BEFORE THE
TASK FORCE ON NEUROSCIENCE AND MEDICINE OF THE
INDEPENDENT CITIZENS' OVERSIGHT COMMITTEE
TO THE
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE
ORGANIZED PURSUANT TO THE
CALIFORNIA STEM CELL RESEARCH AND CURES ACT

REGULAR MEETING

LOCATION: VIA ZOOM

DATE: OCTOBER 18, 2023
9 A.M.

REPORTER: BETH C. DRAIN, CA CSR
CSR. NO. 7152

FILE NO.: 2023-32

I N D E X

OCTOBER 18, 2023; 9 A.M.

(THE MEETING WAS DULY CALLED TO ORDER BY CHAIRMAN GOLDSTEIN.)

CHAIRMAN GOLDSTEIN: CALL THE ROLL.

MS. MORALEZ: SURE. I'LL DO IT.

LEONDRA CLARK-HARVEY.

DR. CLARK-HARVEY: HERE.

MS. MORALEZ: MARIA BONNEVILLE.

VICE CHAIR BONNEVILLE: PRESENT.

MS. MORALEZ: MARK FISCHER-COLBRIE.

DR. FISCHER-COLBRIE: HERE.

MS. MORALEZ: FRED FISHER. JUDY GASSON.

DR. GASSON: HERE.

MS. MORALEZ: LARRY GOLDSTEIN.

CHAIRMAN GOLDSTEIN: I'M HERE.

MS. MORALEZ: DAVID HIGGINS. VITO IMBASCIANI.

DR. IMBASCIANI: HERE.

MS. MORALEZ: STEVE JUELSGAARD. PAT LEVITT.

DR. LEVITT: HERE.

MS. MORALEZ: LAUREN MILLER-ROGEN. MARVIN SOUTHARD.

DR. SOUTHARD: HERE.

MS. MORALEZ: AND KEITH YAMAMOTO.



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CHAIRMAN GOLDSTEIN: ALL RIGHT. SO SORRY. DID I MISS SOMETHING?

MS. MORALEZ: FRED FISHER JUST ENTERED.

CHAIRMAN GOLDSTEIN: OKAY. GOOD. WELCOME, FRED.

LET ME JUST GIVE YOU A BRIEF BIT OF CONTEXT SETTING BEFORE HEARING FROM OUR GUESTS TODAY. YOU WILL RECALL FROM OUR CHARGE THAT WE HAVE A COUPLE OF GOALS. ONE IS TO DEVELOP A GENERAL PLAN FOR THE $1.5 BILLION NEURO PLUS SET-ASIDE. SECOND IS, WHERE POSSIBLE, WE WANT TO IDENTIFY UNUSUAL OPPORTUNITIES WHERE WE MIGHT GET A LOT OF BANG FOR OUR BUCK OR HIGH IMPACT. AND THIRD, WE HAVE TO DO AT LEAST SOME PORTFOLIO ANALYSIS SO WE KNOW WHERE WE ARE IN ORDER TO DECIDE WHAT WE WANT TO DO IN A PLAN.

NOW, YOU WILL RECALL FROM THE NEUROPSYCHIATRIC DISCUSSIONS THAT WE USED DALY'S, DISABILITY-ADJUSTED LIFE YEARS, AS A PROXY FOR SOME OTHER METRICS, BUT DETAILS REVEALED PRETTY CLEARLY THAT NEUROPSYCHIATRIC HAS A BIG BURDEN. FRED FISHER, HOWEVER, POINTED OUT, CORRECTLY, I THINK, THAT DALY'S REALLY UNDERVALUE DISORDERS LIKE ALS OR FTD WHERE EARLY MORTALITY IS PART OF THE PICTURE.

SO IN ORDER TO GET SOME IDEA OF WHERE WE STAND WITH RESPECT TO DISORDERS THAT DO HAVE EARLY



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MORTALITY, WE'VE ASKED FOLKS FROM THE SCHAEFFER CENTER, AND THEY'LL BE REPRESENTED ABLY BY SETH SEABURY IN A MOMENT, TO HELP US THINK ABOUT OTHER WAYS OF EVALUATING DISEASE IMPACT SO THAT IF WE IDENTIFY A DISEASE THAT IS REALLY UNDERRESOURCED, HAS SIGNIFICANT SCIENTIFIC AND MEDICAL OPPORTUNITY, SAY, WE CAN IDENTIFY THAT AND GET TO WORK ON FINDING WAYS TO IMPROVE ITS FUNDING.

SO THAT BRINGS US TO OUR SET OF GUESTS TODAY FROM THE SCHAEFFER CENTER, THEY DID SOME OF THE ECONOMIC ANALYSIS FOR BOTH PROP 71 AND PROP 14, TO GIVE AN IDEA OF THE FINANCIAL IMPACT OF THOSE FUNDING INITIATIVES. AND WE'VE ASKED THEM TO COME TODAY AND, AS I SAID, THEY'LL BE REPRESENTED BY SETH SEABURY, WHO'S A PROFESSOR AT USC AND IN THE SCHAEFFER CENTER, TO GIVE US SOME IDEA OF LOOKING AT DISEASE IMPACT IN SOME OTHER WAYS FROM DETAILS IN PARTICULAR METHODOLOGIES THAT SCORE MORE ACCURATELY BURDENS ON MORTALITY.

AND SO SETH SEABURY, I THINK, IS GOING TO BE THE LEAD SPEAKER FROM THIS GROUP. I'VE ASKED THEM TO PRESENT FOR ABOUT 30 MINUTES, AND THEN WE'LL HAVE 15 MINUTES OR SO OF DISCUSSION BEFORE MOVING ON TO ANOTHER TOPIC THAT WAS REQUESTED BY A COUPLE OF TASK FORCE MEMBERS, WHICH IS WHAT ARE GOOD

METHODOLOGIES WE CAN USE FOR TRACKING WHETHER WE ARE ON TARGET TO AWARD THE APPROPRIATE AMOUNT OF THE ONE AND A HALF BILLION OVER TIME.

SO WITH THAT, I THINK WE'RE GOING TO SURRENDER OUR SCREENS TO SETH SEABURY. I KNOW I SAW HIM HERE A MOMENT AGO. SETH, IF YOU'LL TAKE OVER THE MICROPHONE, WE CAN GET GOING. SO SETH SEABURY.

DR. SEABURY: THANKS FOR HAVING ME HERE. CAN YOU ALL SEE MY SLIDES?

I FIRST WANT TO SAY THANK YOU ALSO TO MY COLLEAGUE BRYAN TYSINGER IS HERE FROM THE SCHAEFFER CENTER AS WELL. BRYAN LEADS OUR MICROSIMULATION GROUP, SO HE CAN CORRECT ANY OF THE MISTAKES THAT I MAKE HERE.

AND SO I JUST WANT TO POINT OUT THIS IS -- THERE HAVE BEEN A COUPLE OF VERSIONS OF THIS PRESENTATION THAT HAVE BEEN POSTED. I BELIEVE THE NEWEST VERSION EITHER IS POSTED OR WILL BE SOON; BUT IF THERE'S ANY DIFFERENCE BETWEEN WHAT YOU MIGHT HAVE SEEN PRIOR TO THAT, A LOT OF THE WORK THAT THIS PRESENTATION IS BASED OFF ON WAS FOCUSED MORE ON BEHAVIORAL HEALTH. SO WE MADE A FEW UPDATES TO KIND OF HIGHLIGHT THE RELEVANCE FOR NEURODEGENERATIVE DISORDERS. BUT I AM TALKING ABOUT THE VALUE OF OUR -- TRYING TO THINK THROUGH HOW TO VALUE RESEARCH

AND DEVELOPMENT FOR DISORDERS OF THE CENTRAL NERVOUS SYSTEM.

JUST TO PROVIDE SOME DISCLOSURES UP FRONT, THE STUDIES THAT I'M GOING TO BE TALKING ABOUT HERE HAD FUNDING FROM A VARIETY OF SOURCES, INCLUDING THE NATIONAL INSTITUTE ON AGING, BUT AS WELL SOME PRIVATE SOURCES, SUCH AS VERILY LIFE SCIENCES, OTSUKA PHARMACEUTICAL, LUNDBECK, ALKERMES. AND ALSO I'VE HAD SOME CONSULTING WORK IN THE PAST WITH BRISTOL MEYERS SQUIBB, PRECISION HEALTH ECONOMICS, AND ENTITYRISK.

ALL RIGHT. SO I'M GOING TO GO REALLY QUICKLY ABOUT JUST A BRIEF OVERVIEW OF THE SCHAEFFER CENTER IF PEOPLE AREN'T FAMILIAR. EVERYTHING I'M GOING TO TALK ABOUT IS UP ON OUR WEBSITE. HAPPY TO ANSWER ANY QUESTIONS, BUT I DO WANT TO JUMP TO THE CONTENT AS QUICKLY AS POSSIBLE. BUT WE ARE A HEALTH POLICY INSTITUTE LOCATED AT USC. WE BRING IN FACULTY MEMBERS AND SCHOLARS FROM ACROSS THE UNIVERSITY. SO I'M A HEALTH ECONOMIST, BUT I WORK WITH MD'S, PHARMACISTS, PEOPLE FROM OUR POLICY SCHOOL, FROM THE ENGINEERING SCHOOL, GERONTOLOGY, ECONOMICS. SO WE REALLY TRY TO TAKE ADVANTAGE OF THE WIDE RANGE OF THOUGHT LEADERS WE HAVE AT THE UNIVERSITY. WE ALSO HAVE A NUMBER OF EXTERNAL



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COLLABORATORS WE WORK WITH. SO PEOPLE FROM LEADING INSTITUTIONS ACROSS THE WORLD, OTHER LEADING RESEARCH INSTITUTIONS HERE IN THE U.S., AND, OF COURSE, A NUMBER OF PUBLIC PARTNERS WE'VE WORKED WITH IN THE PAST HERE IN CALIFORNIA. WE WORK CLOSELY HERE IN L.A. WITH THE COUNTY DEPARTMENT OF PUBLIC HEALTH AND WORKED WITH THE STEINBERG INSTITUTE. OF COURSE, HAVE DONE WORK IN THE PAST FOR CIRM.

SO THE GOAL OF THE SCHAEFFER CENTER IS TO IMPROVE HEALTH, AND BY IMPROVING HEALTH POLICY USING EVIDENCE-BASED SOLUTIONS THAT ARE REALLY DRIVEN BY OUR RESEARCH. AND WE SEEK TO IMPROVE VALUE IN HEALTHCARE DELIVERY.

