much as 20 years.

HARVEY: I would like to raise one point here which I think is fairly important. One of the advantages of the 1,000 aviator study is that when they started I think they took mainly students who were roughly the same age and, therefore, they had similar grouping. We have chosen a cross selection of these in active duty. Therefore, as we go downstream, we're going to lose a large percentage of the people we have in the study due to the aging process, death and what have you. Somewhere along the route I should like some thoughts from you as to whether we should continue to select from that population, or whether we ought to start concentrating perhaps on people in submarine school.

MITCHELL: There was no selection per se in the 1,000 aviator group. They just took an entire class. It wasn't a voluntary thing at all.

GUNDERSON: Returning to your original question, Dr. Enterline, about the - whether it would be possible to find out what the characteristics are of this population in relation to the total submarine population. It should and can be done I think. In addition to having from San Diego medical history tapes on every sailor since 1965, we also are compiling BuPers personnel tapes on all sailors in the Navy who have been in the Navy since 1965. Our intention is to look at the total Navy and the characteristics of the total Navy and then select a particular sub-group which we might want to follow longitudinally and look at the similarities and differences in that particular sub-group with respect to the total Navy. I think that can be done with relation to the submarine sample selected here.

ENTERLINE: I'd like to make a contrast between what I call the paper studies and the hands-on studies. The feeling I get is that the principal thing

to be gained with the longitudinal study is to do something that you never will get out of a retrospective cohort analysis. I want to be on the record with respect to the fact that I think the Hester studies are very important; that those problems be solved. Coming back to this particular question, which is what is unique about the hands-on approach, it would seem to me that the unique thing actually is the possibility of not doing from the onset one study of a group of people for 30 years, but the possibility of doing 10 or 15 studies as you go along on particular risk groups that do identify with these specific environmental problems which you have and are in fact exactly what you say - subacute early detection kinds of studies. It may very well be that if you standardize your procedures you can someday end up with some kind of an aggregate of 10 studies which would be comparable to the studies at Pensacola. I have a feeling that if you do ^a good paper study you don't need to do a Pensacola study. If you do a good series of longitudinal studies you get more bang for your dollar.

DISCHER: What do you mean a series of longitudinal health studies?

ENTERLINE: Allright, let me say this week's problem is - we're worrying about CO₂. Well let's look for the best groups to study. Maybe it's before and after a particular patrol where you can document exposures and get a group of people who repeatedly go in to high risk areas; with good control groups also of a similar selected population of submariners who go into submarines where predictably they do not get these high CO₂ exposures. Go ahead and follow them for a period of several years, much more intensively than every third year, but in fact, as you accumulate, keep those in your longitudinal study group of every three years besides. You're doing short-term epidemiology and at

the same time you're investing in those people who have had something important to study. These are called ad-hoc studies.

GELL: Perhaps this is a good methodology to separate it out piece-by-piece and bone-by-bone but you end up in the area of MIXED stressor mechanisms where one stressor augments the other stressor and unless you study the whole panorama why you don't get the real picture.

ENTERLINE: I wonder if we should take a break.

ENTERLINE: Shall we start with population selection?

KNIGHT: The current methods for selecting subjects for the Longitudinal Health Study are not randomized. Any submarine officer or enlisted man is allowed into the study. A medical department representative of the submariners homeported in New London schedules the subjects for the multiphasic examination. There are problems in obtaining an ideal study population. 1. There are subpopulations of submariners incorporated within the study. 2. The subjects experience variable geographic locations. 3. There is no control group. 4. We are unable to analyze and quantitate the reasons for receiving a population of subjects who volunteer for the study vs. the population of workers who do not participate in the study. Needless to say, it is hoped that an outcome of this session will be that of receiving guidelines on selection of a study population.

ENTERLINE: Can I ask what is the appeal made to the people to get into this study?

HARVEY: Word of mouth is very important. For the first 7 or 8 hundred people that went through the study we had each man that went through

fill out at the end of the day a questionnaire as to what he thought of the study, why he came, what he thought of it; in retrospect, what he thought was best and what he thought was worst about what he'd gone through. We used that to polish our own techniques. So we have gradually improved most of our techniques that will increase their enthusiasm.

Chief McCance works in Sub Group 2. He now solicits the boat corpsmen. By a process which varies from boat to boat he goes to the XO or he goes to the Captain and says "Hey, can I solicit volunteers". The corpsman may go around to the guys and ask them individually. They pop up with quite a few bodies somehow from this system, that then are given by name to Chief McCance, who sends them to us.

HARVEY: We could have gotten a lot more. The problem is not getting people but the problem is our ability to keep up with the workload we do have.

ENTERLINE: Dr. Gell mentioned the fact that there are annual physicals and I think you talked about the annual physical program and whether that could be somehow incorporated or augmented in any way used. I could think of a couple of ways: (1) you could learn about the health of the people who don't respond. One thing to try to find out is are your 1,000 different than the 7,000? If there is an annual physical exam record some place, you might be able to make that comparison between 1,000 and 7,000.

McARDLE: I'm strictly an analyst but there are strict rules when you go to an over-all population to select a sample from and unless these rules are followed, it may not be significant. So, to me you have to start with the over-all population that you have and what would be an

adequate sample from an analyst's point of view. Then, it appears to me that we're talking about different cells in that population. I think risks like disease, age, and certainly an occupation cell. I question having it just at one location with one population on a voluntary basis. I go for something of a random sample by social security number which seems to be about the most acceptable, and then I'd put it in the terms where a person would be in the program and would comply with the follow up. That in general is what I would think would be the approach to selecting an adequate sample. Without that I don't see how you can put much validity on what you find.

After I'd done all that, I'd worry about money. Because if there isn't money, enough money to support the minimum of sample, then you come up 10 - 20 years from now with this study that somebody says "the sample was insignificant".

OSTFELD:

I think that CDR McArdle put his finger on the most important and I think the most difficult problem here. I think that the crucial issue at this point is this - - that in the last analysis what Dr. Harvey said is the way the sample is selected depends on an enterprising corpsman going down to the dock and lining people up and there is unquestionably all kinds of biases. Now the central question is "are you at this point going to say that the means of acquiring men is so erratic and probably biased that you don't have anything?" Therefore, one alternative is to kill it. Now, if you don't want to kill it, are you at this point going to try to get the kind of sample that CDR McArdle talked about. Are you at this point going to try to identify the entire submarine group, stratify and then select a representative

sample with different sampling fractions in each stratum? Or, your third alternative is to say that "we put in an enormous amount of time and money and gotten a great deal of data on these people." You've got an investment that's roughly half a million dollars at this point. Now, your other alternative is to say the group that you've got has all these problems. Can we at least systematically find out whether or not the group we've picked differs from some kind of sampling. Are there differences in obvious demographic characteristics? Are there differences in age, marital status, even education? If it turns out that in fact they don't differ in mean and distribution of age, skin color, marital status, health at initial examination, etc, then I think you have clear evidence that at least the problems that you've looked at are not problems or are in fact problems. It seems to me that the latter approach probably is going to be the most productive. It would be hard for me to see that there would be huge differences between the volunteers and the non-volunteers although I'm prepared to think there might be.

