Captions will appear here.

>> THIS MEETING IS NOW BEING RECORDED.

>> FIRST OF ALL, LET ME INTRODUCE MYSELF. MY NAME IS MISSY HARVEY, I AM THE TECHNOLOGY AND COMMUNICATION COORDINATOR FOR MAR, OUR MIDDLE ATLANTIC REGION. WE HAVE A GUEST SPEAKER TODAY AND I JUST UM, BEFORE I INTRODUCE HERE, I JUST WANT TO, UM, PUT IN A COUPLE LITTLE IF YOU WANT TO CALL IT HOUSE KEEPING DETAILS. FIRST OF ALL, WHILE MARY LOU IS SPEAKING, I'M GOING TO BE MUTING ALL OF US SO THAT WE'RE NOT HEARING BACKGROUND NOISE. SOME OF YOU MIGHT NOTICE ON THE LEFT SIDE OF YOUR SCREEN NEXT TO YOUR NAME THAT I'VE ALREADY MUTED SOME OF YOU AS YOU'VE COME ALONG. WHEN MARY LOU IS DONE SPEAKING TODAY, WHAT I'LL DO IS I'LL UNMUTE EVERYONE AND SO THAT YOU CAN ASK QUESTIONS AND WE CAN HAVE DISCUSSIONS. UM, THE OTHER THING I WANT TO MENTION, UM, ON THE LEFT SIDE OF YOUR SCREEN, I'D SAY YOU'LL SEE A SERIES OF BOXES, THE THIRD ONE FROM THE -- EXCUSE ME, THE THIRD BOX FROM THE TOP SAYS CHAT. IF AT ANY POINT YOU HAVE QUESTIONS OR PROBLEMS OR WHATEVER, PLEASE FEEL FREE TO TYPE IN THAT CHAT WINDOW, BUT ALSO I WANT TO STRESS WE WOULD LIKE TO ASK THAT EVERYONE THAT IS PARTICIPATING TODAY IN -- EXCUSE ME -- IN THAT CHAT WINDOW PLEASE ENTER YOUR NAME AND YOUR ZIP CODE BECAUSE WE DO NEED TO REPORT THAT KIND OF DATA AND THAT KIND OF INFORMATION BACK TO THE NATIONAL LIBRARY OF MEDICINE. SO WE APPRECIATE YOUR TIME. OKAY. SO WE ARE ABOUT TO GET STARTED. FIRST OF ALL, LET ME INTRODUCE MARY LOU KLEM. DR. KLEM RECEIVED HER Ph.D. IN CLINICAL PSYCHOLOGY FROM THE UNIVERSITY OF MEMPHIS IN 1993 AND WENT ON TO COMPLETE HER RESIDENCY IN CLINICAL PSYCHOLOGY AT THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER AND THE JACKSON, MISSISSIPPI VA CENTER. SHE MOVED TO THE UNIVERSITY OF PITTSBURGH AND SERVED AS A POST DOCK ROLL FELLOW AT THE BARRAGE WAIT SCHOOL OF PUBLIC HEALTH. FROM 1999-2003, SHE HELD AN APPOINTMENT AS AN ASSISTANT PROFESSOR OF PSYCHIATRY AT OUR WESTERN PSYCHIATRIC INSTITUTE AND CLINIC AT THE UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE. DURING THIS TIME SHE ALSO CLEATED A MASTERS DEGREE IN LIBRARY AND INFORMATION SCIENCE AND IN 2003, AS PART OF A CAREER TRANSITION FROM CLINICAL PSYCHOLOGIST TO LIBRARIAN, SHE COMPLETED A TRAINEE SHIP IN HEALTH SCIENCES LIBRARIANSHIP AND BIOMEDICAL INFORMATICS. DR. KLEM IS CURRENTLY A FACULTY LIBRARIAN FOR THE HEALTH SCIENCES LIBRARY SYSTEM AT THE UNIVERSITY OF PITTSBURGH, AND ONCE AGAIN, I'D LIKE TO ASK ALL OF YOU TO PLEASE JOIN ME IN WELCOMING DR. KLEM AND PLEASE DO REMEMBER TO TYPE IN YOUR NAME AND ZIP CODE IN THE CHAT WINDOW. THANK YOU SO MUCH. MARY LOU, IT'S ALL YOURS.

>> OKAY. YOU CAN HEAR ME OKAY?

>> VERY MUCH SO.

>> OKAY. ALL RIGHT. WELL THANK YOU EVERYBODY FOR ATTENDING TODAY. UM, WHAT I WANT TO DO IN THE NEXT MAYBE 35-40 MINUTES IS TO TALK WITH

>> THIS MEETING IS NOW BEING RECORDED.

>> FIRST OF ALL, LET ME INTRODUCE MYSELF. MY NAME IS MISSY HARVEY, I AM THE TECHNOLOGY AND COMMUNICATION COORDINATOR FOR MAR, OUR MIDDLE ATLANTIC REGION. WE HAVE A GUEST SPEAKER TODAY AND I JUST UM, BEFORE I INTRODUCE HERE, I JUST WANT TO, UM, PUT IN A COUPLE LITTLE IF YOU WANT TO CALL IT HOUSE KEEPING DETAILS. FIRST OF ALL, WHILE MARY LOU IS SPEAKING, I'M GOING TO BE MUTING ALL OF US SO THAT WE'RE NOT HEARING BACKGROUND NOISE. SOME OF YOU MIGHT NOTICE ON THE LEFT SIDE OF YOUR SCREEN NEXT TO YOUR NAME THAT I'VE ALREADY MUTED SOME OF YOU AS YOU'VE COME ALONG. WHEN MARY LOU IS DONE SPEAKING TODAY, WHAT I'LL DO IS I'LL UNMUTE EVERYONE AND SO THAT YOU CAN ASK QUESTIONS AND WE CAN HAVE DISCUSSIONS. UM, THE OTHER THING I WANT TO MENTION, UM, ON THE LEFT SIDE OF YOUR SCREEN, I'D SAY YOU'LL SEE A SERIES OF BOXES, THE THIRD ONE FROM THE -- EXCUSE ME, THE THIRD BOX FROM THE TOP SAYS CHAT. IF AT ANY POINT YOU HAVE QUESTIONS OR PROBLEMS OR WHATEVER, PLEASE FEEL FREE TO TYPE IN THAT CHAT WINDOW, BUT ALSO I WANT TO STRESS WE WOULD LIKE TO ASK THAT EVERYONE THAT IS PARTICIPATING TODAY IN -- EXCUSE ME -- IN THAT CHAT WINDOW PLEASE ENTER YOUR NAME AND YOUR ZIP CODE BECAUSE WE DO NEED TO REPORT THAT KIND OF DATA AND THAT KIND OF INFORMATION BACK TO THE NATIONAL LIBRARY OF MEDICINE. SO WE APPRECIATE YOUR TIME. OKAY. SO WE ARE ABOUT TO GET STARTED. FIRST OF ALL, LET ME INTRODUCE MARY LOU KLEM. DR. KLEM RECEIVED HER Ph.D. IN CLINICAL PSYCHOLOGY FROM THE UNIVERSITY OF MEMPHIS IN 1993 AND WENT ON TO COMPLETE HER RESIDENCY IN CLINICAL PSYCHOLOGY AT THE UNIVERSITY OF MISSISSIPPI MEDICAL CENTER AND THE JACKSON, MISSISSIPPI VA CENTER. SHE MOVED TO THE UNIVERSITY OF PITTSBURGH AND SERVED AS A POST DOCK ROLL FELLOW AT THE BARRAGE WAIT SCHOOL OF PUBLIC HEALTH. FROM 1999-2003, SHE HELD AN APPOINTMENT AS AN ASSISTANT PROFESSOR OF PSYCHIATRY AT OUR WESTERN PSYCHIATRIC INSTITUTE AND CLINIC AT THE UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE. DURING THIS TIME SHE ALSO CLEATED A MASTERS DEGREE IN LIBRARY AND INFORMATION SCIENCE AND IN 2003, AS PART OF A CAREER TRANSITION FROM CLINICAL PSYCHOLOGIST TO LIBRARIAN, SHE COMPLETED A TRAINEE SHIP IN HEALTH SCIENCES LIBRARIANSHIP AND BIOMEDICAL INFORMATICS. DR. KLEM IS CURRENTLY A FACULTY LIBRARIAN FOR THE HEALTH SCIENCES LIBRARY SYSTEM AT THE UNIVERSITY OF PITTSBURGH, AND ONCE AGAIN, I'D LIKE TO ASK ALL OF YOU TO PLEASE JOIN ME IN WELCOMING DR. KLEM AND PLEASE DO REMEMBER TO TYPE IN YOUR NAME AND ZIP CODE IN THE CHAT WINDOW. THANK YOU SO MUCH. MARY LOU, IT'S ALL YOURS.