AND SO PART OF THAT IN SORT OF THINKING ABOUT WHAT I'M GOING TO BE TALKING ABOUT TODAY IS THINKING ABOUT HEALTH AND HEALTH EXPENDITURES AS INVESTMENTS, NOT JUST EXPENSES. AND INVESTMENTS THAT SHOULD BE JUDGED BY THE IMPROVED OUTCOMES THAT THEY GENERATE OVER THE LONG TERM. AND SO WE REALLY TRY TO THINK OF COST-EFFECTIVE SOLUTIONS ON HOW TO GET BOTH, PROMOTE INNOVATION IN HEALTHCARE AND INNOVATION IN HEALTHCARE DELIVERY.

OKAY. SO HAPPY TO TALK IF PEOPLE HAVE OTHER QUESTIONS ABOUT THE CENTER, HAPPY TO TALK

ABOUT THAT IN THE Q AND A, BUT LET'S GET TO THE MEAT OF THE TALK.

KIND OF WANT TO DO TWO THINGS. FIRST, I WANT TO TALK ABOUT PRIVATE R&D FUNDING AND SOME OF THE BARRIERS IN THIS AREA IN THE PRIVATE SECTOR AND WHY WE THINK PUBLIC INVESTMENT AND INNOVATION HERE IS SO IMPORTANT. AND THEN WE'LL TALK ABOUT SOME GENERAL LESSONS FOR HOW TO VALUE R&D SPENDING AND GIVE A COUPLE OF EXAMPLES OF OUR MODELING APPROACHES.

I KNOW THAT THE GOAL IS FOR ME TO TALK FOR A BIT AND HAVE A Q AND A. BUT I ALSO DON'T WANT PEOPLE TO SIT THERE IF THEY DON'T UNDERSTAND SOMETHING OR THEY HAVE SOME QUESTIONS. PLEASE I'M FINE WITH BEING INTERRUPTED AS WE GO. AND I DO JUST KIND OF WANT TO SAY GENERALLY A LOT OF THE PRIOR WORK THIS IS BASED OFF OF WAS FOCUSED ON MENTAL AND BEHAVORIAL HEALTH CONDITIONS, BUT I DO HAVE SOME EXAMPLES FOCUSED ON NEURODEGENERATIVE CONDITIONS. BUT WHEN I TALK ABOUT THIS SPACE, I'M REALLY JUST TALKING ABOUT DISORDERS OF THE CENTRAL NERVOUS SYSTEM BROADLY, ALL THE METHODS. ANYTHING THAT I'M TALKING ABOUT WITH MENTAL HEALTH WILL GENERALLY APPLY TO OTHER DISEASE AREAS AS WELL. BUT WE CAN TALK AGAIN MORE ABOUT THAT IF THERE ARE QUESTIONS.



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OKAY. SO JUST TO GIVE YOU SOME NUMBERS. WE WERE CURIOUS ABOUT UNDERSTANDING PRIVATE INVESTMENT DECISIONS FOR RESEARCH AND DEVELOPMENT IN THE CNS AREA, CENTRAL NERVOUS SYSTEM DISORDERS. AND SO ONE OF THE THINGS WE DID WAS WE COLLECTED SOME DATA ON ECONOMIC BURDEN. SO WHAT ARE THE COSTS THAT THE LITERATURE -- COST ESTIMATES THE LITERATURE HAS PRODUCED FOR BURDEN ACCORDING TO DIFFERENT DISEASE AREAS. AND SO WE FOUND SOME, USING LITERATURE REVIEW, WE FOUND ESTIMATES FOR DEMENTIA, EPILEPSY, SCHIZOPHRENIA, MAJOR DEPRESSION, AND BIPOLAR DISORDER. SO THESE ARE THE NEUROLOGICAL AND PSYCHIATRIC CONDITIONS WE FOCUSED ON. AND THEN WE COMPARED IT TO BURDEN ESTIMATES FOR SOME OTHER COMMON CHRONIC DISEASES, COPD, DIABETES, RHEUMATOID ARTHRITIS, CARDIOVASCULAR DISEASE, AND THEN WE ALSO COMPARED IT TO CANCER.

AND AS YOU CAN SEE, THESE ARE THE ANNUAL PER-PATIENT BURDEN ESTIMATES. SO THE COST FOR A RANDOMLY SELECTED PATIENT IN THIS AREA THAT THE ESTIMATED ANNUAL BURDEN THAT THEY EXPERIENCE AS A RESULT OF DISEASE. AND YOU CAN SEE, LOOKING AT THE CNS CONDITIONS TO THE NON-CNS CONDITIONS, THE AVERAGE PER-PATIENT BURDEN ESTIMATES ARE QUITE HIGH. SO YOU SEE HIGH BURDEN OF DISEASE IN DEMENTIA, OVER



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60,000 PER YEAR; SCHIZOPHRENIA, CLOSE TO 35,000; AND THEN OTHER CONDITIONS CLOSE TO 20 OR 10,000 PER YEAR. AND WE COMPARED THAT TO THE OTHER CONDITIONS. THESE ARE OBVIOUSLY SERIOUS DISEASES AND IMPOSE SIGNIFICANT COST ON PEOPLE, BUT ON A PER-PATIENT BASIS, THESE NUMBERS HIGHLIGHT THAT THE CNS CONDITIONS ARE QUITE SEVERE.

AND NOW SO PER-PATIENT, THINKING ABOUT THE COST FOR AN INDIVIDUAL PATIENT IS ONE WAY OF LOOKING AT THIS. YOU CAN ALSO THINK AT THE POPULATION LEVEL. WHAT'S THE COST GENERATED BY THE DISEASE? AND SO WE LOOKED AT THE TOTAL ANNUAL BURDEN AND COMPARED ACROSS THE SAME DISEASES. AND SO ONE OF THE THINGS, JUST THINKING WITH THE DIFFERENCE BETWEEN THESE TWO SLIDES, SO IF YOU LOOK AT CARDIOVASCULAR DISEASE HERE, THE PER-PATIENT BURDEN ESTIMATE WAS ABOUT $5,000 PER PATIENT. SO IT WAS AMONG OF THE LOWER IN TERMS OF PER-PATIENT COST, BUT IT'S AN EXTREMELY PREVALENT CONDITION. SO WHEN I LOOK AT THE ACTUAL TOTAL COST AT THE POPULATION LEVEL, WE ARE TALKING CLOSE TO 500 BILLION PER YEAR. SO JUST UNDERSTANDING HOW PREVALENCE AND THE PER-PATIENT COST WORK TOGETHER TO GENERATE THESE NUMBERS.

BUT WHAT YOU CAN SEE IS THAT EVEN THOUGH



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SOME OF THE CONDITIONS WE'RE FOCUSED ON, SOMETHING LIKE SCHIZOPHRENIA IS A VERY UNCOMMON DISEASE, THE PER-PATIENT COSTS ARE SO HIGH THAT WHEN WE LOOK AT THE TOTAL BURDEN ESTIMATES, THEY'RE STILL VERY SIGNIFICANT. AND YOU CAN SEE THAT'S THE CASE IN GENERAL.

ONE OF THE THINGS I DID WANT TO NOTE IS YOU MIGHT HAVE BEEN SURPRISED THE CANCER NUMBER HERE IS SO LOW. JUST WANT TO POINT OUT THERE'S A COUPLE THINGS GOING ON THERE. SOME OF THE BURDEN ESTIMATES IN THE LITERATURE DON'T DO A GOOD JOB OF DEALING WITH THE COST OF PREMATURE MORTALITY. SO IF YOU JUST LOOK AT THE ACTUAL IMPACT ON A CANCER PATIENT, THE BURDEN ESTIMATES CAN BE RELATIVELY LOW BECAUSE THE ESTIMATES AREN'T INCORPORATING MORTALITY. SO I DO WANT TO POINT THAT OUT. THAT'S ONE OF THE IMPROVEMENTS THAT I THINK OUR METHODS INCORPORATE.

SO WHAT WE DID IS THEN -- AS I SAID, THE GOAL OF THIS WAS TO THINK ABOUT R&D EXPENDITURES. SO WHAT WE WANT TO DO IS TO ASSESS THE INVESTMENT BY PRIVATE COMPANIES IN THESE DISEASE AREAS RELATIVE TO THE ACTUAL BURDEN THAT PATIENTS EXPERIENCE. IF YOU THINK OF THE BURDEN AS A MEASURE OF THE SOCIETAL COST OF THE CONDITION, THEN WE MIGHT THINK THAT WE WOULD INVEST SIGNIFICANT FUNDING IN IMPROVING

OUTCOMES FOR SUCH COSTLY CONDITIONS. BUT WHAT WE ACTUALLY FOUND WHEN WE COMPARED THE R&D EXPENDITURES BY THE MARKET, AND THESE ARE ESSENTIALLY PUBLICLY REPORTED R&D EXPENDITURES FOR PHARMACEUTICAL COMPANIES, WHICH IS WHERE WE GOT THE R&D NUMBERS FROM, YOU CAN SEE THAT ACTUALLY THE CNS CONDITIONS, NEUROLOGY, NEUROLOGICAL DISORDERS, SCHIZOPHRENIA, MAJOR DEPRESSION, BIPOLAR, THE ACTUAL SPENDING PER ESTIMATED DOLLAR OF BURDEN IS QUITE LOW. AND CANCER IS A BIT OF AN OUTLIER. I THINK THAT'S, AS I SAID, BECAUSE OF THE ISSUES WITH EVALUATING THE IMPACT ON MORTALITY ON BURDEN. BUT EVEN IF YOU DON'T FOCUS ON CANCER AND LOOK AT THE OTHER CONDITIONS, YOU CAN SEE COPD, RHEUMATOID ARTHRITIS, YOU'RE SEEING MORE R&D EXPENDITURES PER DOLLAR OF ECONOMIC BURDEN BY A WIDE RANGE THAN YOU SEE FOR THESE OTHER CNS CONDITIONS.

I'M NOT HERE TO MAKE THE POINT, I'M NOT TRYING TO -- THERE'S OBVIOUSLY GOOD REASONS TO INVEST MONEY IN IMPROVING OUTCOMES FOR CANCER PATIENTS. SO THIS ISN'T HERE TO TRY TO SAY, OH, WE ARE SPENDING TOO MUCH ON THESE OTHER CONDITIONS. BUT IT'S HELPFUL TO UNDERSTAND WHY WE ARE SEEING RELATIVELY LOW LEVELS OF INVESTMENT IN THESE NEUROLOGICAL CONDITIONS GIVEN HOW SEVERE THEY ARE.