HARVEY: These people were collected over a period of 3 years roughly I'd say. The composition of the crews who did not volunteer has now changed and switched. There is no way we can look back and see who was there at that time and what their characteristics were.

McARDLE: I'm looking at the over-all population of the submarine force which should be fairly consistent and those are the cells that I'm picking up on your point. I would look now at the over-all composition, look at the cells I wanted to identify, look at the sample, the voluntary sample I already have to fill the cells, to see which cells needed filling and then use the random sample to fill those cells. The thing that I

worry about in the bias more than anything else is the geographic location of all the people here and using that as a sample to project against the whole submarine force. I imagine most of the people who come here are New Englanders. They are victims of their previous environment and there are a lot of things that are going to make it questionable.

ENTERLINE: Dr. Harvey raises a very formidable problem here and that is reconstruction of the population that produced these 1,000 men. I suppose the best you can do is see that they are not all cooks or something like that. There is a sampling method called quota sampling, in which you really set about to get some number of people from each occupation or each job class, from each age, etc, and all you do is force the sample to have the same characteristics as the parent population in terms of some 3-or 4-way cross tabulation. Quite surprisingly, that's not a bad sampling method; in fact, about 90% of all the sampling done in the United States is quota sampling, not random sampling.

The problem with random selection is you can go ahead and designate them but then you have the non-respondent problem so you really don't have even a random sample, because the people all don't cooperate.

DISCHER: When you look at what you've gotten out of the quota sample oftentimes it is apparent that you've got some groups that don't qualify. Then it seems logical and is often done to go out to supplement your study group with those missing cells. I subscribe to that as being appropro to what we're talking about here today.

HARVEY: It would be feasible at this point not to change our selection technique but to go back to the boats, pull their medical records

and possibly their personnel records if we were willing to put the manpower to work on it and compare certain commalities between the groups that way. It would take a lot of manpower.

McARDLE: I would not go back to the boats for their personnel records. I'd form the questions I wanted to ask and that's I guess why I'm here, and go to the Bureau of Personnel and say "here's what we want about people" and they'll go down a decision tree and fill in your cells as to what's the average age of the submarine force, how many over 40, over 30, over 20. I'm sure if I get a list of the questions I can sit down with those people and get anything or more than you'll get out of the personnel records on the ships.

DISCHER: You could pull a sample. You'd have a population of this for each cell and you could give the size of the cell. The manpower issue could be addressed in an intelligent way rather than just spraying into the whole group.

ENTERLINE: Well, we seem to be in some kind of agreement that maybe we shouldn't throw away what we've got. It's a lot of money invested and that the thing to do is see if it's non representative in any way, and to see if there's some way it can be supplemented to make it more representative.

HARVEY: I would like to again address the question -- Should we think about concentrating on people in the submarine school who have not entered the at-risk population?

ENTERLINE: My reaction to that is that if you're going to start people when they enter the service you're going to have to get a longer study. For one thing, you won't have any retrospective history of exposure and so forth. I think obviously it's a better way because you have better control of the

men and the records and you can get the kind of information you want, rather than have to use things that may not have been desirable for the study in the first place. I think there's a trade-off there. I think the trade-off is partly economic. If you take the man coming on duty, you've got to wait 30 - 40 years to see what happens to him.

DISCHER: It seems to me that if the investment that you have already put in is going to be realized, it is important to deal with the question of non-respondent at the time that you were sampling the population. Maybe it isn't easy to get information locally but the personnel information existed three years ago and that's the information we're really talking about. It's coincident with the time in which you were laying on your hands. Force yourself into this business of looking at biases at that point in time rather than, as you were describing before, a current question and it has to be forced just that way.

ENTERLINE: Dr. Gell mentioned the fact that there were roughly 5 longitudinal studies.

BORNMANN: As far as I know there were 5 unless Dr. Gunderson has more.

GUNDERSON: The types of data we are looking at are identical with the tapes of Dr. Hester but it's the same data 1969 - 1971, except that our data extends over several more years -- several years before and several years after. We'll continue to accumulate this same type of data for years into the future. This pertains to the entire enlisted and officer population in the Navy and it includes all hospitalizations -- for any reason. It includes all medical board actions; it includes all physical evaluation board actions. We have a complete follow-up from the Bureau of Medicine and Surgery for the entire Navy. Dr. Hester has a portion for submarines. These records are being set up for detailed analysis of the entire population of the Navy with respect to incidence rates by

various sub-groups, age, pay-grade levels, job type, duty station, and certain little population characteristics -- sex, officer, enlisted, etc. We will then follow these populations to determine recurrences, the dispositions from the hospital and from the Navy and the mortality rates for these conditions.

We are constructing some service history records from the Bureau of Naval Personnel. Then we will hopefully attach the medical history to the service history for every sailor who's been in the Navy since July 1965. This file will permit us to do a variety of studies obviously of not so much the detailed environmental stresses and organizational stresses because we won't always know what the specific conditions were under which people were working etc., rather just general incidence rates for gross sampling things out of the Navy population.

ENTERLINE: Now the Hester study is a sub-component to your study ?

GUNDERSON: That is correct. I have not talked to Dr. Hester and I am very anxious to do so to see the overlap and common elements of our interests.

BORNMANN: I would like to know more of what goes into your study. Do you also include admission to the sick list?

GUNDERSON: The cards that are prepared at the time of discharge from the hospital are forwarded from regional centers to the central data processing center in Bethesda. In addition, there is another card prepared if the man is seen by a medical board.

ENTERLINE: I would like to go with some of the things I would like to find out whether you're omitting -- what about visits to a medical officer in a dispensary - not in there?

GUNDERSON: Not in there.

ENTERLINE: What about out-patient visits in a hospital?

GUNDERSON: There is only an individual record kept.

ENTERLINE: If you're hospitalized under Champus does that come into this thing?

McARDLE: That wouldn't apply to the uniform force.

GUNDERSON: There are records kept on dependents who are hospitalized.

ENTERLINE: I am really driving at the point that Dave Discher made. How are you going to follow men when they leave the service and if they leave selectively, what's that going to do to the kind of observations you can make. You don't plan to follow them as they leave the service, or do you?