>> OKAY. YOU CAN HEAR ME OKAY?

>> VERY MUCH SO.

>> OKAY. ALL RIGHT. WELL THANK YOU EVERYBODY FOR ATTENDING TODAY. UM, WHAT I WANT TO DO IN THE NEXT MAYBE 35-40 MINUTES IS TO TALK WITH YOU ABOUT SOME BASICS OF STUDY DESIGN. UM, I'VE TAUGHT THIS SECTION A NUMBER OF TIMES, UM N THE CONTEXT OF OUR WORKSHOP ON THE NUTS AND BOLTS OF SYSTEMATIC REVIEWS FOR LIBRARIANS, AND, UM, THE REASON THAT WE TALK ABOUT STUDY DESIGN IN THAT CONTEXT IS BECAUSE IF AS YOU KNOW IF YOU'RE FAMILIAR WITH SYSTEMATIC REVIEWS THAT THOSE ARE REVIEWS OF THE HIGHEST QUALITY AVAILABLE EVIDENCE THAT ADDRESSES A PARTICULAR CLINICAL QUESTION OR TOPIC, AND SO THERE'S GREAT EMPHASIS PLACED ON NOT JUST LOCATING STUDIES THAT ARE RELEVANT TO THE

TOPIC OR QUESTION BUT ALSO THEN TRYING TO SUMMARIZE, UM, ONLY THE HIGHEST EVIDENCE THAT'S AVAILABLE SO THERE'S AN ISSUE OF QUALITY, AND WHAT WE KNOW IS THAT THE QUALITY OF EVIDENCE [BACKGROUND NOISE] -- BY THE PARTICULAR DESIGN THAT'S USED BY THE INVESTIGATORS. AND IF YOU'RE FAMILIAR WITH THE EVIDENCE PYRAMID THAT'S USED IN EVIDENCE-BASED PRACTICE, UM, THAT IS SIMPLY A VISUAL PRESENTATION OF THE FACT THAT YOU CAN TYPICALLY JUDGE THE QUALITY OF EVIDENCE BY THE PARTICULAR STUDY DESIGN THAT IS USED TO COLLECT THAT EVIDENCE. UM, WHAT DOES THIS MEAN FOR YOU IF YOU'RE HELPING WITH THE SYSTEMATIC REVIEW? IT MEANS YOU MAY BE ASKED BY INVESTIGATORS TO LOCATE NOT JUST ANY STUDIES ON A PARTICULAR TOPIC OR CLINICAL QUESTION, BUT THEY MAY BE INTERESTED IN RESTRICTING THE SEARCH TO PARTICULAR STUDY DESIGNS, UM, AND TYPICALLY WHAT WE TELL PEOPLE IN OUR WORKSHOP IS THAT IF THE INVESTIGATORS, THEMSELVES, DO NOT MAKE A REQUEST TO LIMIT THE SEARCH RESULTS TO A PARTICULAR STUDY DESIGN, THAT THAT'S SOMETHING TYPICALLY YOU SHOULD ASK ABOUT JUST TO MAKE SURE THAT THEY DON'T KIND OF HAVE THAT IN THE BACK OF THEIR HEAD AND HAVEN'T SAID ANYTHING OR NOT. IT ALSO WILL HAVE A LARGE IMPACT ON WHAT YOU'RE DOING WHEN YOU START CREATING THE SEARCH FOR SYSTEMATIC REVIEW. WHEN WE'RE TALKING ABOUT EVIDENCE AND THE QUALITY OF EVIDENCE, THE ONE THING I THINK THAT FOLKS ARE AWARE OF IS THAT THE RANDOMIZED CONTROLLED TRIAL IS TYPICALLY CONSIDERED TO BE THE GOLD STANDARD OR THE HIGHEST LEVEL OF EVIDENCE WHEN YOU'RE TALKING ABOUT ORIGINAL STUDIES. UM, BUT ONE OF THE THINGS THAT I ALSO LIKE TO POINT OUT DURING OUR WORKSHOP IS THAT, UM, ALTHOUGH THE RANDOMIZED CONTROLLED TRIAL IS MOST OFTEN CITED AS A GOLD STANDARD FOR HIGH-QUALITY EVIDENCE, IT'S ACTUALLY POSSIBLE THAT THE BEST EVIDENCE FOR A PARTICULAR TOPIC OR CLINICAL QUESTION CAN BE SOME OTHER STUDY DESIGN OR METHODOLOGY. FOR EXAMPLE, IN THE SLIDE THAT I HAVE UP HERE FOR YOU KNOW, YOU CAN SEE THERE'S TWO CLINICAL QUESTIONS SOMEONE MIGHT ADDRESS IN THE SYSTEMATIC REVIEW. THE FIRST IS A THERAPY QUESTION ASKING ABOUT THE EFFECTS OF A DRUG, AND FOR A THERAPY QUESTION LIKE THAT, WE'RE LOOKING, UM, FOR THE EVIDENCE ON A PARTICULAR TREATMENT, THE PREFERRED METHODOLOGY, THE GOLD STANDARD WOULD INDEED BE A RANDOMIZED CONTROL TRIAL PREFIBLY WITH DOUBLE BLINDING. HOWEVER, AS I SAID, THERE ARE INSTANCES IN WHICH ANOTHER METHODOLOGY MAY BE JUST FINE AND MAY BE THE HIGHEST QUALITY OF EVIDENCE THAT YOU CAN FIND AND THAT'S ILLUSTRATED BY THIS SECOND CLINICAL QUESTION THAT I'VE POSED HERE FOR YOU WHICH IS ACTUALLY A PROGNOSIS QUESTION, SYSTEMATIC REVIEW QUESTION WHERE THEY'RE TRYING TO DETERMINE WHETHER SOMEONE'S SMOKING STATUS, DOES THAT INFLUENCE THE RISK OF MORTALITY IN PATIENT WHO IS MAY HAVE HAD A MYOCARDIAL INFARCTION. WHEN YOU START LOOKING FOR LITERATURE ON THIS TOPIC, WHAT YOU'RE GOING TO FIND IS THAT MOST OF THE STUDIES AVAILABLE OUT THERE ARE SOMETHING CALLED COHORT STUDIES. IT'S EXTREMELY UNLIKELY THAT YOU WOULD EVER FIND A RANDOMIZED CONTROLLED TRIAL THAT WOULD ADDRESS A PARTICULAR QUESTION LIKE THIS. SO THE BEST EVIDENCE THAT'S GOING TO BE AVAILABLE IS A COHORT STUDY AND THAT OBVIOUSLY HAVE IMPLICATIONS FOR HOW YOU WOULD GO ABOUT CREATING THE SEARCH FOR THIS PARTICULAR QUESTION. SO WHAT I WANT TO DO TODAY IN THE TIME THAT I HAVE REMAINING IS JUST TALK A LITTLE BIT ABOUT BASIC STUDY DESIGNED, MAJOR TYPE OF STUDY DESIGNS, AND I WILL HAPPILY ADMIT UP FRONT THAT THERE'S NO WAY I CAN POSSIBLY COVER ALL OF THE NUANCES OF RESEARCH DESIGN OR STUDY DESIGN AND SO WHAT I'M