AND SO THERE ARE A COUPLE OF AREAS THAT WE



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THOUGHT LED TO A COUPLE OF SIGNIFICANT BARRIERS THAT LED TO DISINCENTIVIZE PRIVATE INVESTMENT IN THIS AREA. ONE IS JUST THE DEGREE OF SCIENTIFIC UNCERTAINTY. THIS IS A HARD SPACE TO WORK IN. THERE'S A LOT WE DON'T KNOW ABOUT THE WAY THAT THE BRAIN WORKS, THE NERVOUS SYSTEM WORKS. AND SO WHAT YOU SEE IS THAT, WHEN YOU LOOK AT PRODUCTS THAT REACH A CERTAIN STAGE OF DEVELOPMENT AND THEY BRING THESE PRODUCTS TO THE TRIAL PHASE, THE ACTUAL SUCCESS RATE OF STARTING THE TRIAL TO GETTING MARKET APPROVAL IS ONLY 6.2 PERCENT FOR CNS -- FOR DRUGS TREATING CNS-RELATED DISORDERS. AND THAT'S COMPARED TO 13.2 PERCENT FOR THE NON-CNS PRODUCTS. SO THE ACTUAL SUCCESS RATE OF TAKING MY DRUG DISCOVERY TO MARKET IS LESS THAN HALF FOR A CNS-RELATED PRODUCT THAN A NON-CNS PRODUCT. SO FROM THE STANDPOINT OF PRIVATE INVESTORS THINKING ABOUT WHERE TO DEDICATE THEIR R&D FUNDS, THIS IS A MUCH RISKIER SPACE TO OPERATE IN, WHICH IS GOING TO POTENTIALLY DISINCENTIVIZE INVESTMENT.

THE OTHER THING, WE ALSO NOTICED SOME MARKET CHALLENGES THAT CAN BE PARTICULAR TO THIS AREA. NOW, AGAIN, FOCUSING MORE ON THE PSYCHIATRIC SIDE AND BEHAVORIAL HEALTH, ONE OF THE ISSUES THAT WAS PARTICULARLY RELEVANT HERE IS THE PATIENTS WITH



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PSYCHIATRIC DISORDERS, THE NATURE OF THE DISEASE IS SUCH THAT IT'S HARD TO HOLD DOWN A JOB IN THE U.S., PRIVATE INSURANCE IS TIED TO EMPLOYMENT TYPICALLY. SO PATIENTS WITH PSYCHIATRIC DISORDERS ARE DISPROPORTIONATELY LIKELY TO WIND UP UNINSURED OR COVERED BY MEDICAID, WHICH IS IN GENERAL. IT'S BASICALLY A LESS PROFITABLE PATIENT POPULATION TO PROVIDE TREATMENT FOR.

SO, AGAIN, AS AN INVESTOR THINKING ABOUT WHERE TO DIRECT FUNDING TO GENERATE FUTURE RETURNS, THIS IS A RISKY SPACE AND POTENTIALLY A LESS PROFITABLE SPACE.

NOW, SOMETHING LIKE ALZHEIMER'S WHERE MOST OF THE PATIENTS ARE COVERED BY MEDICARE, THE INSURANCE ISN'T MUCH OF AN ISSUE; BUT MANY OF THE NEURODEGENERATIVE CONDITIONS ARE RELATIVELY RARE AND COULD HAVE UNCERTAIN MARKETS. SO WHEN YOU COMBINE RISKY, RELATIVELY LOW SUCCESS RATES, SO HIGH DEGREE OF RISK, WITH POTENTIAL SMALLER MARKETS OR MARKETS WITH LESS HEALTH COVERAGE, THEN YOU JUST GET IN GENERAL -- IT'S A LESS APPEALING AREA FOR A PRIVATE INVESTOR.

SO WHAT DOES THAT MEAN? IT MEANS WE HAVE A SET OF CONDITIONS THAT IMPOSE SIGNIFICANT BURDEN ON PATIENTS, BUT IT'S AN AREA WHERE PRIVATE MARKETS



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ARE LESS WILLING TO STEP INTO TO PROVIDE FUNDING. THIS GENERATES A LOT OF POTENTIAL VALUE FOR PUBLIC INVESTMENTS IN PROMOTING INNOVATION. AND SO WE THINK THIS IS AN AREA WHERE A PLACE LIKE CIRM OR NIH OR PUBLIC FUNDERS OF RESEARCH, THIS IS AN AREA WHERE IT'S PARTICULARLY NEEDED BECAUSE IT CAN FUND INNOVATIONS THAT HELP PATIENTS NOW, BUT HOPEFULLY IT CAN FUND INNOVATIONS THAT ALSO MAYBE CAN HELP IMPROVE THE 6.2 PERCENT SUCCESS RATE. AND SO NOT JUST PROMOTE NEW DRUGS THAT HELP PATIENTS OR NEW TREATMENT OPTIONS FOR PATIENTS, BUT ALSO HELPS SPUR FUTURE PRIVATE INVESTMENT.

SO THAT'S WHAT I HAD TO TALK ABOUT FOR BARRIERS. SO IF THERE ARE NO QUESTIONS ON THAT, I'LL MOVE AHEAD TO TALK ABOUT FRAMEWORK FOR VALUING R&D SPENDING.

SO BASED ON MAKING THE CASE THAT THIS IS AN AREA WHERE WE THINK PUBLIC INVESTMENT IN RESEARCH COULD BE POTENTIALLY HIGHLY IMPACTFUL, BUT WHAT WE'D ALSO LIKE TO DO IS HAVE A BETTER UNDERSTANDING OF HOW TO QUANTIFY THE BENEFITS OF THAT R&D. AND YOU CAN THINK OF THAT FOR A COUPLE OF DIFFERENT REASONS WHY YOU MIGHT WANT TO DO THAT. ONE IS RETROSPECTIVELY TO LOOK BACK, UNDERSTAND WHEN WE INVEST OUR MONEY IN THE PAST, WHAT KIND OF RETURNS



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DID WE GET? DID WE ALLOCATE THAT MONEY APPROPRIATELY? AND ALSO PROSPECTIVELY THINKING ABOUT, WELL, WHAT ARE THE AREAS THAT HAVE THE BIGGEST POTENTIAL RETURNS FOR A GIVEN TYPE OF INNOVATION?

AND SO PART OF WHAT THIS MEANS IS THINKING ABOUT RESEARCH FUNDING OR RESEARCH AND DEVELOPMENT FUNDS AS AN INVESTMENT. AND SO THE DISCUSSION WE JUST HAD, WE THINK THAT THE BENEFITS OF IMPROVING OUTCOMES FOR INDIVIDUALS WITH NEUROLOGICAL AND PSYCHOLOGICAL DISORDERS ARE POTENTIALLY QUITE LARGE. WE SAW TENS, HUNDREDS OF BILLIONS OF DOLLAR PER YEAR IN ECONOMIC BURDEN THAT HOPEFULLY THAT WE COULD ALLEVIATE WITH NEW TREATMENT OPTIONS, NEW INNOVATIONS. BUT THE BENEFITS ARE DIFFUSE IN THE SENSE THAT THEY GO TO A LOT OF DIFFERENT PEOPLE AND THEY CAN BE REALIZED OVER A LONG TIME HORIZON. SO FOR PSYCHOLOGICAL DISORDERS WHERE PEOPLE OFTEN CHANGE INSURERS OR JUST IN GENERAL IN THE U.S. SYSTEM WHERE THERE'S A LOT OF CHURN ACROSS DIFFERENT PAYERS, THE POTENTIAL BENEFITS OF IMPROVING OUTCOMES FOR PATIENTS IS THEY'RE COST SAVING. THOSE COSTS AREN'T NECESSARILY GOING TO GO TO HELP TODAY'S PAYER.

A LOT OF THE COSTS THAT ACTUALLY ARE

GENERATED BY THESE DISEASES ARE NOT NECESSARILY HEALTHCARE COSTS OR ONLY COSTS. THEY COULD ACCRUE OUTSIDE THE HEALTHCARE SYSTEM. SO IF YOU IMPROVE OUTCOMES FOR NEURODEGENERATIVE CONDITIONS, ONE OF THE BIG BENEFITS THAT'S GOING TO HAPPEN FROM THAT WOULD BE A REDUCTION IN CAREGIVER BURDEN. AND CAREGIVER BURDEN IS NOT SOMETHING THAT'S DIRECTLY RECOGNIZED BY THE HEALTHCARE SYSTEM.

AND FOR SOME OF THESE CONDITIONS THAT AFFECT PEOPLE OVER THE COURSE OF THEIR LIFE, THEN THESE BENEFITS ARE POTENTIALLY REALIZED WITH A VERY LONG TIME HORIZON. WHEREAS, MOST CLINICAL TRIALS, MOST OTHER KIND OF DATA SOURCES REALLY FOCUS ON NARROW TIME WINDOWS. AND FROM THE STANDPOINT OF SOMETHING LIKE A NEURODEGENERATIVE CONDITION OR SOMETHING THAT REDUCES A PATIENT'S LIFE EXPECTANCY, THEN YOU HAVE TO CONSIDER NOT JUST WHAT HAPPENS TO A PATIENT WHILE THEY'RE ALIVE, BUT WOULD HAVE HAPPENED HAD THE PATIENT SURVIVED, AND YOU NEED TO INCORPORATE THAT INTO THE VALUE CALCULATION.

AND PART OF THE PROBLEM IS EVERYTHING I'M SAYING IT MEANS TAKE THE VALUE CALCULATION IS COMPLEX AND HARD TO DO, WHICH MEANS THE INDIVIDUAL AGENTS OR AGENCIES MAY NOT RECOGNIZE THE BENEFITS OF TREATMENT INNOVATIONS. AND THAT TENDS TO LEAD TO A



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FOCUS ON COSTS. AGENCIES FOCUS ON BUDGETS. BUDGETS ARE DONE FOR THE FISCAL YEAR. AND THERE REALLY USUALLY ISN'T THAT KIND OF LONG-TERM THINKING IN TERMS OF THE POTENTIAL BENEFITS FOR -- THIS IS PARTICULARLY TRUE WHEN YOU THINK ABOUT ACCESS DECISIONS BY PAYERS, BUT IT CAN ALSO BE TRUE FOR PEOPLE THINKING ABOUT HOW TO VALUE AN INNOVATION OR AN INVESTMENT.

SO JUST TO KIND OF DOUBLE DOWN ON THIS POINT, THAT THE VALUE OF INNOVATION IS COMPLICATED, RESEARCH AT THE SCHAEFFER CENTER AND ELSEWHERE HAVE PUT A LOT OF THOUGHT INTO UNDERSTANDING HOW YOU CAN MEASURE AND QUANTIFY THE VALUE OF IMPROVED HEALTHCARE. AND SO THIS CHART IS ONE WE LIKE TO SHOW THAT JUST KIND OF SHOWS SOME COMMON AND LESS COMMON ELEMENTS OF POTENTIAL VALUE. SO THERE'S KIND OF TWO KIND OF CORE ELEMENTS HERE, THE QALY'S, THE QUALITY-ADJUSTED LIFE YEARS, AND NET COSTS. YOU CAN MAKE A SIMILAR ARGUMENT IF YOU SUBSTITUTED QALY'S FOR DALY'S. SO THE QALY'S ARE MORE COMMONLY USED IN HEALTH TECHNOLOGY ASSESSMENT DECISIONS.