GUNDERSON: If a man is injured or has a serious illness, which is judged to be service connected, that is, related to his service in the Navy, he may be eligible for compensation. Now, these individuals go into the Veterans Administration system. We have done one follow-up study, a 5-year follow-up study of psychiatric patients, mainly relying on the Veterans Administration records on these patients. There will be a re-evaluation of that individual every 18 months by a compensation board but prior to the end of 5 years by law there must be a determination of the permanent degree of disability of that individual, so there is a built-in system of follow-up which is quite accessible, and it is a very good one. We have plans to utilize that system for follow-up with respect to our population. Now, individuals who are separated from the Navy without compensation or perhaps with a lump sum compensation we have not attempted and will not attempt to follow up. It's too difficult.

ENTERLINE: Of course, most of these men would have an insurance policy when they leave and you could follow them up.

GUNDERSON: That's correct. My understanding is that over 90% of deaths of service personnel can be very easily traced -- because of insurance.

BORNMANN: On the military's term-life insurance it has to be converted when you leave the Navy -- is that correct? What is the rate of conversion? Do you have any guess?

GUNDERSON: 90%.

GELL: I doubt that very much. A lot of these kids are getting out, you know, and then when they turn in their policy why they get a little cash, and that looks a lot better to them than 40-year retirement -- I don't think it would even be 50%.

DISCHER: I'd like again to distinguish between studies where the intention is to be examining everybody -- using standardized methods vs paper studies. What we've just heard from Dr. Gunderson, and about Dr. Hester's study, I would distinguish those as 2 retrospective cohort studies. I do think they should be distinguished from the standpoint of the thrust of what we're doing as largely as you indicated before as hypotheses generators for the longitudinal study here rather than the same kind of longitudinal study as we're talking about.

ENTERLINE: One statistic would help me -- would be some estimate of how many of these thousand men you would expect to be in the Navy 5 years from now, 10 years from now, 15, 20 to get some idea as to what the losses would be.

McARDLE: If you start with a recruit it would be roughly 25 to 30% would be in the Navy. If you start with the new man first turn going through submarine school, twenty-five to thirty percent of them stay through the second tour, after the next six years, it's about 80 to 90% say, and after that I'd say 100% stay for the 20.

KNIGHT: The switchover from selection of 3 or more years experience to open policy occurred when the arrangement was made with group 2, and Chief McCance started to select our population. Prior to that, Dr. Tansey adhered to the policy of selecting people with probability of retention.

HARVEY: That means we have probably 500 or 600 of our people who were selected based on that. We do have a high retention rate in submariners.

BORNMANN: What -- 50% of the first enlistment?

HARVEY: I guess it's in that range.

GUNDERSON: Would the re-enlistment examination itself be a point in which one could screen perhaps and determine whether this subject is suitable or not for follow up.

HARVEY: I would say it would be

Afternoon Session

HARVEY: There are some questions people wanted to address to Dr. Hester.

OSTFELD: I might ask Dr. Hester if he has any hypotheses that he has been able to generate from data on the submariners. In other words, do they appear to be unusual in any way?

HESTER: Unusually healthy I would say. There's one question I mentioned to Dr. Gunderson that's bound to come up. It is, "does exposure to the submarine environment tend to produce malignant neoplasms?" This is a question I had in mind when I set the study up.*

*My work is a retrospective study of submarine personnel health based upon existing records and documents. Attention thus far has been limited to the two large relevant data systems on magnetic tape: the BuPers Master File tapes and the BuMed Inpatient Data System.

The question considered is this: "Do existing data suggest that prolonged exposure to the nuclear submarine has an adverse effect upon crew health?" My aim has been to obtain essential tape files and to try to put the material together in a way that will give an answer.

Do I have any evidence? No.

I really have not tried to look at anything specific. I tried to develop the whole system as a unit to try to build the machinery to put the information together. I have a group of about 50,000 people with submarine and diving experience.

ENTERLINE: Your idea is to make a comparison with the rest of the Navy?

HESTER: No, the idea was a simple matter that the submariners were a legitimate interest of this Laboratory and so were divers. We asked for that material from BuPers. The submarine force at a given point is a very definite organization and you can attach meaning to it, but when you ask what happens to people on board submarines, you get a different picture. You draw a distribution something like this *. This is months of SSN/SSBN duty. It's fairly comprehensive, and months of the conventional submarine duty here, when you look at that you see that it's quite an adequate distribution within the table itself. The problem was how do you accumulate enough experience to establish meaningful rates and what I'm trying to do is put incidence here and man-years at risk for the period of the medical data available

*The distribution we wish to make is between (a) a population at risk defined as personnel assigned to submarine duty and (b) a population defined in terms of cumulative submarine exposure. It is not assumed that morbidity experiences in populations defined the two ways are necessarily of the two populations. (a) is easier to identify since it corresponds roughly to the submarine personnel force at some point in time.

A risk base defined in terms of cumulative exposure, however, appears essential for present purposes. This permits a distribution something like the following:

Months SSBN/SSN Duty

	None	1 - 24	25 - 48	48 +	Total
	M1 / R1	M2 / R2			
1 - 24					
25 - 48					
48 +					
Total					

here and establish the hospitalization rate. It's just man-days in the hospital per man-year at risk type of function. Now, obviously, you can ask the question "How does this jibe with the rest of the Navy's experience"? It has to make sense somehow but there is no specific effort to bring in a separate population. I thought there might be until I looked at distributions and that it just didn't seem to be necessary because you have such wide range of actual exposure conditions within the group that I have studied.

ENTERLINE: So you have internal control. You're saying the numbers are really big enough in themselves.

HESTER: I think so. Within the scope of the amount of information I have, it really provides for reasonable internal control.

DISCHER: Dr. Hester, I wonder if there's a difference in the selectivity between people in the three cells that you're talking about.

HESTER: I'm sure there may be but then there is selectivity of people coming into the submarines in the first place.

ENTERLINE: I was going to suggest that if you drew upon some rather conventional techniques, and there are a few in the field of occupational health, one way that you might look at the submariners is to get an expected incidence of hospitalization based on the whole population that Dr. Gunderson is working with, and then calculate relative risks in all those cells.

HESTER: That is reasonable. As a matter of fact, I've used this risk technique with working once upon a time at the V. A. The thing is, I published a little paper here some four years ago. I estimated risk from the latest published 1964 data which the Navy published. I used exactly that technique; it was all I could do. So I am familiar with that technique. It was a person/years technique. What you're trying to do is to be reasonably sure that the submarine is not injuring people.

ENTERLINE: Have you any evidence that the submariners are selected on health factors?