DOING SHEER REALLY GIVING YOU JUST SORT OF AN INKLING OR A TASTE OF WHAT IS ACTUALLY A VERY COMPLEX AND BROAD TOPIC, BUT IT'S JUST ENOUGH TO HOPEFULLY TEACH YOU A LITTLE BIT MORE THAN YOU KNOW NOW AND MAYBE REFRESH YOUR MEMORY IF IT'S SOMETHING THAT YOU'VE LEARNED PREVIOUSLY. UM, THE MAIN DISTINCTION THAT I WANT TO MAKE -- AND IT'S A FUNDAMENTAL DISTINCTION BETWEEN STUDY DESIGNS -- IS THIS ISSUE OF A DESIGN BEING EITHER EXPERIMENTAL OR OBSERVATIONAL. THIS IS REALLY SORT OF A FUND TALL DISTINCTION YOU CAN MAKE BETWEEN STUDIES. IF A STUDY IS WHAT'S CALLED AN EXPERIMENTAL DESIGN, UM, WHAT EXPERIMENTAL MEANS, BASICALLY IS THAT THE INVESTIGATOR INTENTIONALLY MANIPULATES A VARIABLE OF SOME SORT AND THEN GOES AHEAD AND LOOKS AT THE EFFECT OF THAT MANIPULATION ON AN OUTCOME THAT HE OR SHE IS INTERESTED IN. THE RANDOMIZED CONTROLLED TRIAL IS THE CLASSIC EXAMPLE OF THIS. IF AN EXAMPLE, FOR EXAMPLE, IS INTERESTED IN THE EFFECTS OF A DRUG, THEY WILL RECRUIT PARTICIPANTS, THEY WILL RANDOMLY ASSIGN THEM TO RECEIVE THE DRUG OR TO RECEIVE SOME OTHER CONTROLLED CONDITION AND THEN LOOK AT THE EFFECT OF THE TREATMENT OR THE CONTROL GROUP ON AN OUTCOME SUCH AS A DISEASE STATE OR MORTALITY. SO THE INVESTIGATOR IS ACTIVELY INVOLVED ON SOME LEVEL IN DETERMINES WHICH PARTICULAR TREATMENT OR EXPOSURE THE PARTICIPANTS EXPERIENCE. IN CONTRAST AND IN OBSERVATIONAL STUDY DESIGN, THE INVESTIGATOR IS NOT IN THERE AND IS NOT DELIBERATELY MANIPULATING OR CHANGING ANYTHING. INSTEAD WHAT THEY'RE DOING IS TAKING ADVANTAGE OF A NATURALLY-OCCURRING DIFFERENCE OR A PREEXISTING DIFFERENCE BETWEEN PARTICIPANTS AND ENROLLS THOSE PARTICIPANTS AND THEN SIMPLY FOLLOWS THEM OVERTIME. IT CAN BE FORREGARDWARD, IT CAN BE A BACK WARD KIND OF THING, BUT THE MAJOR POINT IS THAT THE INVESTIGATOR IS SIMPLY OBSERVING OUTCOMES OF A NATURALLY-OCCURRING DIFFERENCE AS OPPOSED TO CREATING A DIFFERENCE OF SOME SORT BETWEEN GROUPS OF PARTICIPANTS. WHAT YOU CAN SEE, UM, ON THIS SLIDE AGAIN IS SOME OF THE EXAMPLES OF THE COHORT STUDIES I'VE MENTIONED. CASE CONTROL AND CASE SERIES CAN BE EXAMPLES AS WELL. JUST TO SHOW YOU A DIAGRAM AND EXPLAIN ABOUT THE CHARACTERISTICS OF A RANDOMIZED CONTROLLED TRIAL T WAY THAT THESE WORK ARE THAT THE INVESTIGATOR FINDS A POPULATION -- THESE ARE POTENTIAL PARTICIPANTS WHO ARE THE KIND OF FOLKS THAT THEY WANT TO STUDY. WE RECRUIT THESE PEOPLE AND ONCE THEY COME IN THEY GO THROUGH A PROCESS CALLED RANDOMIZIZATION. RANDOMIZATION MEANS THAT THESE FOLKS ARE GOING TO BE RAND COME TOLY ASSIGNED TO, FOR EXAMPLE, A TREATMENT GROUP. THIS RANDOMIZATION, THIS ASSIGNMENT IS DONE WITHOUT REGARD TO ANY PERSONAL CHARACTERISTIC OR PREFERENCES OF THE PATIENT OR THE PARTICIPANT. AND ACTUALLY THAT'S WITHOUT REGARD TO PREFERENCES OF THE INVESTIGATOR AS WELL OR ANYBODY ELSE. IT'S A COMPLETELY RANDOM PROCESS. THE INVESTIGATOR CONTROLS THE RANDOMIZATION PROCESS, UM, IN THAT THEY'RE SORT OF THE ONE THAT OPENS THE ENVELOPE THAT TELLS THE PARTICIPANT WHICH GROUP THEY'RE BE ASSIGNED TO BUT THE INVESTIGATOR AS WELL AS THE PATIENT HAS NO CONTROL OVER WHICH OF THE TREATMENT GROUPS OR CONTROL GROUPS THE PARTICIPANT WOULD WIND UP IN. AND THIS IS OBVIOUSLY A CRITICAL PART OF THIS. I MEAN THIS IS THE EXPERIMENTAL MANIPULATION THAT'S GOING ON, AND THE PURPOSE OF THIS RANDOMLY ASSIGNING PEOPLE TO A GROUP OF EITHER A TREATMENT GROUP OR CONTROL GROUP IS THAT WHAT YOU WANT TO HAVE TO HAPPEN IS THAT THE ASSIGNMENT OCCURS RANDOMLY AND SO ALL THE GROUPS WILL BE EQUIVALENT ON ANY SOURCE OF MEASURES THAT YOU CAN THINK ABOUT. YOU DON'T WANT TO ASSIGN PEOPLE KEEPING