BUT THE SORT OF STANDARD APPROACH TO COST-EFFECTIVENESS ANALYSIS HAS LOOKED AT A MEDICAL TREATMENT, COMPARED THE QUALITY-ADJUSTED LIFE YEARS GAINED THROUGH THE TREATMENT, APPLIED SOME DOLLAR



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VALUE TO THAT, PARTICULARLY SOMETHING IN THE RANGE OF A $100,000 PER QUALITY GAINED, AND THEN LOOKED AT THE COST OF TREATMENT AND THEN TRIED TO ASSESS WHETHER THE TREATMENT PROVIDES VALUE BASED ON WHETHER THE QUALITY GAINED TIMES A 100,000 EXCEEDS THE COST.

BUT THEN THE PROBLEM WITH THAT IS IT'S A VERY LIMITED APPROACH TO ASSESSING THE VALUE OF TREATMENT. AND THERE ARE MANY OTHER WAYS IN WHICH IMPROVED TREATMENT COULD AFFECT PEOPLE AND IMPROVE THEIR LIVES.

SO SOME COMMONLY USED, BUT INCONSISTENTLY USED MEASURES OF VALUE INCLUDE PRODUCTIVITY. SO IF YOUR HEALTH IMPROVES YOUR ABILITY TO FUNCTION IN THE LABOR FORCE, THEN THOSE ADDITIONAL EARNINGS THAT YOU GET AS WELL AS THE ECONOMIC ACTIVITY THAT YOU GENERATE FOR YOUR EMPLOYER ARE ELEMENTS OF VALUE THAT ARE IMPORTANT, BUT ARE NOT ALWAYS CAPTURED.

JUST ONE THING ELSE ABOUT THE CHART. THE BLUE LINES REPRESENT THINGS THAT ARE CAPTURED BY THE HEALTHCARE SYSTEM WHILE THE RED LINES REPRESENT THINGS THAT ARE NOT CAPTURED BY HEALTHCARE.

PAYERS WILL VALUE SOMETIMES THINGS THAT IMPROVE ADHERENCE. SO, FOR EXAMPLE, IF A PILL HAS TO ONLY BE TAKEN ONCE A DAY AS OPPOSED TO THREE OR

FOUR TIMES A DAY, WE TEND TO GET BETTER ADHERENCE. AND SO PAYERS WILL VALUE THAT POTENTIALLY, BUT THAT'S NOT ALWAYS CONSIDERED IN COST-EFFECTIVENESS DECISIONS.

AND THEN YOU HAVE ALL THESE OTHER ELEMENTS OF VALUES OF THINGS THAT ARE THINGS THAT ARE IMPORTANT TO PEOPLE THAT ARE TYPICALLY NOT RECOGNIZED. THINGS LIKE THE VALUE OF HOPE, THE INSURANCE VALUE PROVIDED, REDUCTIONS IN UNCERTAINTY. THESE ARE ALL THINGS THAT IMPROVE A PERSON'S QUALITY OF LIFE POTENTIALLY AND GENERATE VALUE FROM TREATMENT, BUT ARE NOT USUALLY RECOGNIZED BY PAYERS.

SO WHAT THIS MEANS -- AND THE CHALLENGE HERE, REALLY A LOT OF THE GOAL OF HEALTH ECONOMICS IS TO COME UP WITH AN UNDERLYING ECONOMIC FRAMEWORK TO BETTER QUANTIFY THE VALUES THAT ARE GENERATED BY NOVEL TREATMENTS AND TREATMENT OPTIONS.

AND SO AT THE SCHAEFFER CENTER, ONE OF THE KEY TOOLS THAT WE USE TO DO THIS IS WHAT'S CALLED MICROSIMULATION. AND SO IN THE SCHAEFFER CENTER REALLY GOING BACK TO 2004 BEGINNING WITH SOME OF THE FOUNDING MEMBERS OF THE CENTER, THEY'VE USED MICROSIMULATION TO ADDRESS A NUMBER OF POLICY QUESTIONS.

I'M GOING TO BE TALKING ABOUT RESULTS FROM



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TWO MODELS, THE FUTURE ELDERLY MODEL, WHICH IS THE ORIGINAL MICROSIMULATION MODEL GENERATED BY SCHAEFFER CENTER RESEARCHERS, AND THEN THE SORT OF EXPANSION, THE FUTURE ADULT MODEL. I'LL GIVE SOME MORE DETAIL, BUT THIS WAS DEVELOPED WITH SUPPORT FROM NIA. IT'S BEEN USED TO STUDY INNOVATIONS, TREATMENT OPTIONS, PUBLIC HEALTH QUESTIONS, INCLUDING AGING, EARLY CHILDHOOD INVESTMENTS, SERIOUS MENTAL ILLNESS, OBESITY, CARDIOVASCULAR RISK. IT REALLY APPLIES TO A HOST OF TEXT CONDITIONS, REALLY ANYTHING THAT WE ARE ABLE TO GET DATA THAT WE ARE ABLE TO LINK BACK TO THE MODEL.

SO WHY DO WE USE MICROSIMULATION? WE'VE BEEN ABLE TO USE THIS TO TACKLE A NUMBER OF IMPORTANT QUESTIONS FACING THE FUTURE OF THE HEALTHCARE SYSTEM IN THE U.S., INCLUDING BURDEN OF DISEASE, DISPARITIES IN ACCESS TO CARE, RISING HEALTHCARE COSTS, THE IMPLICATIONS FOR GOVERNMENT PROGRAMS, SUCH AS DISABILITY PROGRAMS, PUBLIC HEALTH INSURERS, PUBLIC PAYERS.

NOW, THESE ARE COMPLEX PROBLEMS BECAUSE YOU HAVE MULTIPLE PROCESSES, BEHAVIORS ALL MOVING AT THE SAME TIME. SO WHAT THE MICROSIMULATION MODELS ALLOW US TO DO IS TO PROJECT FUTURE RISK FACTORS, TO UNDERSTAND CHANGES IN POPULATION HEALTH, AND THEN



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UNDERSTAND HOW THESE FACTORS WORK TOGETHER WITH A DATA-DRIVEN METHODOLOGY.

SO I'M USING THIS WORD "MICROSIMULATION," WHAT DOES IT MEAN? MICROSIMULATION MODELS CAPTURE INTERACTIONS BETWEEN MULTIPLE PROGRAMS AND POLICIES AND BASICALLY ALLOW US TO CREATE WHAT-IF HYPOTHETICAL SCENARIOS AND ESTIMATE HOW DEMOGRAPHIC, BEHAVORIAL, OTHER POLICY CHANGES IMPACT INDIVIDUAL AND SOCIETAL OUTCOMES. AND SO BY POLICY CHANGE, THAT'S BROADLY DEFINE. SO AN INNOVATION, A MEDICAL INNOVATION THAT LEADS TO A NEW TREATMENT THAT EITHER REDUCES THE SEVERITY OF DISEASE, REDUCES THE INCIDENCE OF DISEASE, WE CAN MODEL THAT THE WAY WE WOULD MODEL POLICY CHANGE.

SO AS I SAID, I'M GOING TO TALK ABOUT THE RESULTS OF TWO MODELS. THERE'S THE FUTURE ELDERLY MODEL, WHICH WAS DEVELOPED FOR A POPULATION AGED 51 PLUS. THIS IS CENTERED AROUND A DATASET CALLED THE HEALTH AND RETIREMENT STUDY, WHICH IS A PANEL STUDY THAT PROVIDES THE FOUNDATION FOR MUCH OF THE ANALYSES. IT'S OVER TEN YEARS OF MODEL DEVELOPMENT. IT'S BEEN APPLIED INTERNATIONALLY TO THE U.S., CALIFORNIA. REALLY BEEN ABLE TO APPLY IT AS BROAD AS THE COUNTRY LEVEL AND AS SPECIFIC AS AN INDIVIDUAL COUNTY.



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AND THEN THE FUTURE ADULT MODEL WAS DEVELOPED THAT EXTENDED THE MODEL TO LOOK AT PEOPLE NOT FOR AN AGING POPULATION, BUT GOING DOWN TO 25 PLUS. AND AGE 25 IS ABOUT WHEN PEOPLE TEND TO -- MOST PEOPLE HAVE COMPLETED THEIR EDUCATION, ENTERED THE LABOR FORCE. IT'S SORT OF A PERIOD OF WHERE THEIR LIVES ARE RELATIVELY MORE STABLE.

BEFORE MOVING ON, I DO WANT TO NOTE WE ARE NOT THE ONLY PEOPLE WHO DO MICROSIMULATION AT THE SCHAEFFER CENTER. WE ARE PROUD OF OUR CAPABILITIES HERE. THIS IS SOMETHING THAT OTHER INSTITUTIONS DO AS WELL. I'M GOING TO TALK MORE ABOUT THE SORT OF METHODOLOGY AS OPPOSED TO JUST OUR SPECIFIC MODELS.

LET ME GIVE YOU AN EXAMPLE WHERE WE USED THE FAM TO ESTIMATE THE LIFETIME BURDEN OF PATIENTS WHO SELF-REPORT BEING DIAGNOSED WITH SERIOUS MENTAL ILLNESS. SO THINKING OF SCHIZOPHRENIA, BIPOLAR DISORDER, OR MAJOR DEPRESSION BY AGE 25.

AND THE WAY WE DO THIS, USING THE MODELS, WE ESTIMATE THE LIFE TRAJECTORY OF HEALTH AND ECONOMIC OUTCOMES. SO WE SEE SOMEONE AGE 25, WE LOOK AT AS THEY AGE, WE SEE HOW THEIR HEALTH CHANGES, WHAT'S THE INCIDENCE OF DISEASE, WHAT'S THE PROBABILITY THAT THEY'RE WORKING, HOW MUCH DO THEY EARN, ALL THESE DIFFERENT FACTORS CONDITIONAL ON

DEMOGRAPHIC INFORMATION, EDUCATION, AND WE ARE ABLE TO ESTIMATE, BASICALLY SIMULATE A LIFETIME FOR SOMEONE AGED 25. AND THEN WHAT WE DO IS WE PROJECT SIMILAR TRAJECTORIES FOR THE OBSERVABLY SAME PERSON, BUT THEY WERE DIAGNOSED WITH SMI BY AGE 25. AND SO THE DIFFERENCE IN LIFE-TIME TRAJECTORIES REPRESENTS THE IMPACT OF THE DISEASE.

CHAIRMAN GOLDSTEIN: COULD YOU DEFINE SMI FOR THE GROUP PLEASE?