HESTER: This is not an unselected population by any means. It has never been, as far as I know. There's any interesting phenomenon in relation to epidemiology in submarines. One time the Navy medical statistics did publish an incidence of illness by types of service and the submarines were characteristically and without exceptions very very low on any form of illness. We know that the submarines when going on patrol do leave people out that are ill. So, just taking the people that are attached to submarines at the moment, may or may not be relevant. In the data that I do have there is certainly a low incidence for submariners of over-all diseases than you got from the early medical statistics. I mean, they may be lower than average but not all that much, they are just like other people. I mean the over-all incidence of illness is pretty much characteristic with all the population. *

Again I come back to the point that unless you can find evidence of increased morbidity or increased morbidity in the submarines then in a sense our job is done.

ENTERLINE: There is a very interesting observation. The whole idea is that life force is at a low ebb in February and is very high in October and if you look at mortality statistics they fluctuate up and down - high in February - low in October. If you go to So Africa the thing flip-flops - it reverses - obviously the season reverses. The question really is in any event if something is as controlled as the submarine environment if you get this up and down sort of thing in illnesses -- as you do in the general population --

* For personnel attached to nuclear submarines during 1956-59, representing a risk base of about 52K years. The total incidence of reported disease and injury was about 4K. For the population now under study, the 04 files have been searched for the 18-month period 1 July 1968-Dec 1969, for which the risk base is less than 84K man-years and the total incidence of disease and injury is about 12K. Note that the two different definitions of risk-base appear to give a morbidity incidence rate contrast of almost 1:2.

BORNMANN: In the submarine at sea there is one season which does not change.

DISCHER: You wouldn't expect a submariner to be hospitalized when he's at sea because there is another psychological stress -- the stress of getting the job done and getting back which would tend to downgrade the thing which then might come pouring out when he gets back home and has the availability and the time to relax a little bit and then go in and see the Doctor.

HESTER: I'm going to back away from saying that could be easily done because the reports that I have published -- they don't have the cycle in them.

ENTERLINE: Of course your non-effective ratio follows the cycle very nicely.

HESTER: But this over-all thing one can easily do and I will have that information.

ENTERLINE: It's not a very important point. Someone in human biology would be interested in publishing something like that.

GELL: You definitely have a diurnal variation that's interesting that you also would have any yearly variation. I was just wondering are there any rhythms in between that?

Well the one thing you can always spot - the flu epidemics. I studied in 1967/^{the} world-wide flu epidemic. The interesting thing about that was that it took place almost simultaneously just BANG all over the world -- you wonder how in the world it managed to do that.

HARVEY: I would point out one other thing. The crews that go out here on the submarines may go to Rota or to Holy Loch and spend 30 days refitting the sub and going ashore and mingling with civilian personnel periodically and being exposed to Lord knows what different

type of epidemiological type things. The point I'm making is the off-crew time has a different experience in different locations.

ENTERLINE: What is the underseas record -- how long do they stay out at sea ?

HARVEY: Well, in a routine patrol the crew will go there for 30 days, refit while they do their preventative maintenances and 60 days at sea and then they turn it over to the other crew and come back here for 90 days.

ENTERLINE: Well, can you randomize those cycles somehow?

HARVEY: No, they're pretty well stabilized on a given boat.

DISCHER: Is there any reason to consider that within the group of attack vs patrol, either or these, there are gross differences in exposure? And, is there any reason to believe that any of the environmental contaminants are different between the two?

HARVEY: As a general rule I would say there is no gross difference in the level of contaminants. The FBM's will often stay buttoned up, if you will, longer than they'll stay down, 60 whole days, and perhaps without changing the atmosphere other than what they artificially created, so that I would say the unbroken exposure tends to be longer than on the more regular cycling basis in the FBM's.

ENTERLINE: Well, wouldn't you observe the men during that period to see if there was a change in blood chemistry and wouldn't you have a chance to see what goes on with the men?

HARVEY: We no longer carry doctors aboard our FBM's on patrol. We have corpsmen ready to treat any emergencies and monitor certain life-support systems. Generally speaking, people are not monitored during the patrols.

ENTERLINE: So you do know that if you're submerged for 90 days whether there's a difference before and after.

HARVEY: I would say we have limited knowledge on that. I'd say there's room for finding out a lot more.

BORNMANN: There is another difference between the FBM polaris submarines and the fast attacks. Your two crews for polaris may go on a periodic schedule, so that they are on 90 days and off 90 days. Some skippers of nuclear attack submarines will go longer periods in intense activity and claims have been made that that's the most stressful, the most fatiguing type of submarine duty, whereas the polaris duty, even though it's longer at a stretch is more relaxed and more easy going.

DISCHER: Of the 500 people that you have had for three or more years, how are they distributed?

HARVEY: I can't give you an honest answer on that. I would have to tell you the big majority are FBM, but I cannot give you a breakdown now. The SSBN is ballistic missile sub with the big nuclear missiles. SSN is the attack submarine. It carries a crew of around 100 opposed to 150 or so that are aboard the SSBN. So it has a smaller number of people and only one crew.

DISCHER: In terms of design it would seem to me that you would want to have a higher sample of the second group, being the SSN. This is the group as I understand it that has part of the stress, the very erratic schedule and as I understood this was an area of concern.

HARVEY: There simply is a difference in their exposure patterns.

ENTERLINE: Someone in the Pentagon a few years ago did a lot of work on serum cholesterol as it fluctuates around the stressful periods.

Can you only measure stress in these terms in these crews?

Do you notice any fluctuation.

HARVEY: Somewhere I have an article on cholesterol and people aboard subs. There is a considerable amount of literature built up here in the Laboratory studying an individual stress parameter -- cholesterol or blood platelets or hemoglobin changes or something else. There are quite a few of the individual studies of this nature which can, if pooled together, give us something of a picture. We have also had certain isolation studies. I don't think anybody has ever really done a time motion stress level 24-hour EKG.

There are several question areas that I was hoping we could get into this afternoon and if it's appropriate I'll go ahead into some. One of the areas that has to come up in a longitudinal health thing of this nature is availability of the sub groups that actually do the examinations. For instance, our Dental Branch is about to be phased out. This means the dental longitudinal health study comes to a screeching halt as of that point in time. If one is going to do a study like this, there must be some way of keeping continuity so that you don't change things as you go down stream. In fact all of us are rather jealous of the program, trying to keep what we've got without losing, so I point out that one must continue to watch this problem. This comes down to the changeover in personnel and their interests and motivation and I just want to point out we recognize this. I don't know anything we can do except try to get people who are interested to keep plugging. Recall techniques are a problem. None of us associated with the study at the moment really think we're adequately set up to locate and recall these people. There has been no actual contact mechanism set up and when they're on active duty we can find them through Bureau of Naval Personnel. We're in the process now of trying to rectify this somewhat by getting to their last known command and trying to find out whatever we can.

HESTER: This is the hard part of using enlisted men and I'm afraid they're going to become anonymous once they leave the service. In theory the V. A. records are available. This is what I would see as my next big project once I get through this, trying to get to them.