IN YOUR MIND SOME PARTICULAR CHARACTERISTIC. LIKE YOU WOULDN'T WANT TO THINK, WELL I WANT ALL THE WOMEN IN ONE GROUP AND MEN IN THE OTHER GROUP. WHAT YOU REALLY WANT ARE EQUAL PROPORTIONS OF MEN AND WOMEN IN EACH OF THE TWO GROUPS, AND THAT GOES FOR ANY OTHER CHARACTERISTIC THAT THE PARTICIPANTS MAY BE DIFFERENT ON. SO THAT REGARDLESS OF THE CHARACTERISTIC THAT YOU CHOOSE, PEOPLE IN EITHER OF THE TWO GROUPS ARE REPRESENTED EQUALLY, THERE'S THE SAME PROPORTION OF THAT CHARACTERISTIC ACROSS ALL THE TREATMENT GROUPS AND CONTROL GROUPS. BASICALLY, WHAT'S GOING TO HAPPEN IS THAT BEFORE TREATMENT BEGINS, THESE TWO GROUPS OR WHATEVER MANY THERE ARE, ARE GOING TO LOOK EQUIVALENT. THEY'LL LOOK THE SAME. THE ONLY DIFFERENCE BETWEEN THE TWO GROUPS IS GOING TO BE THE TREATMENT OR THE EXPOSURE THAT THEY RECEIVE, AND THE BEAUTY OF THAT IS THAT AT THE END OF THE TRIAL IF THERE ARE DIFFERENCES BETWEEN THE GROUPS ON A PARTICULAR OUTCOME, YOU CAN ATTRIBUTE IT TO THE ONLY KNOWN DIFFERENCE BETWEEN THE GROUPS WHICH IS THE TREATMENT THAT WAS ADMINISTERED. SO THAT'S THE PURPOSE OF RANDOMIZATION. AS I'VE MENTIONED, THERE TYPICALLY ARE GOING TO BE MULTIPLE GROUPS. THERE WILL HAVE TO BE AT LEAST TWO GROUPS AND SOMETIMES EVEN MORE. THERE'S ALWAYS GOING TO BE ONE GROUP, AT LEAST ONE THAT RECEIVES SOME SORT OF ACTIVE TREATMENT AND THEN THERE'S GOING TO BE A CONTROL OR A COME PARSON GROUP, THAT'S WHERE THE RANDOMIZED CONTROL TRIAL COMES FROM. THIS IS A GROUP THAT DOES NOT RECEIVE THE TREATMENT OF INTEREST OR THE EXPOSURE. THEY CAN BE ANOTHER TREATMENT -- [NO AUDIO]. -- -- CURRENTLY WHAT'S GIVEN FOR A PARTICULAR DISORDER -- [NO AUDIO]. -- CURRENTLY WHAT'S GIVEN FOR A PARTICULAR DISORDER -- [NO AUDIO]. CURRENTLY WHAT'S GIVEN FOR A PARTICULAR DISORDER -- [NO AUDIO]. CURRENTLY WHAT'S GIVEN FOR A PARTICULAR DISORDER -- [NO AUDIO]. -- TREATED GROUP TO ANOTHER GROUP. OKAY. AS I SAID, AT THE END OF THE RANDOMIZED CONTROL TRIAL, YOU COMPARE TREATED TO CONTROL AND LOOK FOR DIFFERENCES IN AN OUTCOME. THAT'S SORT OF THE BASIC CHARACTERISTICS OF A RANDOMIZED CONTROLLED TRIAL. I THINK AS IS OBVIOUS FROM THE WAY I'VE BEEN TALKING ABOUT IT, AN RCT IS DESIGNED TO ASSESS THE WHAT'S CALLED THE EFFICACY OR EFFECTIVENESS OF AN INTERVENTION LOOKING AT THE EFFECT THAT IT HAS ON A CLINICAL OUTCOME. THE PURPOSE OF THE RANDOMIZATION WHICH IS CRITICAL IS THAT YOU WANT TO MINIMIZE ANY DIFFERENCES BETWEEN THE GROUPS OTHER THAN THE TREATMENTS THAT THEY HAVE BEEN ASSIGNED TO, AND IF YOU ARE ABLE TO DO THAT, IF RANDOMIZATION IS SUCCESSFUL, THEN AT THE END OF THE RANDOMIZED CONTROLLED TRIAL IF YOU ARE SEEING DIFFERENCES BETWEEN THE TWO GROUPS YOU CAN BE FAIRLY CONFIDENT THAT THE TREATMENT THAT YOU ADMINISTERED IS RESPONSIBLE FOR THOSE CHANGES AS OPPOSED TO MAYBE SOME OTHER FACTORS THAT MIGHT BE DIFFERENT BETWEEN THE TWO GROUPS. AS I SAID, THE RANDOMIZATION IS THERE TO DESIGN TO ENSURE THAT THE GROUPS ARE ESSENTIALLY THE SAME EXCEPT FOR THE DIFFERENCE IN THE TREATMENT THAT THEY'RE RECEIVING. THAT'S SORT OF THE DESIGN AND THE THEORY BEHIND A RANDOMIZED CONTROL TRIAL. AN EXAMPLE OF AN OBSERVATIONAL STUDY -- REMEMBER THAT'S THE TYPE OF STUDY WHERE THE INVESTIGATOR ISN'T MANIPULATING ANYTHING, THEY'RE JUST GOING TO OBSERVE OUTCOMES OF A NATURALLY-OCCURRING DIFFERENCE -- WOULD BE THIS COHORT STUDY THAT I'VE MENTIONED A COUPLE OF TIMES. THE PARTICULAR DESIGN THAT YOU SEE ON THE SLIDE HERE IS A PROSPECTIVE COHORT STUDY SO IT STARTS AT ONE POINT AND MOVES FORWARD, AND WHAT THE INVESTIGATOR DOES IN A STUDY LIKE THIS IS THAT THEY WOULD GO OUT AND FIND PATIENTS WHO, UM, ARE