DR. SEABURY: YES. SO THIS IS THE TERM REALLY THAT IS USED TO REFER TO SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS, BIPOLAR DISORDER, AND MAJOR DEPRESSION DISORDER. SO IT'S NOT INCLUDING ALL DEPRESSION CASES. IT'S SPECIFICALLY DIAGNOSIS OF MAJOR DEPRESSION.

SO USING THE MODEL, THIS GIVES YOU AN EXAMPLE OF HOW WE GENERATE BURDEN ESTIMATES USING THE MODEL. SO THE GRAY BARS HERE REPRESENT THE PROJECTED OUTCOMES FOR A PERSON. AGAIN, SO THE IDEA BEING THIS WOULD BE A RANDOMLY SELECTED, A REPRESENTATIVE 25 YEAR OLD, AND THEN WHAT THAT INDIVIDUAL COULD EXPECT OVER THE COURSE OF THEIR LIFE. AND THE GRAY BAR REPRESENTS FOR SOMEONE WHO WAS NOT DIAGNOSED WITH SMI BEFORE AGE 25 COMPARED TO SOMEONE WHO WAS DIAGNOSED. SO TRYING TO UNDERSTAND



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THE LIFETIME IMPACT OF THE DISEASE ON THIS PATIENT POPULATION. AND.

SO WHAT THE GRAPH PRESENTS ON OUTCOMES. SO THE GRAY BAR REPRESENTS THE LIFE EXPECTANCY AT AGE 25 OF A PERSON. SO A LIFE EXPECTANCY OF 56 YEARS ESSENTIAL TO AGE 81 AND COMPARE THAT TO SOMEONE WITHOUT AN SMI DIAGNOSIS. AND YOU SEE THAT THE IMPACT ON THEIR LIFE EXPECTANCY IS HUGE, TEN YEARS OF LIFE.

NOW, IF WE DO QUALITY ADJUSTMENT, SO IN THE DATA WE HAVE THE SELF-REPORTED QUALITY OF LIFE MEASURES NEEDED TO DO AN ADJUSTMENT FOR QALY'S. AND YOU CAN SEE THE QUALITY-ADJUSTED LIFE YEAR IMPACT IS EVEN LARGER. SO ABOUT 11.6 FEWER QUALITY-ADJUSTED LIFE YEARS FOR SOMEONE WITH SMI. HALF AS MANY DISABILITY FREE LIFE YEARS. AND ALSO -- SO YOU CAN THINK OF THESE ARE HEALTH-RELATED IMPACTS. WE ALSO SEE SIGNIFICANT ECONOMIC IMPACTS AS WELL.

AS I MENTIONED, SMI IS PSYCHIATRIC CONDITIONS LIKE SMI HAVE A HUGE NEGATIVE IMPACT ON A PERSON'S ABILITY TO WORK. AND YOU SEE THAT A 25-YEAR-OLD WITH SMI CAN EXPECT TO WORK 15 FEWER YEARS IN THE LABOR MARKET. AND SO IF WE TRANSLATE THAT INTO LIFETIME EARNINGS, YOU SEE IT'S ALMOST CUT IN HALF, THEIR LIFETIME EARNINGS. SO HUNDREDS OF



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THOUSANDS OF ECONOMIC COSTS. SLIGHTLY HIGHER MEDICAL SPENDING.

YOU MIGHT BE SURPRISED THAT THE MEDICAL SPENDING DIFFERENCE ISN'T HIGHER; BUT ONE OF THE IMPACTS OF SMI'S, AS I SAID, IS YOU'RE MORE LIKELY TO BE UNINSURED OR MORE LIKELY TO BE ON MEDICAID, WHICH HAS LOWER REIMBURSEMENT RATES ON AVERAGE. SO THE IMPACT ON MEDICAL SPENDING IS LESS THAN WHAT YOU MIGHT THINK IT IS PROBABLY BECAUSE OF POOR ACCESS TO CARE.

SO THE POINT I WANT TO MAKE, LARRY AS MENTIONED AT THE START OF THE MEETING THAT THE IMPACT ON -- FOCUSING ON SOMETHING JUST LIKE DALY'S DOESN'T NECESSARILY INCORPORATE THE IMPACT OF LOSS OF LIFE. WHEREAS, IT'S NOT NECESSARILY A GOOD MEASURE OF COST FOR NEURODEGENERATIVE DISORDERS THAT DO LOWER LIFE EXPECTANCY. AND YOU CAN SEE THAT EVEN IN THE CASE OF SMI, THE ACTUAL -- ABOUT 63 PERCENT OF THE TOTAL LIFETIME PATIENT BURDEN COMES FROM THE DECLINE IN QUALITY-ADJUSTED LIFE YEARS. SO PART OF THAT IS THE REDUCTION IN THE QUALITY OF LIFE WHILE THE PERSON IS ALIVE. BUT AS WE SAW, SMI IS ASSOCIATED WITH SIGNIFICANT REDUCTIONS IN LIFE EXPECTANCY, TEN FEWER YEARS OF LIFE. AND SO WHEN YOU THINK ABOUT THE REDUCTION IN THE YEARS THAT YOU



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WOULD HAVE HAD, THE HEALTHY YEARS THAT YOU WOULD HAVE HAD IN THE ABSENCE OF THE CONDITION, THIS IS A SIGNIFICANT GENERATOR OF VALUE OR OF THE BURDEN OF DISEASE. AND SO THAT MEANS IT WOULD ALSO BE A SIGNIFICANT ELEMENT OF THE VALUE OF IMPROVING OUTCOMES FOR PATIENTS.

SO MOVING US A LITTLE BIT, ONE OF THE OTHER ADVANTAGES OF MICROSIMULATION IS NOT JUST -- SO BASICALLY WHAT WE JUST DID IS TO USE THE MODEL TO GENERATE BURDEN OF DISEASE ESTIMATES. BUT WHAT YOU CAN ALSO DO, ONE OF THE REAL STRENGTHS OF MICROSIMULATION IS BECAUSE YOU'RE DOING THESE HYPOTHETICAL WHAT-IF SCENARIOS, IT GIVES YOU THE OPPORTUNITY TO CHANGE THE MODEL PARAMETERS AND BY DOING SO SIMULATE THE POTENTIAL VALUE OF SOME NEW INNOVATION. SO, FOR EXAMPLE, IF YOU CHANGE RISK FACTORS, SO YOU CAN LOOK AT WHAT'S THE IMPACT OF INCREASING CIGARETTE TAXES ON SMOKING BEHAVIOR. AND THEN BY CHANGING THE FREQUENCY OF SMOKING IN THE MODEL, YOU'RE ABLE TO EVALUATE WHAT THAT IMPACT ON THE CHANGE IN TAXES WOULD DO IN TERMS OF THE COST OF SMOKING.

YOU CAN ALSO SIMULATE CHANGES IN POLICY CHARACTERISTICS. FOR EXAMPLE, SUPPOSE YOU CHANGE THE MEDICARE ELIGIBILITY AGE OR YOU CHANGE FEDERAL



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BENEFIT LEVELS. WHAT WOULD THE IMPACT BE ON ECONOMIC OUTCOMES FOR PATIENTS?

AND THEN YOU CAN THINK OF TREATMENT INNOVATIONS THAT IMPACT THE PREVALENCE OR SEVERITY OF DISEASE. SO, FOR EXAMPLE, IF YOU WERE TO CONSIDER SOME INNOVATION THAT DECREASED THE LIKELIHOOD OF DEVELOPING DISEASE, CURE THE DISEASE, OR WERE TO DELAY ONSET. SO EACH OF THESE PROVIDES THE OPPORTUNITY TO QUANTIFY THE POTENTIAL VALUE OF A NEW HEALTH INNOVATION.

SO I'M GOING TO TALK ABOUT AN EXAMPLE THAT WE LOOKED AT IN THE PAPER WHERE WE GENERATED THOSE BURDEN ESTIMATES I JUST TALKED ABOUT, WHICH WAS TO ASK WHAT IF EVERYONE WITH SMI RECEIVED A SUPPORTED EDUCATION PROGRAM? SO THIS IS INFORMATION MODELED ON USING DATA FROM WHAT'S CALLED THE RAISE-ETP CLINICAL TRIAL AT NIMH. SOME OF YOU MAY BE FAMILIAR WITH IT. IT WAS A VERY FAMOUS CLINICAL TRIAL. IT DID MANY THINGS, BUT ONE OF THE THINGS THAT THEY INCLUDED WAS INFORMATION ABOUT THE RECEIPT OF SUPPORTED EDUCATION PROGRAM TO HELP NEWLY -- NEW ONSET CASES OF PSYCHOTIC DISORDERS, PATIENTS RECEIVING -- IMPROVING THEIR EDUCATIONAL ATTAINMENT.

AND SO WHAT THAT MEANS IS THAT THE CLINICAL TRIAL DATA ACTUALLY INCLUDED INFORMATION ON



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EDUCATIONAL ATTAINMENT OF THE PARTICIPANTS. AND EDUCATIONAL ATTAINMENT IS SOMETHING THAT'S IN OUR DATA. SO WE ARE ACTUALLY ABLE TO MODEL WHAT THE IMPACT OF IMPROVED EDUCATIONAL ATTAINMENT IS ON AN SMI PATIENT. AND WHAT WE FOUND IS THAT IF YOU WERE TO SIMULATE THE EFFECTS OF THE PROGRAM, WHICH IS ABOUT A ONE-YEAR INCREASE IN EDUCATIONAL ATTAINMENT, THIS REDUCED THE ECONOMIC BURDEN TO INDIVIDUALS WITH SMI BY ABOUT 4 PERCENT. SO IT'S A SMALL IMPACT, BUT IT'S STILL AN IMPROVEMENT IN OUTCOMES FOR THESE PATIENTS OVER THE COURSE OF THEIR LIFE. AND WHEN COMPARED TO THE REPORTED DATA ON THE COST OF THE PROGRAM, IT WAS ABOUT A TWO TO ONE RETURN ON INVESTMENT. AND WE THOUGHT THIS WAS CONSERVATIVE BECAUSE IT UNDERESTIMATES THE BENEFIT BECAUSE IT ASSUMES FULL PROGRAM COSTS, IGNORED SOME OF THE OTHER PROGRAM BENEFITS, SUCH AS IMPROVED MEDICAL TREATMENT.

SO I JUST WANT TO KIND OF HIGHLIGHT THE KEY IS THAT WE ARE ABLE TO ESTIMATE THE IMPACT OF THE PROGRAM BECAUSE THE CLINICAL TRIAL INCLUDED INFORMATION THAT WAS ALSO INCLUDED IN OUR MODEL. SO THIS IS ONE OF THE THINGS THAT I WANT TO KIND OF POINT OUT IS THAT IF YOU WANT TO UNDERSTAND THE VALUE OF SOME NEW INNOVATION, MOST OF THE TIME TRIAL



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RESEARCHERS AREN'T NECESSARILY THINKING IN TERMS OF ECONOMICS. BUT IF WE COULD INCORPORATE SOME OF THESE DATA INTO TRIALS IN A MORE SYSTEMATIC WAY, IT WOULD GREATLY IMPROVE OUR ABILITY TO UNDERSTAND THE VALUE OF INNOVATION.