HARVEY: Well, this brings up the question in ethics and there are several ethical questions involved in all this. Does the V. A. have the right to release their addresses to us for this particular purpose? How do we get this established. There are other ^{ethical} questions too. What about our information? If a man has a problem, do you let the Navy officially know about it with potential to disqualify him? If the man has an insurance company write to us for records what clearances do we have to insist on to send them out? I think the biggest one I can address is the question of our release of our information. It has been our policy up to this time that if a man had a problem, whether it's a blood sugar elevation or something else, we referred him to the clinical side for further evaluation. Out of this several people have been disqualified as having latent diabetes. This kind of publicity does not help the study in its reputation in any sense of the word.

HESTER: A death certificate is probably record, so if you could get those . .

McARDLE: Could I interrupt and go back to locating the people because theoretically we have a system in BuPers. When a guy is released from active duty, the information goes to the Navy recruit command who has follow-up actions. I'll look into it when I get back and tell you who to contact on that because that's actually the follower and you would have a pretty good percentage of a year or two later of being able to locate people to see if they want to come back in the Navy. So, that shouldn't be ignored!

ENTERLINE: Well I can speak for the V. A. problem. You know there was a large study on in which the Veterans Administration did give names and addresses of all veterans who were carrying insurance at the time the study started. I do a lot of follow-up studies in industrial populations and the V. A. has been very helpful. If I give them a social security number the V. A. will tell me if that person has been hospitalized in their system. I used to have to use the Armed Forces serial number but they now have a cross index at the V. A. and I can go in with one and come out with the other. So, just to say that I found in industrial studies that there are a lot of follow-up mechanisms that are really open. If I send them a list of Social Security Numbers, they'll tell me who has died.

MITCHELL: Is that right? We've been turned down by them.

PURDY: Just recently you know, two laws have been passed concerning privacy of the individual and government records. We're having some trouble now with Social Security as I understand getting some information and we're known for keeping confidences as far as records are concerned.

OSTFELD: It seems to me that the most important issue in follow up is the energy and ingenuity of the people doing it and if you've got good people who really want to do it. So it seems to me if you've really got a person who wants to follow the group you will use all kinds of ingenuity and try all your resources. They will do very well and I think that's the crucial issue to get those people. About the ethical and moral aspects of what we've discussed, NIH is going to come out on April 30th with a statement about how they feel people in human experimentation should be handled, and preparing the details on the ethics of human experimentation, and I suspect that you will have to go along with that pretty much anyway. It's a little difficult not knowing what

they're going to come up with. Whatever they've come up with will probably be standard and you'll have to adhere to that.

HARVEY: I will toss out one thing that has put a bit of pressure on us. One of them is that when we do the longitudinal health physical we usually fill out their annual physical as a correlator to this, simply saving somebody having to do another physical.

DISCHER: I'm going to answer that point you made which had to do with the departure of the dentists. My feeling about what you done so far is a perfectly reasonable baseline and there is probably little need to repeat in your follow-up examinations that much information anyway. It would seem to me that the energy being spent to retrieve annual physical examinations on particularly the individuals who are going to accumulate plenty of person years in various kinds of environments that you're interested in would be the important thing to do. That would imply to me the importance of having the annual examination done as closely similar to what you are doing. As to the ethics I don't think there's any question in my mind that you have to deal with that individual administratively just as you would whether he was in the study or not and that if there's good reason to discharge him and he's a hazard to other people on board or to himself then you're going to have to proceed.

MITCHELL: What are you using for standards for pulmonary functions? I was going to mention that if you have no standards I don't how you can disqualify.

HARVEY: Let me lead into one other very related area here at this point. When you're doing a study like this and spend a lot of money and time and effort, who wants it, --- who are we giving it to that's going to make some use of it? A question is "what are we going to give to BuPers

that they can use to pick up a better group of people who will not fail out? What are we giving the Bureau of Medicine and Surgery to prevent or cure or work with disease? Who's going to use this information? I think one of the things that has come out of this is that we can indeed and are working with Dr. Baker to suggest changes that perhaps would be worthwhile in the submarine physical. Everybody in the study is open to comments on who you think will use this information and who we ought to be getting for it and what value it has.

MITCHELL: Go back to the 1000 aviator study. We have altered the physical standards for aviation in significant areas and I'm sure the same thing would apply with the submariners' physical exams. I think that's the practical application. That's one of the reasons why we're running into a problem now -- BuMed says -- these people are all beyond the age when they're going to be serving on active duty, therefore, why should we fund the program -- which makes sense, I suppose. I find that a little hard that we can't follow them literally to the end of their days and find out what happens to them because I think there's going to be some practical application to the aging processes.

ENTERLINE: I think the answer to "who wants it", is what we started with this morning. It seems to me that there were two purposes for the study -- one was long range to find out if there are these hazards. I presume if you found some you'd correct them or try to do something about it. The short term, I guess, was that of observing a cohort. It might be sort of like the Framingham study in the sense that you could find some precursors to the disease or pre-clinical conditions.

DISCHER: I guess along with that the important thing to know is whether these early precursors mean anything in terms of job performance, another aspect which may come out of the long-range consequences. If you see progression with these people toward decrements in function or whatever, that's maybe a good indication to change your qualifications.

PURDY: Of course the diving material that you're putting together is going to be very valuable. As far as I know, it's the only comprehensive study in the United States along this line. Burke will be doing something shortly and I think we could probably learn from looking at your study, of the mistakes you've made and/or that you know you've made, and areas where you think you could have done better and so on.

HARVEY: One of the problems in studying these people downstream is the question -- "do we bring the individuals back here, do we need a team that goes to a centralized location where groups of them may be, do we try to set up something that could be handled by another institution with no involvement with our people whatsoever" . There are a lot of techniques open to us -- what are your thoughts on this?

OSTFELD: It seems to me that probably if you have them all come back here your problem would be payment for travel particularly. I think in order to keep the bills down that the most logical thing to do would be to have a group that could do these examinations on the West Coast, a smaller group which would come here and observe what's being done here precisely and then on a very small group of men with a high degree of tolerance for repetition you could have the group that's going to do them on the West Coast and the group that's here make all of those observations on the men. The subjects would be asked to put up with two exams on hearing let's say or vision or two blood pressure measurements and when you get to the point where the group that's

training has let's say 95% agreement on something absent and something present or the group that's here then they're calibrated and they go on to the West Coast. For example, it would seem to me that that would be a lot cheaper than bringing the men back here all the time. You'd lose a little by setting up a satellite which would be calibrated against the group here but I don't think you'd lose a lot.

MITCHELL: This is what we had hoped to do with the 1,000 aviator group. We felt this could be done and I still feel it could be done.