ALREADY DIFFERENT ON A VARIABLE THAT IS OF INTEREST TO THE INVESTIGATOR. UM, FOR EXAMPLE, MISSY MENTIONED BRIEFLY THAT I WORKED IN THE PSYCHIATRY DEPARTMENT BEFORE I BECAME A LIBRARIAN. WHEY DID THERE WHEN I WAS ON FACULTY WAS I ACTUALLY DID A NUMBER OF TRIALS LOOKING AT THE EFFECTIVENESS OF DIFFERENT COGNITIVE BEHAVIORAL WEIGHT LOSS INTERVENTIONS. SO IF I WERE DOING A COHORT STUDY, UM, IN MY PREVIOUS LIFE AS AN INVESTIGATOR, UM, WHAT I MIGHT HAVE DONE WAS TO HAVE, UM, TRIED TO RECRUIT, FOR EXAMPLE, A GROUP OF PEOPLE WHO WERE CURRENTLY USING WEIGHT WATCHERS. OKAY. I DIDN'T RANDOMLY ASSIGN THEM TO THAT, THEY WERE PEOPLE WHO'D GONE AHEAD AND SIGNED UP ON THEIR OWN, AND IN CONTRAST TO THEM, I MIGHT GO OUT AND TRY TO FIND ANOTHER GROUP OF PEOPLE WHO ARE USING SOME OTHER WEIGHT LOSS PROGRAM, FOR EXAMPLE MAYBE JENNY CRAIG OR MY PERSONAL FAVORITE WHICH IS RICHARD SIMMONS DEAL A MALE. NOW I'VE GOT TWO DIFFERENT GROUPS USING TWO DIFFERENT METHODS OF WEIGHT LOSSES. THE PARTICIPANTS, THEMG THEMSELVES, HAVE CHOSEN THE TREATMENT THEY'RE USING. WHAT I WOULD DO THEN IS FOLLOW THOSE TWO GROUPS FORWARD IN TIME AND LOOK PERIODICALLY AT A PARTICULAR OUTCOME THAT I'M INTERESTED IN. SO, FOR EXAMPLE, IF I WANT TO SEE HOW MUCH WEIGHT THEY'RE LOSING OR CHANGES IN BODY MAZ INDEX. I MIGHT HAVE EVERYDAY COME IN ONCE A YEAR AND LOOK AT CHANGES IN BMI OR BODY WEIGHT. THOSE FOLKS ARE DOING IT ON THEIR OWN. I'M NOT MANIPULATING IT, I'M JUST SIMPLY FOLLOWING THEM OVER TIME AND LOOKING AT DIFFERENCES. NOW, THE COHORT STUDY, YOU MIGHT WONDER SINCE I'VE BEEN TALKING SO MUCH ABOUT THE RANDOMIZED CONTROL TRIAL AND HOW IMPORTANT RANDOMIZATION IS AND HOW MUCH MORE CONFIDENT IT CAN MAKE YOU FEEL ABOUT YOUR OUTCOMES; WHY WOULD SOMEONE GO WITH THE USE OF COHORT STUDY WHERE THERE'S A LACK OF RANDOMIZATION. THERE COULD BE INSTANCES IN WHICH IT'S NOT POSSIBLE TO RANDOMIZE PEOPLE TO A TREATMENT OR PARTICULAR EXPOSURE. A LOT OF TIMES IT WOULD BE UNETHICAL, OTHER TIMES WHEN IT'S JUST NOT POSSIBLE. IF YOU THINK BACK TO ONE OF THE FIRST SLIDES I SHOWS YOU WHERE THERE WAS A QUESTION ASK WHETHER SMOKING INCREASES MORTALITY. YOU CAN IMAGINE THAT'S A PARTICULAR QUESTION THAT YOU REALLY COULD NOT USE RANDOMIZATION OR RANDOMIZED CONTROL TRIAL TO ANSWER. RIGHT. THAT WOULD INVOLVE IF YOU TRIED TO DO SOMETHING LIKE THAT, IT WOULD INVOLVE FINDING PATIENTS WHO'D HAD A RECENT HEART ATTACK, RANDOMLY ASSIGNING THEM TO BEGIN SMOKING CIGARETTES OR NOT AND THEN FOLLOWING THEM OVER TIME TO SEE WHO DIED AND WHO DID NOT. THAT'S NOT REALLY ETHICAL AND IT'S CERTAINLY NOT GOING TO GET BY AN IRB THESE DAYS. IN A CASE LIKE THAT WHAT YOU MIGHT DO IS RESORT TO SOMETHING LIKE A COHORT STUDY WHERE YOU WOULD FIND PEOPLE WHO HAD MADE THE DECISION TO START SMOKING OR NOT, HAD RECENTLY HAD A HEART ATTACK AND FOLLOW THOSE GROUPS OVERTIME. I ALSO LIKE TO MENTION THAT A LOT OF THE OBSERVATIONAL DESIGNS, COHORT AS WELL AS SOME OTHERS, ARE CAN BE EASIER TO DO AND LESS EXPENSIVE TO DO THAN A RANDOMIZED CONTROLLED TRIAL. RCT s CAN BE VERY INVOLVED AND VERY EXPENSIVE. SO PARTICULARLY WHEN AN INVESTIGATOR IS JUST STARTING TO THINK ABOUT A QUESTION, NOT A LOT OF RESEARCH HAS BEEN DONE, IT'S NOT CLEAR HOW PRODUCTIVE PURSUING A PARTICULAR LINE OF RESEARCH IS GOING TO BE, INVESTIGATORS WILL START WITH OBSERVATIONAL SDE SINES SUCH AS A COHORT STUDY, LOOK TO SEE WHAT KINDS OF RESULTS THEY'RE GETTING AND KIND OF BUILD UP TO THE POINT WHERE THEY DECIDE IT'S TIME TO GO AHEAD AND DO A RANDOMIZED CONTROLLED TRIAL. NOW, INVESTIGATORS WHO DO COHORT

STUDIES ARE VERY WELL AWARE OF THE LIMITATIONS OF SHORT COMINGS OF THESE SORTS OF DESIGNS, AND THEY REALIZE IN PARTICULAR THAT LACK OF RANDOMIZATION CAN CREATE AN ISSUE IN TERMS OF UNEQUAL GROUPS OR GROUPS THAT DON'T LOOK THE SAME AS EACH OTHER.

SO TYPICALLY WHAT HAPPENS WHEN A COHORT STUDY IS BEING DESIGNED IS THAT THE INVESTIGATORS WILL MAKE AN EFFORT TO TRY TO CHOOSE SUBJECTS IN SUCH A WAY THAT THE TWO GROUPS THAT THEY END UP WITH RESEMBLE EACH OTHER ON CERTAIN CHARACTERISTIC THAT MIGHT HAVE AN EFFECT ON OUTCOME. THERE'S A NUMBER OF DIFFERENT THING DHAS DO, NVKT TORS CAN DO TO TRY TO MAKE THESE TWO GROUPS EQUAL AND THEY TYPICALLY MAKE AN EFFORT, BUT THE FACT THAT RANDOMIZATION DID NOT OCCUR IS ALWAYS STILL SORT OF LURKING IN THE BACKGROUND AND WE HAVE TO BE AWARE OF THAT WHEN YOU'RE WRITING UP THE RESULTS OF AN OBSERVATIONAL STUDY OR A COHORT STUDY. THERE'S STILL IS ALWAYS THE POSSIBILITY THAT NO MATTER HOW HARD THE INVESTIGATOR HAS TRIED TO CREATE TWO GROUPS THAT LOOK THE SAME THAT THEY MAY NOT BE IN SOME WAY THAT WE FAILED TO ANTICIPATE, UM, AND SO WHEN PEOPLE ARE DRAWING CONCLUSIONS FROM OBSERVATIONAL STUDIES THEY ARE TYPICALLY VERY CAREFUL NOT TO INFER CAUSE AATION. THEY MAY NOT BE ABLE TO SAY TREATMENT A CAUSED CHANGE IN THIS VARIABLE I'M INTERESTED IN. A LOT OF TIMES WHAT THEY'LL SAY IS IT'S CORRELATED. SO EXPOSURE TO THIS PARTICULAR TREATMENT IS CORRELATED WITH A DIFFERENCE IN OUTCOME, BUT THEY'RE GOING TO BE MUCH MORE CAGE GI ABOUT TALKING ABOUT CAUSATION. THIS IDEA THAT THERE'S THIS POTENTIAL DIFFERENCE OUT THERE THAT WE DON'T KNOW LURKING IN THE BACKGROUND IS SOMETIMES REFERRED TO AS THE THIRD VARIABLE PROBLEM. THAT IS, THERE ARE TWO VARIABLES WE KNOW ABOUT; THERE IS THE TREATMENT TOR EXPOSURE THAT THE PARTICIPANTS HAVE BEEN EXPOSED TO AND THEN THERE IS THE OUTCOME THAT WE'RE INTERESTED IN, AND WE MAY KNOW THAT THERE'S A RELATIONSHIP OF SOME SORT BETWEEN THE TWO BUT WHAT WE CANNOT RULE OUT IS THE POSSIBILITY OF A THIRD VARIABLE OUT THERE SOMEWHERE THAT WE'RE NOT AWARE OF THAT'S ACTUALLY CREATING RELATIONSHIP BETWEEN THE TWO. MY FAVORITE EXAMPLE OF THIS IS A SAYING AND ACTUALLY I THINK SIT A RESEARCH FINDING THAT THERE IS A WELL-KNOWN RELATIONSHIP BETWEEN THE AMOUNT OF ICE CREAM CONSUMED AND RISK OF DROWNING. SO AS ICE CREAM CONSUMPTION GOES UP, SO DOES SOMEONE'S RISK OF DROWNING. RIGHT. THAT'S A CORRELATION. WHAT'S ACTUALLY GOING ON THERE, THOUGH, IS THAT THERE'S A THIRD VARIABLE THAT IS DRIVING THAT RELATIONSHIP AND THAT THIRD VARIABLE AS YOU MIGHT HAVE ANTICIPATED IS ACTUALLY GOING TO BE TEMPERATURE OR SEASON. BOTH ICE CREAM CONSUMPTION AND RISK OF DROWNING ARE TIED TO WHAT TIME OF YEAR IT IS; THE SUMMERTIME, RIGHT? THAT'S ONE OF THE CLASSIC THIRD VARIABLES. SO THE OBSERVATIONAL STUDIES HAVE THEIR USE, BUT THEY HAVE A LIMITATION THAT YOU DON'T TYPICALLY SEE IN THE EXPERIMENTAL DESIGNS. FINALLY, WHAT I WANTED TO DO WAS JUST TO SHOW YOU, UM, A PARTICULAR ISSUE THAT IN WHICH DESIGN OF STUDIES DID HAVE A LARGE AND SIGNIFICANT IMPACT ON THE OUTCOME AND CONCLUSIONS WHICH WERE BEING DRAWN ABOUT A PARTICULAR TREATMENT. ONCE WE DO THAT WE'LL BE FINISH AND I'LL OPEN IT UP FOR QUESTIONS, BUT I WANT TO SPEND A LITTLE MORE TIME GIVING YOU EXAMPLES OF THESE TWO STUDY DESIGNS AND HOW THE DIFFERENCES MADE AN IMPACT ON A TREATMENT DECISION. WHAT I'M GOING TO BE TALKING ABOUT OVERALL IS THE USE OF HORMONE REPLACEMENT THERAPY ON RISK OF HEART DISEASE IN POSTMENOPAUSAL WOMEN. JUST