I'M GOING TO SKIP OVER THE NEXT SLIDE IN THE INTEREST OF TIME. BASICALLY ALL WE DID IS WE TOOK THE INFORMATION FOR THE RESULTS OF OUR HYPOTHETICAL SCENARIO OF IMPROVING EDUCATIONAL ATTAINMENT AND BASICALLY APPLIED IT TO CALIFORNIA SPECIFICALLY. SO THE POINT OF THE MICROSIMULATION MODEL IS YOU CAN TAILOR THE PATIENT POPULATION YOU'RE LOOKING AT. AND SO WE DID SO TO FOCUS ON CALIFORNIA TO HELP CALIFORNIA POLICYMAKERS UNDERSTAND WHAT THE IMPACT OF THIS PROGRAM OR THIS TYPE OF INNOVATION WOULD BE. AND SO THIS IS SOMETHING THAT COULD BE DONE ALSO IN THE CASE OF NEURODEGENERATIVE DISORDERS FOR UNDERSTANDING POTENTIAL VALUE OF INNOVATION.

SO NOW I'VE BEEN FOCUSING ON MENTAL HEALTH BECAUSE THE EXAMPLES THAT WE DID FROM THE PRIOR STUDY, I THINK, ARE INSTRUCTIVE. BUT WHAT HAPPENS IF WE THINK MORE SPECIFICALLY ABOUT NEURODEGENERATIVE DISORDERS? AND SO I WANT TO JUST GIVE YOU -- AS ANOTHER EXAMPLE GIVE YOU SOME RESULTS



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IF THE FEM, THE FUTURE ELDERLY MODEL. SO THIS IS ONLY THE SMI POPULATION. YOU HAVE MUCH HIGHER RATES OF EARLY ONSET. SO IT'S MUCH MORE LIKELY TO AFFECT PEOPLE EARLY IN THEIR LIVES; WHEREAS, OBVIOUSLY ALZHEIMER'S AND DEMENTIA ARE MORE LIKELY FOR AN OLDER POPULATION. SO THIS MODEL IS FOCUSING ONLY ON 50 PLUS POPULATION.

AND SO THE RESEARCHERS USED THE FEM TO ESTIMATE THE ANNUAL PER-PATIENT COST OF TREATMENT FOR PATIENTS WITH ALZHEIMER'S DISORDER. IT WAS BASED ON DATA 2010 AT THE TIME, BUT THEY ALSO LOOKED AT PROJECTIONS OUT TO 2050. SO, AGAIN, ONE OF THE BENEFITS OF MICROSIMULATION IS USING DATA ON TRENDS, YOU CAN PROJECT FORWARD AND TRY TO ESTIMATE WHAT THINGS WILL LOOK LIKE IN THE FUTURE IF FUTURE TRENDS FOLLOW PAST TRENDS.

AND SO THE STUDY BROKE DOWN COSTS INTO FORMAL MEDICAL SPENDING AND ALSO THE COST OF INFORMAL CARE, INCLUDING CAREGIVER BURDEN. AND ALSO I'LL SHOW YOU THE RESULTS OF A SIMULATED POLICY EXPERIMENT WHERE THEY CONSIDERED DELAYED ONSET BY ONE OR FIVE YEARS.

SO LOOKING AT THE LIFETIME BURDEN OF ALZHEIMER'S DISEASE. SO THE APPROACH HERE WAS SIMILAR TO WHAT I TALKED ABOUT WITH SMI WHERE YOU



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TOOK A PERSON -- YOU TOOK THE COHORT OF PEOPLE AGE 50 PLUS AND YOU COMPARE OUTCOMES FOR PATIENTS WITH AN ALZHEIMER'S DIAGNOSIS TO PATIENTS WITHOUT. AND SO HERE FOR PEOPLE, LOOKING SPECIFICALLY AT THE 70 PLUS POPULATION, COMPARING TREATMENT COST WITH -- MEDICAL COSTS WITH AND WITHOUT AD OR ALZHEIMER'S, YOU CAN SEE THAT IN 2010, IT WAS ABOUT A $26,000 LIFETIME INCREASE IN TOTAL MEDICAL SPENDING IN THE FORMAL SECTOR. SO MEDICARE SPENDING, PRESCRIPTION DRUG SPENDING, ET CETERA. BUT THAT WAS PROJECTED TO INCREASE TO NEARLY 70,000 BY 2050 BASED ON RISING HEALTHCARE COSTS AND THE POTENTIAL FOR NEW TREATMENT OPTIONS IN THE SPACE.

NOW, IF YOU LOOK AT INFORMAL CARE, COUPLE THINGS TO NOTE HERE IS THERE'S LESS OF A TREND SO LESS OF A PROJECTED INCREASE, BUT IT'S STILL A SIGNIFICANT COMPONENT. SO I MENTIONED CAREGIVER BURDEN, A SIGNIFICANT COMPONENT OF SPENDING AND THE COST OF ALZHEIMER'S. AND SO WHEN YOU LOOK AT THE TOTAL COSTS, YOU SEE IT IS ABOUT 53,000 IN 2010, BUT EXPECTED TO RISE TO CLOSE TO 100,000 BY 2050. SO THIS SHOWS YOU, AGAIN, THE POTENTIAL -- THE SEVERITY OF THE CONDITION AND THE POTENTIAL VALUE FOR A NEW OPTION THAT IMPROVED PATIENT OUTCOMES.

AND THINK ABOUT HOW WE ACTUALLY QUANTIFY

THE POTENTIAL VALUE OF A NEW TREATMENT OPTION, AS I SAID, THE STUDY ESTIMATED TWO HYPOTHETICAL SCENARIOS. ONE IS WHERE THERE WAS A ONE-YEAR DELAY. I THINK THEY ACTUALLY DID THREE. I THINK THEY HAD THREE YEARS ALSO IN THE PAPER. I'M JUST FOCUSING ON ONE- AND FIVE-YEAR DELAYS. SO LOOKING AT 70- TO 74-YEAR-OLDS, THINKING ABOUT WHAT WE SEE THE COST OF THE IMPACT ON PATIENTS OF ONSET, AND THEN THINKING ABOUT SUPPOSE WE ARE ABLE TO DELAY ONSET BY A YEAR OR DELAY ONSET BY FIVE YEARS, HOW DOES THAT IMPACT THE LIFETIME OUTCOMES FOR THESE PATIENTS?

YOU CAN SEE THAT AT BASELINE, YOU SEE ABOUT 15.6 TOTAL LIFE YEARS REMAINING. IF WE ARE ABLE TO DELAY ONSET OF ALZHEIMER'S BY ONE YEAR ON AVERAGE, THAT LEADS TO A ONE-YEAR INCREASE IN AVERAGE LIFE EXPECTANCY AND ABOUT A 2.7-YEAR INCREASE WITH A FIVE-YEAR DELAY.

IF WE LOOK AT YEARS WITHOUT AD, THOSE ALSO INCREASE SIGNIFICANTLY IN TIME IN A NURSING HOME. SO FOR A FIVE-YEAR DELAY, THAT'S ABOUT JUST OVER A THIRD OF A YEAR LESS TIME IN A NURSING HOME. SO FOUR MONTHS THAT A PERSON DOESN'T HAVE TO LIVE IN NURSING HOME OVER THE COURSE OF THEIR LIFE.

AND THEN, FINALLY, LOOKING AT THE IMPACT ON MEDICAL TREATMENT COSTS, MEDICAL SPENDING IN THE



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FORMAL MEDICAL SPENDING, YOU DO SEE SOME INCREASE IN TOTAL SPENDING. SO YOU ARE DELAYING THE ONSET OF A DISEASE, BUT THAT -- PEOPLE LIVE LONGER. SO THEY DO ACCUMULATE SOMEWHAT HIGHER MEDICAL COSTS, ALTHOUGH THAT'S GOING TO BE OFFSET POTENTIALLY BY LESS ALZHEIMER'S-RELATED SPENDING. WHERE YOU SEE THE REAL VALUE IN TERMS OF MEDICAL COSTS IS FROM REDUCTION IN THE INFORMAL SECTOR. SO YOU SEE ABOUT 200,000, JUST OVER 200,000 EXPECTED COSTS FOR 70- TO 74-YEAR-OLDS. SO ABOUT $20,000 LOWER ON AVERAGE WITH A ONE-YEAR DELAYED ONSET AND ABOUT $50,000 LESS WITH A FIVE-YEAR DELAYED ONSET.

SO THIS IS A DIFFERENT STUDY THAN THE SMI STUDY. SO THEY DIDN'T DO THE FULL RANGE OF COSTS THAT WE DID IN OUR STUDY. SO I DON'T HAVE THE NUMBERS SAYING WHAT'S THE SPECIFIC VALUE GENERATED BY EXTENDING LIFE EXPECTANCY, FOR EXAMPLE. BUT EVEN JUST FOCUSING ON MEDICAL SPENDING, COMPARING THE INCREASE THAT YOU GET FROM LONGER LIFE VERSUS THE REDUCTION IN INFORMAL CARE REQUIRED, YOU CAN SEE A SIGNIFICANT VALUE GENERATED BECAUSE YOU ARE GENERATING SOME INCREASE IN MEDICAL SPENDING IN THE FORMAL SECTOR, BUT THAT'S MORE THAN OFFSET BY REDUCTIONS IN THE INFORMAL SECTOR. SO EVEN NOT INCLUDING SOME OF THOSE OTHER ELEMENTS OF VALUE WE



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ARE TALKING ABOUT, WE ARE ABLE TO MODEL THE POTENTIAL IMPACT OF SOME INNOVATION THAT WE ARE ABLE TO DELAY ONSET.

CHAIRMAN GOLDSTEIN: SETH, WE ARE RUNNING A LITTLE TIGHT ON TIME. SO IF YOU COULD ACCELERATE A TOUCH, THAT WOULD BE HELPFUL.

DR. SEABURY: OKAY. BASICALLY I WAS JUST GOING TO FINISH UP HERE. SO JUST KIND OF WANT TO MAKE THE POINT THAT A COMPREHENSIVE APPROACH IS NEEDED TO UNDERSTAND RETURNS TO INNOVATIONS THAT IMPROVE OUTCOMES. NEED TO LOOK BEYOND LINE ITEM ACCOUNTING OF COST SAVINGS, CONSIDER TOTAL SPENDING, FORWARD LOOKING MEASURES THAT CONSIDER THE LIFETIME EFFECTS ON SOME INNOVATION, AND CONSIDER BOTH DIRECT AND INDIRECT EFFECTS. SO I THINK IN THE CASE OF PSYCHIATRIC DISORDERS, LABOR MARKET PRODUCTIVITY, OUTSIDE SOCIAL IMPACTS ON OTHER SOCIAL SYSTEMS, AS WELL AS CAREGIVER BURDEN.