OSTFELD: Well, we've done it. I've even trained high school graduates to do neurological examinations that have 94% agreement on presence or absence of Parkinson's Disease or stroke - - this compared to four certified neurologists.

The worst alternative is simply to rely on information that civilian physicians or civilian hospitals or navy hospitals and physicians all over would give you. Best would be to have them come back here with the same people but I think that what I've just been talking about is pretty good too.

DISCHER: I've dealt with the same thing in the National Health Examination and the practice there is to have with each relocation a reliability check, whether there is a turnover or not -- so the quality control persists continuously (it's not really very expensive. You just build an extra 5% into your budget for this kind of overlapping.). In the quality control, you can easily run into difficulty if you don't set it up on a regular basis.

ENTERLINE: I wonder if the examination that you give while they are on active duty would have to be continued intact or if there aren't some parts that could be dropped, and simplify the follow-up exam. The other

thing that occurs to me is that some of the information on this follow-up exam could be hard copy information such as electrocardiograms that might be read centrally in some standardized way. It just occurs to me, therefore, that there are some things that will be fairly standard whether taken in San Diego or Boston and there were bits of information that you may not want to continue in order to make it logistically possible to carry out.

HARVEY: Yes, you're right. There are things that could be left out. The question is what do you want to sacrifice and what don't you. Arriving at a sensible decision as to what to drop is a bit of a logistics problem in terms of the individual investigators, and every one of them will justify what he's got so this becomes an arbitrary choosing that has to be done.

DISCHER: It seems to me that when cutting back you can cut all the way back to what constitutes the basic essential annual examination anyway and then merely deal with this kind of detail every 5, 10 years. You could even go to that extreme.

OSTFELD: You know, just as an example, in Framingham looking / as a risk factor, the first determination of cholesterol was as good a predictor as subsequent coronary heart diseases -- a meeting of the first 5 cholesterol determinations or even a meeting of the first 10 examinations and I think that kind of thing exists in other areas. I think it might be possible to decide that some of the things would not even be measured every cycle -- which might be 3 or 4 years -- might be perfectly well to do it every second cycle and there might even be some things there would be no point in measuring more than once. I really think that one of the temptations in a study like this is to measure and then not to pay so much attention to the records that are generated in between by hospitals or physicians' offices and I

think the latter is a lot cheaper to get and is every bit as important and the longer you go, the more important the follow-up data becomes and the less important the annual or biennial subsequent examinations become. So I would like to see some real careful attention devoted to what might be omitted in part from subsequent examinations and some of that energy and some of those bucks go into the follow-up process.

BORNMANN: May I ask a question? Is it possible that BuMed now computerizes the information on the Form 88 that is submitted for these annual physicals and if not is there any prospect that they may do that?

MITCHELL: They are not now at least from the aviation standpoint. It is not being computerized. It's being microfilmed now. That's as far as the retrieval system goes.

HARVEY: I want to raise one other question. We have been, up until this time, funded by the Bureau of Medicine and Surgery for this study and there is obviously outside interest in what we've been generating from this study. Is this something that should continue as an all-Navy, Bureau of Medicine and Surgery-funded research activity or is this something that should somehow be expanded to have other interested parties funding and using it?

BORNMANN: Do you have something specific in mind?

HARVEY: Well, that comes down to who wants what we've got.

GELL: Well, as far as who wants what we've got -- the Navy wants what we've got and we're serving the Navy. I think that we'd be in one fix if we weren't getting money from our normal source and that is the Navy.

OSTFELD: I think there would be a pricetag to pay if you got somebody else in to fund it, like NIH.

PURDY: It seems to me that one of the things that could make this study more valuable would be a drive toward uniformity of quality of the information you receive from the Navy in general and perhaps to be able to apply it to this study. Perhaps you could convert some of your expertise by automation as you looked at this. Maybe you can find methods of reading x-rays of the chest. We're working on reading them by computers -- and coming up quite well -- contrary to predictions.

HARVEY: We have done exactly this. We have secured an automated spirometer that even makes you predict curves. We have an automatic blood pressure cuff on order. We're looking into San Diego's efforts to get a computerized EKG analysis system.

DISCHER: In that regard I think it's probably been obvious to you that this is important to keep your own signals, both in written records as well as on tape so that if you want to use another set of refreshing equations for pulmonary function, for example, you can always redo it.

BORNMANN: I think that the Navy as a whole should look at this movement toward mechanization of the examination because it has a lot more application in thousands of physicals. If the whole Navy goes to this type of automation, then it simplifies the problem you raised of "where to do the physical?" You can do it practically anywhere. I would like to ask what is the capital cost of this chest x-ray system that you're talking about.

PURDY: We've got about four hundred thousand in our system right now. That sounds like a lot of money but when you consider the amount hanging on this machinery it's not very much. We spend six hundred thousand dollars a year on reading x-rays -- so four

hundred thousand for a system if it works is really not too much, especially if it makes it uniform. We find that 30% variation, for instance, among board-certified radiologists, so it's worth it to us to nail the thing down if we get a machine to do it and it looks like we're winning this particular battle with the mathematicians and the machinery. You have to pay a scientist or a group of scientists and you have to faithfully use a computer and nobody, even NIH, has backed away from this particular problem as being too difficult. It's solvable.

HARVEY: We have just faced the same problem in our dysbaric osteonecrosis study, in trying to figure ways to analyze the films.

PURDY: I can recommend people who might do the job -- the group at USC and it might pay to contact them. Since we paid for most of the research machinery, you wouldn't have that investment to consider. You would, however, have to supply some funds for the use of the systems and we'd be delighted to have you go in there Think about it.

HARVEY: Sounds like an excellent idea.

BORNMANN: I have another question. Have you decided that a separate control examination is not necessary or is necessary?

ENTERLINE: I don't think we really talked about it very much. I know we discussed Dr. Hester's study in terms of an internal control. I can see the great problem of getting external controls though and that is the selectivity factor.

DISCHER: I can lean toward finding another control group.

ENTERLINE: You mean you're saying you'd actually set up another population to study like the submariner's that are being studied?

DISCHER: I would look within the Navy.

HARVEY: We have our divers who admittedly are exposed to a totally different stress -- simultaneously with the submariners in smaller numbers present.

HESTER: It seems to me the external group is almost unnecessary and it's conceivable that I am wrong. It's entirely conceivable that the new men are going to be much more stable, career oriented toward staying in subs so that you're going to get a pretty uniform experience base from them all in which case you'll sort of be out on a limb.

ENTERLINE: Let's say I have a bias against internal controls from a statistical standpoint; you have to study about four times as many people as you do if you have a large external control group. I sure would look hard for the large external group that's already made. You know what you're really talking about is duplicating this whole study. You're going to double the cost, double the problems. You get the same problem of who's going to come in. Are they going to be selected in the same way. Are they going to have the same kind of incentives to come in to stay in the study and you get into a lot of problems in trying to make the comparisons and then it's all over -- different appeals in different locations -- selected differently in the first place.