TO QUICKLY TELL YOU IF YOU'RE NOT AWARE OF THIS AS WOMEN GO THROUGH MEN PAUSE, THERE'S A DECREASE IN THEIR HORMONE LEVELS; YOU SEE DROPS IN ESTROGEN AND PROGESTERONE. THIS CAUSES OTHER SORTS OF CHANGES GOING ON. THERE ARE SOME ACUTE SYMPTOMS. THE MOST WELL KNOWN OF WHICH IS PROBABLY HOT FLASHES, BUT WHAT IS OF EQUAL OR GREATER CONCERN TO BOTH WOMEN AND PHYSICIANS IS THAT THERE IS OVERTIME AN INCREASE IN WOMEN'S RISK OF HEART DISEASE AND OTHER DISEASES AS WELL. THIS RELATIONSHIP BETWEEN A DECREASE IN HORMONES AND AN CREASE IN RISK OF HEART DISEASE HAS BEEN ESTABLISHED FOR A NUMBER OF YEARS, AND WHAT HAS GONE ON IN THE PAST 30 YEARS, PROBABLY STARTING BACK IN THE LATE 1970 s, 80 s, IS THAT THERE WAS INTEREST IN THE CLINICAL POPULATION IN LOOKING AT WAYS TO BLUNT THE EFFECT OF THIS DECREASE IN HORMONES. A NUMBER OF PEOPLE STARTED DOING STUDIES, MOST SCIENCE FOR OBSERVATIONAL STUDIES, LOOKING AT THE POSSIBILITY THAT ADMINISTRATION OF HORMONE REPLACE AMOUNT THERAPY, WHICH WOULD BE ESTROGEN WITH OR WITHOUT PRO JEST ROAN, MIGHT BLUNT OR DECREASE THIS RISK OF HEART DISEASE. WHAT YOU'RE SEEING ON YOUR SCREEN RIGHT NOW IS ONE OF THE EARLIER STUDIES THAT WAS OUT THERE BY BUSH ET AL IN 18987. THERE WAS A PROSPECTIVE COHORT DESIGN. BUSH AND COLLEAGUES WENT OUT AND RECRUITED A GROUP OF POSTMENOPAUSAL WOMEN. -- -- 1987 -- -- SOME OF WHOM HAD ALREADY MADE THE DECISION TO START HRT AND SOME WHICH HAD NOT. BUSH HAD NO CONTROL, THEY JUST SIMPLY WENT OUT AND FOUND WOMEN SOME OF WHOM WHO WERE ALREADY USING THE DRUG AND SOME NOT. THEY BEGAN TO FOLLOW THEM OVERTIME AND HAD THEM COME IN FOR ANNUAL ASSESSMENTS LOOKING AT THE OCCURRENCE OF CARDIOVASCULAR DISEASE, CERTAIN CARD KNOW VASCULAR EVENTS AS WELL AS OTHER THINGS. THEY FOLLOWED THESE WOMEN OVERTIME FOR ABOUT EIGHT-AND-A-HALF YEARS AND AT THE END OF THAT PERIOD, WHAT THEY FOUND WERE THAT THOSE WOMEN WHO HAD COME INTO THE STUDY ALREADY USING HRT AT THE END OF THAT EIGHT-AND-A-HALF YEARS WERE LESS LIKELY TO HAVE DIED OF CERTAIN CARDIOVASCULAR E EVENTS. IT LOOKS LIKE THAT HRT ADMINISTERED TO POSTMENOPAUSAL WOMEN HAD SOME SORT OF HEART-PROTECTIVE EFFECT. THIS, HAS I SAID IT WAS A ONE OF A NUMBER OF STUDIES THAT WERE GOING ON. TONS OF THEM ACTUALLY AND IT LED TO A VERY REAL AND SIGNIFICANT INCREASE IN PRESCRIPTIONS BEING GIVEN FOR HORMONE REPLACEMENT THERAPY FOR WOMEN WHO HAD STARTED TO GO THROUGH MEN MENOPAUSE. WHAT WAS ALSO GOING ON AT THE SAME TIME AS PRESCRIPTION RATE FOR GOING UP IS THERE CONDITIONED TO BE CONCERN ABOUT THE HUS USE OF HRT. PART OF THE REASON A LARGE PART OF THE REASON THERE WAS CONCERN ABOUT THE USE OF HRT WAS BECAUSE THERE WAS A LACK OF RANDOMIZED CONTROLLED TRIALS. THESE WERE ALL OBSERVATIONAL STUDIES AND THIS ISSUE OF NON-RANDOMIZATION WAS OUT THERE, AND FINALLY IN THE EARLY 2000 s, NIH DECIDED TO GO AHEAD AND FUND A VERY, VERY LARGE COMPLEX RESEARCH PROJECT CALLED THE WOMEN'S HEALTH INITIATIVE. WHAT YOU'RE SEEING ON YOUR SCREEN IN FRONT OF YOU IS ACTUALLY JUST ONE PART OF THE TOTAL STUDY DESIGN THAT WAS DEVELOPED BY THE WOMEN'S HEALTH INITIATIVE INVESTIGATORS. THIS WAS A RANDOMIZED CONTROLLED TRIAL. THEY BROUGHT IN WOMEN, THEY RECRUITED WOMEN POSTMENOPAUSAL WOMEN, ALL OF WHOM WERE TREE OF HRT. NONE OF THEM WERE USING HRT, THEY DID NOT HAVE A HISTORY OF USE OF HRT. SO THEY WERE SORT OF NAIVE POST MEN WAS A PAUZ L WOMEN, SO TO SPEAK. THEY WERE RANDOMLY ASSIGNED TO RECEIVE EITHER HORMONE REPLACEMENT THERAPY OF ONE SORT OR ANOTHER OR A PLACEBO. OKAY. AND AGAIN THE WOMEN