AND, FINALLY, JUST WANTED TO MAKE THE POINT THAT WE NEED TO ALSO -- IF YOU WANT TO DO COMPREHENSIVE VALUE MEASURES, YOU NEED TO THINK ABOUT THE DATA THAT YOU NEED TO GENERATE THESE MEASURES. SO IF YOU LOOK AT SOME OF THE IMPACT, SOME OF THE VARIABLES THAT WE HAVE IN THE FEM AND THE FAM, THESE INCLUDE THINGS LIKE CHRONIC

CONDITIONS FOR PATIENTS, ACTIVITIES OF DAILY LIVING, SOME OF THEIR FUNCTIONAL LIMITATIONS, SELF-REPORTED MEASURES SUCH AS DEPRESSION, BEHAVIORS, AND RISK FACTORS, AS WELL AS ECONOMIC OUTCOMES, SUCH AS WHETHER THEY'RE WORKING, WHAT KIND OF INSURANCE THEY HAVE. THERE'S A WHOLE BATTERY OF INFORMATION THAT ARE IN OUR MODELS, MEDICAL SPENDING, UTILIZATION, SUCH AS HOSPITAL ENCOUNTERS, INFORMAL CARE, CAREGIVER BURDEN. ALL OF THESE THINGS ARE IMPORTANT COMPONENTS THAT GENERATE VALUE, BUT THEY'RE NOT ALWAYS CONSIDERED BY PEOPLE RUNNING CLINICAL TRIALS.

SO WE THINK THAT THE CNS DISORDERS IMPOSE SIGNIFICANT LIFETIME COSTS ON PATIENTS. WE THINK THAT PRIVATE R&D SPENDING IS CHALLENGED BECAUSE OF SCIENTIFIC UNCERTAINTY AND ECONOMIC HURDLES, WHICH IMPROVES THE POTENTIAL BENEFITS FROM PUBLIC FUNDING IN THESE AREAS. WE THINK THAT MICROSIMULATION, AND MICROSIMULATION IS ONE APPROACH. THERE ARE OTHERS CERTAINLY ACKNOWLEDGED. AND WE THINK THAT IN GENERAL ECONOMIC MODELING TECHNIQUES CAN PROVIDE AN IMPORTANT METHODOLOGY FOR HELPING STAKEHOLDERS ASSESS THE RETURN THAT IS GENERATED BY INVESTMENT IN THESE AREAS, BUT TO DO SO IN A SYSTEMATIC WAY MIGHT REQUIRE ADDITIONAL DATA COLLECTION.

SO I THINK IT WOULD BE GREAT IF FUNDERS



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COULD CONSIDER THE POTENTIAL BENEFITS OF ENCOURAGING INVESTIGATORS TO NOT JUST FOCUS ON CLINICAL ENDPOINTS, BUT TO THINK ABOUT SOME OF THESE OTHER HEALTH AND ECONOMIC OUTCOMES THAT THEY COULD POTENTIALLY, SINCE OFTEN IN CLINICAL TRIALS, YOU HAVE A BATTERY OF THINGS THAT YOU'RE LOOKING AT AND YOU DO HAVE CONTACT WITH PATIENTS, GETTING SOME ADDITIONAL DATA FROM THEM COULD HELP IMPROVE THE ACCURACY OF THESE VALUE ASSESSMENTS.

SO THAT'S EVERYTHING I HAVE. SO I'M HAPPY TO TAKE ANY QUESTIONS.

CHAIRMAN GOLDSTEIN: THANK YOU, SETH. THAT WAS FASCINATING.

LET ME LAUNCH THE FIRST QUESTION, AND THEN I'LL CALL ON LEONDRA SUBSEQUENTLY.

I GUESS -- YOU'VE PRESENTED A REALLY USEFUL WAY TO MODEL THESE DISORDERS AND THE RETURN ON INVESTMENT, BUT IT'S A FAIRLY INVOLVED ANALYSIS AS NEAR AS I CAN TELL. I GUESS THE QUESTION IS IS THERE A SIMPLE-TO-MEASURE PROXY VARIABLE THAT MIGHT CAPTURE 70 OR 80 PERCENT OF WHAT YOU GET FROM A FULL MODELING EXERCISE? AND IN PARTICULAR I THINK WHAT WE WOULD WORRY ABOUT DOING IS TO LOOK THROUGH, SAY, OUR NEURODEGENERATIVE PORTFOLIO AND ASK THE QUESTION: IS THERE AN AREA WHERE WE ARE

SIGNIFICANTLY UNDERFUNDED WHERE WE MIGHT WANT TO DEVELOP SPECIAL PROGRAMS OR FIND SOME OTHER WAY TO ACCELERATE PROGRESS?

DR. SEABURY: I'D LIKE TO --

DR. FISHER: CAN YOU STOP THE SCREEN SHARE SO WE CAN ACTUALLY SEE EACH OTHER?

CHAIRMAN GOLDSTEIN: GREAT POINT.

DR. SEABURY: SO, YES, TO RESPOND TO THE QUESTION, I MEAN I'D LIKE TO SAY YES, THAT YOU COULD MAKE IT SIMPLE. BUT AT THE SCHAEFFER CENTER WE SPEND A LOT OF OUR TIME CRITICIZING MORE SIMPLE ANALYSES. SO IT'S HARD AS A RESEARCHER TO SAY THAT YOU ACTUALLY DON'T NEED TO DO THE INVOLVED STUDY AND YOU CAN GO ON SOMETHING SIMPLE. THAT SAID, THERE ARE SIMPLER APPROACHES. I MEAN YOU COULD DO KIND OF THE ENVELOPE CALCULATIONS. YOU COULD LOOK AT QALY'S, BASICALLY THAT'S THE METRIC THAT PEOPLE TEND TO USE. SO YOU COULD COLLECT SOME INFORMATION ON THE IMPACT OF DISORDER ON QALY'S. YOU COULD DO A SIMPLE MARKOV MODEL THAT JUST INCORPORATES MORTALITY RISK. AND SO YOU COULD TRY TO SAY THESE ARE THE EXPECTED LIFE YEARS LOST FROM THE CONDITION, MULTIPLY THAT BY A 100,000, AND THAT WILL TELL YOU SORT OF A BACK OF THE ENVELOPE CALCULATION AS TO WHAT THE COST OF THE CONDITION IS GOING TO BE.

AND I DON'T KNOW IF THAT'S GOING TO GET YOU 60 OR 70 PERCENT OF THE VALUE, BUT IT WILL GIVE YOU A SENSE OF THE COST OF THE CONDITION THAT YOU COULD USE. THAT IS THE MOST STANDARD APPROACH.

BRYAN, DO YOU HAVE ANYTHING ELSE THAT YOU WANT TO BRING UP?

DR. TYSINGER: I DON'T HAVE A HEURISTIC FOR HOW TO DO THAT CORRECTLY, BUT I THINK YOU COULD LOOK DISEASE BY DISEASE AND THINK ABOUT IS THIS AN EARLY AGE INCIDENT THING OR SOMETHING THAT HAPPENS LATER IN LIFE. AND THAT WILL TELL YOU HOW MUCH OF THE EMPLOYMENT PICTURE ARE YOU MISSING AND THOSE PIECES. SO I WOULD BE CAREFUL, BUT I THINK YOU CAN DO SOMETHING REASONABLE AS LONG AS YOU'RE ACKNOWLEDGING WHEN THE DISEASE IS AFFECTING PEOPLE.

CHAIRMAN GOLDSTEIN: INTERESTING. THANK YOU. LEONDRA.

DR. CLARK-HARVEY: HI. I JUST WANT TO THANK YOU FOR YOUR VERY GOOD PRESENTATION. AND IN ALL CANDOR, I HAVE HISTORICAL ISSUES WITH COLLEAGUES AND MOSTLY JUST BECAUSE OF HOW THEY CAN BE USED TO DISCRIMINATE AGAINST ACCESS AND TREATMENT FOR SOME PATIENT POPULATIONS. SO UNDERSTAND THE PREMISE AND THE NEED FOR THEM AND ALSO UNDERSTAND THE IMPACT AND HOW THAT KIND OF ROLLS OUT AND IMPACTS PATIENTS IN



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THE END. SO I REALLY LOVE THAT IN THIS PRESENTATION AROUND THE MICROSIMULATION YOU FOCUS ON THE SOCIAL DETERMINANT OF HEALTH IMPACTS BECAUSE I THINK THAT'S A MAJOR THING THAT'S MISSING.

EXCUSE ME. I HAVE A LITTLE COLD. MY CHILDREN GIVE ME THE PLAGUE EVERY OTHER WEEK.

BUT I ALSO REALLY APPRECIATE YOUR FOCUS ON MORE THAN JUST CLINICAL ENDPOINTS. I THINK THAT'S SUCH A POWERFUL STATEMENT THERE, WHICH OPENS THE DOOR FOR LOOKING AT THIS MORE BROADLY AND INCLUDING A LOT MORE OF THOSE DETERMINANTS LIKE THE EMPLOYMENT, CAREGIVER BURDEN, LOTS OF THINGS THAT YOU MENTION THAT WERE UP ON THE SLIDE ARE VERY CRITICAL.

SO MY QUESTION TO YOU WOULD BE DO YOU HAVE A NUMBER OF EXAMPLES OF HOW MICRO HAS BEEN USED WITH NEUROLOGICAL OR NEURODEGENERATIVE DISORDERS THAT WE COULD POINT TO EASILY TO BE ABLE TO SAY THIS WORKS WITH THIS POPULATION. THIS WOULD BE SOMETHING THAT WE COULD LOOK AT.

ALSO, WITH THE PREVIOUS COMMENTER, OUR CHAIR, AROUND NOT HAVING A LOT OF SIMPLICITY IN THIS MODEL, IT DOES MAKE IT DIFFICULT; BUT I STILL IF THERE'S A WAY TO POINT TO STUDIES THAT HAVE ALREADY BEEN DONE WITH THIS POPULATION, THAT WOULD BE

HELPFUL. SO I HOPE THAT MAKES SENSE. BUT LET ME KNOW IF THERE -- WHAT YOUR ANSWER IS.