OSTFELD: I'd like to take the position that you don't need an external control study. Let's look at two kinds of hypotheses that you want to check out. First, let's say that you have the hypothesis that exposure to a given condition is going to be associated with increased risk of this or that

disorder. It seems to be that within the submarine group you will have a dose response effect as the duration of exposure and intensity of exposure to certain occupation factors of living in a submarine increases, so will the incidence increase. It doesn't seem to me that external controls will be crucial for establishing the fact that the more the exposure increases, the greater the likelihood of a certain illness appearing will increase. Now, secondly, you're looking at the hypothesis that characteristics of men measured at the time that they come into the study are going to influence subsequent morbidity and mortality. All you really need there is to be sure that you have a reasonable range of variations in the characteristics of the men as they come into the study. Now the dose is what the guy brings on his own carcass into the study and an external group may not add a lot to that.

DISCHER: I think the biggest problem is that it doesn't work out to be quite nice. Dose response curves and the reasons for that are multiple but probably the most persuasive thing is -- you can never know what your low exposure group really represents. They may represent a fourfold increase in risk whereas the high exposure group represents a ninefold increase in risk.

OSTFELD: So you cannot get a threshold effect.

MITCHELL: May I go into the matter for just a moment here? With regard to the prisoners-of-war study, we don't have a control group because we haven't gotten the funding for it. What we have done is collect 140 active naval aviators with about 8 or 10 variables on the computers. We need this control group because we're seeing some lung changes. We're seeing some changes that we cannot explain as being necessarily related to personal experience. Now with the 1,000 aviator group

first we have a really very beautifully built in control because half of these individuals, and it's sheer coincidence, approximately half of them, almost exactly half of them left the service at the end of World War II and have been in the non-aviation population. So, we've had these two groups which has had its own internal control.

DISCHER: Glad to hear you say that because you really put your finger right on it; you were lucky.

MITCHELL: That's right.

DISCHER: But when you talk about this kind of money, do you really want to take a chance?

HARVEY: We have had a couple of efforts in that direction of controls. For instance, Dr. Kinney for visual controls has gone to the Coast Guard Academy to get a control group to match the people she studied.

OSTFELD: So, we've heard two good reasons for having external control -- one is when you can't pick up the threshold, and the other one is that there is so little data in man on functions measured longitudinally over years that you don't know what the meaning is of anything that you find unless you've got some sort of control.

MITCHELL: You've got to be very careful that you're not attributing things to one thing when in fact they might well be more or less just normal variations.

ENTERLINE: Could I make a suggestion that combines these two ideas? I calculate for every exposure level, a relative risk -- relative to some standardized population. So I can tell two things simultaneously -- I can tell whether or not it's a standard population. My risk is increasing as dose increases. I also know where I am relative to the standard

population in every risk group, relative risk by exposure level. Dave points out that you don't know where the threshold is. You don't know where you are with your start. So there is a way of combining these two ideas and when you combine them and use the person/years approach that I mentioned you do standardize also for time and age. You do that all simultaneously.

Anything that would have to do with aging for example could be analytically handled with this technique. The problem is to find a standard, but after all you do settle for standards. A lot of these tests you're doing, there are some kinds of standards for them, so that you might roughly standardize this data to get those populations.

DISCHER:

I wanted to comment on the direction of the discussion. It's certainly going to be difficult to pick out any cause in this because as you told us before what you have is multiple possibilities and perhaps it's going to be very difficult for you to even assign high, low and medium to anybody other than just simply years per hours. So, you're going to talk about the submarine environment in person hours rather than in any other terms of an agent. If there is anything you could incorporate in there so you could separate out high, medium and low into another series of cells where you could be saying "allright, this guy's -- maybe he's high in years, but he happens to represent a group that's high in some specific age." I just finished a study where we did this, we had high, medium and low and a control group and it was in the aluminum industry. It turns out that I could plot on the other axis two different processes where in one case they have -- in both cases they have high fluoride -- but in one case they have a carcinogen and in the other case they have very little. That helps a great deal, if you can construct such subgroups. If you don't have it, you don't have it, that's all.

BORNMANN: I just wondered if we could now go back and ask the principal investigator if there is anything unusual about the divers' LHS that is not true of the submarine study.

HARVEY: The divers are subject to perhaps more physical and environmental stress than the submariners are in my opinion, and therefore, more apt to show pathological changes if they show it. We have also coupled that with the dysbaric osteonecrosis studies to look at their long bones which is in a separate study very closely aligned to what we're doing. We, I think, have a better chance of having the divers stick to the study longitudinally than we do with the submariners. They tend to be more motivated toward this kind of an approach. They tend to be a younger group on the whole than the submariners because the average length of time that a man sticks to diving is not really all that long in his life. We also tend to have a better handle on what happens to them, at least in terms of diving-related accidents of any kind because of the study going on at Norfolk Naval Safety Center where we can at least in more recent years get good data on what kind of accidents they might have had, what kind of diving experience they might have had. So, it's easy to quantitate the actual exposures to the risk stress.

ENTERLINE: You're doing both studies?

HARVEY: Yes, we are doing them both. They're funded as separate entities but run very closely together.

BORNMANN: I would like to extend that by my views of the problem they certainly are a younger group -- they're a smaller group -- 3,300 approximately, right? -- rather than 25,000 approximately. They're a much more widely scattered group and they operate in smaller teams -- much more difficult to handle on what a diver is because we have underwater demolition team swimmers, we have sea teams, sea/air/land commandoes -- basically, we have explosive disposal, we have

first class, second class divers, deep-sea divers, salvage divers, et cetera. It is much more difficult to categorize the type of diving they do, even though there is a statistical center because these people get paid anywhere from \$1,000 to \$3,000 a year for having on their record 8 dives -- whether they make the dives or not. You have difficulty in both the submarine and the diving series of answering the objective, which is listed as "document relationships between health disorders and environmental stresses". You cannot really define the environmental stress that well in either study and you'll have a hard time linking the two, even if you find health disorders. I say it's easy to document the submariners because they go in groups of 150 and they stay on board for 90 days.

DISCHER: What would be the value of getting this information as part of the occupational history -- in the following manner:

you have in front of you at the time of your interviews supposedly what happened, and then sit down with the man and get at that on an annual basis.

BORNMANN: Which man.

DISCHER: The diver.

BORNMANN: You mean at the time of their physical examination? That's a very good suggestion. I never thought of it.

DISCHER: At the University, that's what we do because we have the same problem -- everybody was wondering why all the university divers were all lying.

HARVEY: It is a perfectly feasible technique to be done. It would take manpower.