WERE FOLLOWED OVER TIME. IT'S INTERESTING TO NOTE ABOUT THIS, IF YOU'RE NOT FAMILIAR WITH THE WOMEN'S HEALTH INITIATIVE, IS THAT THE ORIGINAL DESIGN CALLED FOR WOMEN TO BE FOLLOWED OVERAN EIGHT-YEAR PERIOD OF TIME. VERY SIMILAR TO THE PERIOD OF TIME THAT BUSH ET AL USED IN THEIR COHORT STUDY. BUT WHAT HAPPENED WITH THIS IS THAT THE TRIAL WAS ACTUALLY HALTED AT YEAR FIVE. THEY DIDN'T WANT TO WAIT UNTIL YEAR EIGHT BECAUSE WHAT THEY BEGAN TO SEE BY THE TIME FIFTH ANNUAL ASSESSMENT CAME BY FOR THESE WOMEN WAS THAT WOMEN WHO'D BEEN RANDOMLY ASSIGNED TO HORMONE REPLACEMENT THERAPY WERE ACTUALLY HAVING HIGHER RATES OF CARDIOVASCULAR DISEASE, STROKE, AND PULMONARY EMBOLISM. WHAT YOU'RE SEEING IS A DRAMATIC TURN ARPD IN THE APPARENT EFFECTS OF HORMONE REPLACEMENT THERAPY AFTER RANDOMIZATION TO HRTT WOMEN WHO WERE GIVEN THAT PARTICULAR DRUG COMBINATION WERE MORE LIKELY TO DEVELOP CARDIOVASCULAR DISEASE. OF COURSE, IF YOU'RE FAMILIAR WITH THE HISTORY OF WOMEN'S HEALTH INITIATIVE WHAT YOU KNOW IS THAT ONCE THESE FINDINGS WERE RELEASED, UM, THAT LED TO A RATHER DRAMATIC DECREASE IN PRESCRIPTION RATES FOR HORMONE REPLACEMENT THERAPY. JUST AN ASIDE, WHAT ALSO HAPPENED AT THAT POINT WERE FOR WOMEN WHO WERE IN Y, THEY WERE UNBLINDED -- THEY HAD BEEN BLINDED ORIGINALLY SO THEY DID NOT KNOW WHICH OF THE DRUGS THEY WERE RECEIVING -- EVERYONE WAS UNBLINDED AND GIVEN THE OPTION OF GOING OFF OF THE HRT IF THEY DECIDED TO DO SO. SO A VERY, VERY DIFFERENT OUTCOME WHEN GOING FROM AN OBSERVATIONAL TO AN EXPERIMENTAL DESIGN, AND WHAT'S PARTICULARLY INTERESTING IS THINKING BACK TO THE COHORT STUDIES LIKE BUSH ET AL AND WHAT MIGHT HAVE BEEN GOING ON THERE THAT LED THEM TO HAVE CONCLUSIONS THAT WERE SO DIFFERENT FROM THOSE THAT WERE SEEN LATER IN THE WOMEN'S HEALTH INITIATIVE. THIS IS JUST A SCREEN SHOT AGAIN OF THE BUSH ET AL DESIGN, AND I WANT TO JUST SHOW YOU QUICKLY SOME THOUGHTS THAT SOME PEOPLE HAVE HAD ABOUT WHAT MIGHT HAVE BEEN GOING ON WITH THAT STUDY. UM, ONE OF THE THINGS THAT'S BEEN SUGGESTED IS THAT IN THE BUSH ET AL STUDY THAT THE WOMEN WHO CAME INTO THE STUDY ALREADY ON HRT MAY HAVE BEEN WOMEN WHO HAD ACCESS TO IN ADDITION TO HORMONE REPLACEMENT THERAPY, BETTER ACCESS TO HEALTH CARE SERVICES IN GENERAL, AND THAT ACTUALLY MAKES A LOT OF SENSE. IF YOU THINK ABOUT HRT IS NOT SOMETHING YOU CAN SCAMPER DOWN TO THE CORNER AND GET A DRUGSTORE, YOU TO HAVE A PRESCRIPTION, SOME SORT OF ENTRY INTO THE HEALTH CARE SYSTEM, AND SO IT'S VERY, IT'S POSSIBLE -- THEY DON'T KNOW FOR SURE -- BUT IT'S POSSIBLE THAT THIS GROUP WHO WAS ALREADY USING HRT NOT ONLY WAS USING HRT BUT HAD BETTER ACCESS TO HEALTH CARE IN GENERAL THAN THE WOMEN WHO WERE NOT CURRENTLY USING HORMONE REPLACEMENT THERAPY AND THAT BETTER ACCESS OF HEALTH CARE SERVICES WAS ACTUALLY WHAT WAS DRIVING THAT PROTECTIVE EFFECT THAT THERE WAS A LOT ELSE THAT THEY WERE RECEIVING THAT WAS HELPING THEM TO AVOID ANY CARDIOVASCULAR DISEASES. THE OTHER POSSIBILITY THAT HAD BEEN THROWN OUT IS SOMETHING CALLED COMPLIANCE WITH BIAS. REMEMBER THESE WERE WOMEN WHO WERE USING HRT. SO THEY WERE WOMEN WHO WERE GIVEN A PRESCRIPTION AND WERE ACTUALLY USING IT. SO THEY WERE VERY GOOD AT ADHERING TO A PRESCRIPTION AND THEY WERE JUST GENERALLY POSSIBLY MORE COMPLIANT. IT COULD BE AMONG THE WOMEN WHO WEREN'T USING HRT WOULD BE WOMEN WHO WERE GENERALLY LESS COMPLIANT, LESS ABLE TO DO THE OTHER KINDS OF PROTECTIVE THINGS THAT WE URGE WOMEN TO DO LIKE WATCHING WHAT THEY'RE EATING, EXERCISING ON A REGULAR BASIS, ETC, ETC. SO AGAIN,

THERE MAY HAVE BEEN OTHER THINGS THAT THIS GROUP WAS DOING THE HRT GROUP WAS DOING; GETTING MORE EXERCISE, DOING LOW-FAT EATING, THAT WAS HELPING TO PROTECT THEM FROM CARDIOVASCULAR DISEASE. AND THAT MAY HAVE BEEN THE SO-CALLED THIRD VARIABILITY THAT WAS DRIVING WHAT WAS HAPPENING WITH THEM. WHAT HAPPENED THEN WITH THE WOMEN'S HEALTH INITIATIVE, RIGHT, IS THIS PROCESS OF RANDOMIZATION. SO RATHER THAN SORT OF UNEQUALLY DISTRIBUTING THESE HEALTHY WORKERS OR COMPLIANT PATIENTS -- THEY'RE SUPPOSEDLY ALL OVER HERE IN BUSH. WHAT MAY HAVE HAPPENED WAS THERE WERE HEALTHY WORKERS IN THE WOMEN'S HEALTH INITIATIVE, BUT THEY WERE DISTRIBUTED ACTUAL EQUALLY BETWEEN THE TWO TREATMENT GROUPS. THERE WAS A SIMILAR PROPORTION IN THE HRT GROUP AND SIMILAR PROPORTION IN THE PLACEBO GROUP. AS A RESULT THE TWO GROUPS WERE TRULY EQUAL IN A WAY THAT THE BUSH GROUPS WERE NOT. AS A RESULT, THAT ALLOWS THE TRUE EFFECT OF HORMONE REPLACEMENT THERAPY TO BE OBSERVED. [LOW AUDIO]. ANYWAY, SO THAT WAS MY QUICK OVERVIEW OF STUDY DESIGNS. AS I SAID AT THE BEGINNING OF THIS TALK, THE REASON THAT I LIKE TO CHAT A LITTLE BIT ABOUT THESE BASIC DIFFERENCES IN STUDY DESIGN IS BECAUSE FROM OUR PERSPECTIVE IT'S SOMETHING THAT CAN COME UP A LOT WHEN YOU'RE TALKING ABOUT SYSTEMATIC REVIEWS, ASSISTING SOMEONE WITH ONE. AND SO WHEN YOU ARE WORKING WITH SOMEONE, ONE OF THE THINGS TO KEEP IN MIND IS THAT YOU MAY WANT TO ASK THEM IF THEY THOUGHT ABOUT LIMITING THEIR SEARCH TO A PARTICULAR DESIGN, AND IT'S ALSO USEFUL TO KEEP IN MIND THAT WHEN YOU'RE THINKING ABOUT CITY STUDY DESIGN EVEN IF YOU'RE NOT QUITE SURE YOU DON'T KNOW A LOT ABOUT THEM THAT REALLY ONE OF THE DESIGNING CHARACTERISTICS OF THEM IS THAT THEY'RE EITHER EXPERIMENTAL IN WHICH THE INVESTIGATOR IS DELIBERATELY MANIPULATING A VARIABLE, RANDOMLY ASSIGNING PEOPLE TO ONE TREATMENT GROUP OR ANOTHER, OR IT'S AN OBSERVATIONAL STUDY WHICH THEY'RE NOT MANIPULATING ANYTHING BUT WATCHING A NATURALLY-OCCURRING CHANGE IN A VARIABLE AND TEFECTS OF THAT ON A PARTICULAR OUTCOME. AND THAT IS PRETTY MUCH IT. SO I'M GOING GET OUT OF HERE, I THINK.

>> THIS IS MISSY HARVEY AGAIN. MARY LOU, WE'D LIKE TO THANK YOU SO MUCH. LET ME FIRST JUST SAY TWO THINGS TO EVERYONE THAT IS ATTENDING TODAY. FIRST OF ALL, A REMINDER, IF YOU HAVEN'T DONE IT ALREADY, ON THE LEFT SIDE YOU SEE A CHAT WINDOW AND PLEASE MAKE SURE TO ENTER YOUR NAME -- JUST YOUR FIRST NAME IS FINE -- AND YOUR ZIP CODE. IF ANYONE WANTS TO ASK QUESTIONS OF MARY LOU OR OF US IN MAR, UM, ALL OF YOU ARE RIGHT NOW MUTED SO WE DON'T HEAR THE BACKGROUND NOISE. SO TO UNMUTE YOUR OWN PHONE, YOU HAVE TO PRESS STAR SIX. SO DOES ANYONE HAVE ANY QUESTIONS? AND IF YOU DO HAVE ANY TROUBLE UNMUTING, YOU CAN ALSO TYPE INTO THE CHAT WINDOW AND I'LL READ THE QUESTION. NO QUESTIONS?

>> THIS IS REBECCA CALLING. ON SOME OF THESE TRIALS, HOW MANY PEOPLE DO YOU NEED ON SOME OF THESE TO BE VALID? [LOW AUDIO].

>> RIGHT. SO? -- WOW, GETTING AN ECHO. THE QUESTION WAS, YEAH, ON RANDOMIZED CONTROL TRIALS HOW MANY PEOPLE DO YOU NEED TO BE VALID. YOU KNOW, THAT'S A GOOD QUESTION. IT DEPENDS ON THE PARTICULAR OUTCOMES THAT YOU'RE TRYING TO MEASURE. THAT IS ACTUALLY, IT'S A STATISTICAL CALCULATION THAT PEOPLE HAVE TO DO. THEY HAVE THEIR OUTCOME MEASURES, THEY KNOW WHAT THEY WANT TO TRY TO MEASURE, AND TYPICALLY WHAT THEY DO IS

SIT DOWN WITH A STATISTICIAN AND TRY TO CALCULATE SOMETHING CALLED POWER, AND THAT IS HOW BIG OF A SAMPLE SIZE DO WE NEED TO BE ABLE TO DETECT ANY TRUE DIFFERENCES ARE THERE. SO IT'S NOT A -- I CAN'T GIVE YOU A SPECIFIC NUMBER, IT JUST KIND OF DEPENDS ON WHAT THEY'RE INTERESTED IN ASSESSING.

>> THIS IS MISSY. IF I COULD INTERJECT REAL QUICKLY. SOMEONE HAS TYPED IN A QUESTION SAYING; YOU KNOW, WILL THESE SLIDES BE MADE AVAILABLE? AND YES, WE WILL PROBABLY BE PUTTING THEM UP EITHER THIS AFTERNOON OR TOMORROW MORNING ON OUR MAR WEB SITE. OTHER QUESTIONS?

>> MISSY, IF THERE AREN'T ANY OTHER QUESTIONS AND BEFORE WE FINISH UP FOR THE DAY, I WOULD LIKE TO TAKE THE OPPORTUNITY TO DO A SHAMELESS PLUG FOR OUR WORKSHOP ON SYSTEMATIC REVIEWS. AS I MENTIONED AT THE BEGINNING, THIS PARTICULAR SECTION THAT I'VE DONE HERE IS ONE OF A BUNCH OF THEM THAT WE DO AS PART OF OUR WORKSHOP, AND IF ANYBODY IS INTERESTED IN OUR WORKSHOP WE'RE OFFERING THAT NOW THREE TIMES A YEAR. IT'S ONCE IN APRIL, ONCE IN JULY, AND IN NOVEMBER. OUR JULY WORKSHOP IS ACTUALLY FULL AT THIS POINT. WE WILL BE OFFERING THE WORKSHOP AGAIN IN NOVEMBER. WE HAVE NOT YET SET THE DATES FOR THAT, UM, BUT WHEN WE DO, WE'LL BE ANNOUNCING THEM ON OUR WEB SITE AND THE URL FOR OUR WEB SITE IS ON THE FIRST SLIDE THAT I SHOWED TODAY. WE'LL ALSO, I BELIEVE, WE SEND OUT ANNOUNCEMENT ON THE MEDLINE PEW LISTSERV AS WELL. IF ANYONE IS INTERESTED, WE'LL BE OFFERING THAT WORKSHOP APPARENTLY FOR THE REST OF OUR LIVES. [LAUGHTER]

>> WE IN MAR, WE'LL PROBABLY BE SENDING THAT OUT AS WELL. IN FACT, THAT'S A REMIND TORE EVERYONE WHO'S LISTENING TODAY IS IF YOU DO HAVE THESE TYPES OF THINGS THAT YOU'D LIKE TO ADVERTISE, PLEASE FEEL FREE TO SEND E NILE ME AND I'LL ADD THEM TO WEEKLY POSTINGS WE SEND OUT EVERY FRIED. ANY OTHER QUESTIONS? WELL WE'D LIKE TO THANK ALL OF YOU FOR ATTENDING. IT'S JUST BEEN REMARKABLE TO SEE HOW MANY OF US HAVE JOINED US, AND ONCE AGAIN WE DO LOOK FORWARD TO YOU JOINING US FOR OUR NEXT LUNCH WITH THE RML AND OUR BOOST BOX SESSION AGAIN NEXT MONTH. MAKE SURE TO KEEP CHECKING OUR WEB SITE AND OUR LISTSERV AND RSS FEEDS FROM OUR BLOG. WE'LL KEEP YOU POSTED ON WHEN THESE ARE ALL TALKING PLACE. THANK YOU SO MUCH. WE APPRECIATE YOUR TIME AND MARY LOU, THANK YOU FOR YOUR PRESENTATION AND YOUR TIME AS WELL. HAVE A GOOD DAY, EVERYONE.

>> YOU'RE WELCOME.

>> THANKS.