DISCHER: Yes, but how long would it take?

HARVEY: It depends on how much the man's been diving, but half an hour to an hour.

PURDY: How are your dives automatically recorded, that is, decompression dives? Those are the ones that will probably hurt the divers more as far as sickness is concerned.

HARVEY: All of our dives are recorded.

PURDY: By hand?

HARVEY: By hand, on this flip sheet.

PURDY: I don't think those are very accurate.

HARVEY: I agree with you. It would seem to me desirable from our study to find out where we have problems healthwise. So that, I think, a prospective study looking at them healthwise as they go and examine their status at a period of time and then retrospectively. Looking back at this kind of a history seems a desirable approach.

DISCHER: Are you talking about a sequential design or are you talking about a retrospective study?

HARVEY: Basically, I'm talking about a retrospective study in terms of what their experience has been. We're not looking for a cause and effect right now either. We're looking for a statistical correlation.

GUNDERSON: Is there a question of brain damage in divers under certain conditions?

HARVEY: There has been to my knowledge no decrements in central nervous system functions other than those that have had actual decompression sickness where we can document a long-term effect. There are known hearing losses which are known to occur in divers. There is also the dysbaric osteonecrosis study.

PURDY: Have you run into the problem of vestibular type problems?

HARVEY: Yes, there have been vestibular problems as you know. There's been sudden onset of vestibular problems with no obvious barotrauma

of any kind. There's been vestibular problems secondary to barotrauma and decompression sickness. I would also say that really the incidence of illness among the divers is pretty low.

ENTERLINE: You know, what you ought to do is if you just take some people with a tremendous amount of diving and match them with people without diving experience and if there's no difference between these people, anything you can measure, you begin to suspect that the diving experience is not important.

HARVEY: We had hoped to compare our divers to our submarine population since we're doing the same health parameters on them and we can pick out a group that we can match with age, weight, sex, race, whatever else you want to talk about within our limitation of recording. The one problem is that the submariners have all had escape training so there have been some pressure exposures but it's pretty nominal, so it makes it sort of a control group we have immediate access to, if you will.

PURDY: That makes it a bit sticky though for osteonecrosis since there are records of one dive leading to osteonecrosis.

HARVEY: We still have to finish figuring out what our prevalence to osteonecrosis is.

KNIGHT: On osteonecrosis, if we can show a distinct difference between the two populations it would build up a case for "chronic exposure" or "single dive exposure". It would be a fruitful avenue to investigate by comparing the two populations.

HARVEY: I would toss out one other thing. We're not x-raying our submariners for osteonecrosis, only the divers.

PURDY: It might be interesting to do that however because as far as I know there has been no study of another population, and the only one I ran across was in some village in Germany where they found a 10th of one per cent of osteonecrosis prevalence.

HARVEY: The best control group I know of is one the British had for their Clyde Tunnel. They found highly significant differences in their study by their interpretation.

PURDY: What are the civilians or the non-participants showing?

HARVEY: I will quote you less than 1%.

PURDY: You're aware that we have now proposed at NIOSH to do an epidemiological study of the divers on the Gulf Coast. Our intent is to go through a series of exams, probably quite similar to what you already set up and we hope to learn from you on this. I didn't find any neurological examinations that looked in depth anyway and one would think that this would very important for divers because one would expect that somewhere along the line that the nervous system would be in trouble.

HARVEY: Can I toss out one additional question? Assume for a moment that we're faced with limits of manpower -- limited funds -- and we're faced with in the next several months making a decision as to whether to go ahead with new subjects, start recalling old subjects, or to apply our techniques to sub-acute studies. Which of these, and in what priority would you say from what you know now would be important?

ENTERLINE: More slowly now -- new subjects, old subjects, recalls or . . .

HARVEY: Say, taking a submarine and checking everybody pre-patrol, studying them during the patrol and post-patrol. In other words, using our longitudinal examination techniques for short-term we had studies. Where would you say we should put our priorities assuming/a limited staff and limited money. Is it time to recall the 1,000 -- should we split ourselves and try to go with both? If we start recalling these people, in order to get them recalled within say three years, we're going to have to go at that pretty full time. If we start feeding new people into the system, obviously this affects our ability to do the recall of subjects as well. Now, I'm trying to say -- where do you think our priorities should lay, --- should we expand our base and recall the people later? should we concentrate on recalls at this period? -- it now being three years.

ENTERLINE: Well, there are two possibilities. The third one was to do some after studies. I think you ought to offer one more possibility that the group here considered a little while ago and that was how about categorizing the people you have and finding out whose missing and filling in and then going with that group.

McARDLE: I agree with the point there and then I would seriously, as a first cut, look at the information on gathering, when it was discussed and how I'm gathering it and why I need a unique group to gather it because it appears to me you're going to transfer it to a data base. You're going to have areas that you transfer. I'd make that decision before I'd even consider the steps you pointed out.

ENTERLINE: First you'd have to take that matter up. What could you do with 1,000? Do you really need 2,000? I certainly wouldn't continue to examine men who have less than three years of service. I quite honestly, in the absence of really good hypotheses on this thing, would be very interested in this special study kind of idea -- see if

you could -- if there are any differences you can detect before and after cruises or with the most exposed and the least exposed -- you really need some more hypotheses in this whole thing. I'm looking at this purely from an occupational epidemiological standpoint -- I recognize that there is another way of looking at it and that is just to watch people. Seems to me those overlap. I think hypotheses generating activities could be very useful in this study.

GELL: I'd like to direct a question to Claude. I would feel that we make a close scrutiny as to how many we can do in a matter of three years. I think we can do more than that.

HARVEY: I would agree with you in terms of our potential capability but our realistic world is that the people who are doing the study are also spread into other jobs and you come down to the row of dominoes. I was just looking at the realistic package; it's taken us three years to do 1,000.

BORNMANN: It is true that BuMed requires an annual physical of these people and that if it wasn't done by you, it would be done by the hospital at the Submarine Medical Center. I think you ought to play on that a little bit.

McARDLE: This is what has me hung up. I see a normal process. I don't see why you need unique individuals to perform the physical you want performed.

HARVEY: Let me make one brief statement. The majority of the tests we run along in the LHS are not carried out in the routine physical examination. The SMA 12 is not carried out. The hearing test is carried out with several additional tests. The vision test is not carried out. Fundus photography is not carried out. Pulmonary function test is not carried out. By far, the majority of our tests are unique in terms of the standard physical that is done.

SPHAR:

I think we've come to the point in the proceedings where my job is extremely easy. Thank you very much for providing a stimulating and interesting session for us. I hope that you will all continue to be interested in the LHS and associate with us from time to time in conducting periodic peer reviews of the study. Thank you very very much, gentlemen.

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