DR. SEABURY: SO I DON'T KNOW OFF THE TOP OF MY HEAD A NUMBER OF SPECIFIC EXAMPLES. I KNOW AT THE CENTER WE'VE DONE SOME. AND, BRYAN, I KNOW YOU HAVE ONGOING WORK SPECIFICALLY IN ALZHEIMER'S AND DEMENTIA. I DON'T KNOW THAT WE'VE EVER USED THE MODEL FOR OTHER NEURODEGENERATIVE CONDITIONS SUCH AS ALS. HAVE WE DONE THAT, BRYAN, OR IN PARKINSON'S? I DON'T THINK THAT WE HAVE SPECIFIC EXAMPLES THAT WE HAVE DONE. THERE MAY BE SOME OTHERS IN THE LITERATURE. I'D HAVE TO LOOK FOR THOSE.

BUT I DO THINK THAT IT IS AN AREA THAT IS RIPE FOR ADDITIONAL WORK CERTAINLY. I THINK SOME OF THE ISSUES OF INVESTMENT BY THE PRIVATE MARKET THAT I TALKED ABOUT HAVE LED TO PROBABLY UNDERRESEARCH IN THESE AREAS IN THIS FIELD AS WELL BECAUSE SOMETIMES THOSE TWO OFTEN WORK IN TANDEM. SOME OF THE WORK TO UNDERSTAND THE IMPACT OF THE DISEASE IS MOTIVATED BY THESE HEALTH TECHNOLOGY -- THE DESIRE TO DO THESE HEALTH TECHNOLOGY ASSESSMENTS. SO I THINK IT'S PROBABLY NOT. SO I THINK THERE ARE A LOT OF EVIDENCE GAPS IN THIS AREA.

BUT THAT SAID, THERE COULD BE MORE WORK THAT I'M JUST NOT AWARE OF.



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DR. CLARK-HARVEY: YEAH. I'VE SEEN A LOT ON LIKE DIABETES, HEARING LOSS. AND SO I THINK THERE'S -- THIS IS EXCITING FOR THIS AREA. AND I THINK IT'S ALSO HELPFUL TO HAVE SOME EVIDENCE IN OUR BASKET TO BE ABLE TO THINK ABOUT HOW THIS MIGHT APPLY. THANKS FOR CONSIDERING.

DR. SEABURY: JUST TO FOLLOW UP, I DO THINK SOME OF THE RESULTS BEING GENERATED ON ALZHEIMER'S CAN CERTAINLY BE RELEVANT FOR OTHER NEURODEGENERATIVE CONDITIONS. THE ONLY CAVEAT BEING -- AND SOME OF THE -- THE CAVEAT BEING THAT IT'S AFFECTING A VERY SPECIFIC POPULATION, AN AGING POPULATION. SO THE RESULTS WILL BE LESS RELEVANT FOR DISEASES WHERE THEY HAVE EARLIER ONSET. BUT CERTAINLY YOU COULD TAKE, I THINK, SOME OF THE ALZHEIMER'S AND DEMENTIA-RELATED RESULTS AND TRY TO GET A SENSE THERE, MAYBE COMPARE THEM TO SOME OF THE QALY STUDIES TO SEE HOW COMPARABLE THEY ARE. THAT MIGHT GIVE YOU A SENSE OF HOW ACCURATE SOME OF THESE SIMPLER METRICS ARE DOING.

DR. CLARK-HARVEY: THANK YOU.

CHAIRMAN GOLDSTEIN: PAT.

DR. LEVITT: THANKS VERY MUCH, SETH AND BRYAN.

TWO THINGS. ONE IS TWO TAKE-HOME MESSAGES



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THAT STRUCK ME. ONE IS WE SHOULD BE THINKING ABOUT IT, MAYBE THE SCIENCE SUBCOMMITTEE FOR CIRM COULD THINK ABOUT THIS, THAT YOU MADE A VERY IMPORTANT POINT, THAT DATA OTHER THAN CLINICAL ENDPOINT MAY BE IMPORTANT FOR US TO THINK ABOUT IN TERMS OF HOW DO YOU INCORPORATE IT INTO STUDIES THAT WE FUND, CLINICAL STUDIES, WHICH WOULD THEN PROVIDE MANY MORE OPPORTUNITIES IN WHAT WE HAVE GENERATING AT CIRM TO DO EVALUATIONS AND DO ANALYSES SUCH AS WHAT YOU'RE TALKING ABOUT. WE WOULD NEED TO KNOW THE MOST IMPORTANT ELEMENTS THAT WOULD NEED TO BE INCLUDED, AND THAT, OF COURSE, COULD BE EVALUATED BY THE SCIENCE SUBCOMMITTEE AND THEN RECOMMENDED. BECAUSE WE ALWAYS -- WE HAVE SPECIFIC REQUIREMENTS IN TERMS OF DATA COLLECTION. THAT WAS ONE THING.

THE OTHER, WHICH IS FAR MORE DEPRESSING AND NO SOLUTION, IS THE PRIVATE SECTOR INVESTMENT IN NEURO DISORDERS IN GENERAL. WE KNOW PRACTICALLY IT'S EASY. YOU DON'T NEED A MARKOV MODEL TO DEMONSTRATE THAT PHARMACEUTICAL COMPANIES ARE WITHDRAWING FASTER THAN A FINGER OVER A FLAME.

SO HAVE YOU HAD ENCOUNTERS OR DISCUSSIONS WITH PHARMACEUTICAL COMPANIES SHOWING SOME OF THE NONCLINICAL OUTCOME DATA THAT ARE POSITIVE ASPECTS OF INVESTMENT IN NEURO DISORDERS THAT WOULD ENHANCE



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THEIR INTEREST OR SPUR THEIR INTEREST OR REINVIGORATE THEIR INTEREST? HOW DO WE GET OUT OF THIS CONUNDRUM BECAUSE PUBLIC INVESTMENT CAN'T DO IT ALL. THERE'S JUST NO WAY. AND HOW DO WE GET OUT OF THIS MESS BECAUSE THE DATA YOU SHOWED IS REALLY DEPRESSING?

DR. SEABURY: I THINK THAT'S A GREAT QUESTION. AND I THINK THAT THERE ARE EXAMPLES OF USING PUBLIC PROGRAMS TO INCENTIVIZE FOCUSED GOVERNANCE. THE ORPHAN DRUG ACT CERTAINLY DID MOTIVATE, FOR EXAMPLE, NEW INNOVATIONS FOR NEW PRODUCTS. NOW, THERE ARE ALWAYS PROBLEMS THAT COME UP AND THERE'S ALWAYS WAYS THAT PEOPLE TRY TO GAME THE SYSTEM. BUT I DO THINK IN GENERAL IT HAS BEEN SUCCESSFUL IN PROMOTING RESEARCH AND DEVELOPMENT IN DRUGS THAT WE TREAT RELATIVELY SMALL PATIENT POPULATIONS. SO I DO THINK YOU COULD TRY TO WORK -- USE PUBLIC INCENTIVES, PUBLIC PROGRAMS TO PROVIDE PRIVATE COMPANIES WITH MORE INCENTIVES TO RESEARCH IN CERTAIN AREAS.

OTHER THAN THAT, I DON'T KNOW HOW TO SOLVE THE PROBLEM, RIGHT, OTHER THAN TRYING TO PROVIDE THEM WITH SOME FINANCIAL INCENTIVES TO DIRECT AREAS. THE ONLY OTHER WAY I CAN SEE, LIKE I SAID, IS NEW INNOVATIONS COULD POTENTIALLY SPUR FUTURE INVESTMENT

IF IT'S SOMETHING THAT PROVIDES A SCIENTIFIC PLATFORM TO OPERATE OFF OF. BUT THAT'S -- HOPE IS NOT A PLAN, I GUESS. SO THAT'S SOMETHING THAT YOU CAN HOPE FOR, BUT THERE COULD BE AN EFFECT.

DR. LEVITT: JUST LET ME GET ONE OTHER THING. SO ONE OF THE VARIABLES YOU HAD WAS WHAT YOU CALL SPILLOVER, WHICH I ASSUME MEANT THAT A DRUG DEVELOPED FOR DISEASE X TURNS OUT TO BE VALUABLE FOR TREATING DISEASE Y OR Z. YOU HAVE EXAMPLES OF THAT WHERE SOMETHING WAS DEVELOPED, LET'S SAY, IN A NON-NEURO DISEASE THAT THEN GOT APPLIED IT TO NEURO DISEASE OR VICE VERSA SO THAT THE VALUE OF INVESTING IN NEURO -- MAYBE VICE VERSA, INVESTMENT IN NEURO THEN TURNED OUT TO BE REALLY VALUABLE FOR TREATING WHATEVER?

DR. SEABURY: THERE ARE PROBABLY OTHERS HERE WHO HAVE BETTER EXAMPLES FROM THE SCIENTIFIC PERSPECTIVE IN NEURO. THE FIRST THING THAT COMES TO MIND FOR ME IS A VERY SPECIFIC EXAMPLE WOULD BE -- I FORGOT WHAT THE -- BASICALLY IT'S A CANCER TREATMENT THAT LED TO THE DEVELOPMENT OF ANTI-VEGF'S FOR TREATING MACULAR DEGENERATION AND OTHER EYE CONDITIONS. SO THAT'S AN EXAMPLE OF WHERE A NEW DRUG CLASS -- A CANCER DRUG LED TO NEW OPHTHALMOLOGY DRUG CLASS.



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SO THERE ARE, I THINK, MANY EXAMPLES OF SPILLOVERS. WHEN YOU TALK ABOUT SPILLOVERS, ALSO WE THINK ABOUT SOMETHING LIKE THE HUMAN GENOME PROJECT WHERE THAT LED TO MANY ADVANCES ACROSS MANY DIFFERENT FIELDS. SO WE TEND TO THINK OF R&D AS HAVING THE POTENTIAL FOR ENORMOUS SPILLOVERS IN THAT KNOWLEDGE GENERATED IN ONE AREA CAN HELP SPUR INNOVATION IN OTHER AREAS. SORT OF WHAT I WAS SAYING BEFORE. IT'S HARD TO PREDICT THOSE THINGS EX ANTE.

ONE THING -- IF I CAN GO BACK, ONE THING I DID WANT TO MENTION FROM AN EARLIER COMMENT ABOUT DATA COLLECTION AND UNDERSTANDING SORT OF HOW TO COLLECT DATA IN THESE AREAS. I WAS INVOLVED IN THE TRACK-TBI PROJECT FOR TRAUMATIC BRAIN INJURY. SO THEY WERE CREATING A REGISTRY OF TBI PATIENTS. AND THEY DID SPEND AN ENORMOUS AMOUNT OF TIME ON THE COMMON DATA ELEMENTS ISSUES. THERE ARE SOME -- AND MANY OF THOSE WOULD INCLUDE SYMPTOMS AND ISSUES RELEVANT FOR, I THINK, NEURODEGENERATIVE CONDITIONS. SO THAT MIGHT BE AN AREA TO LOOK AT, SOME OF THE WORK THAT THEY DID IN TERMS OF UNDERSTANDING -- TRYING TO PROMOTE CONSISTENCY IN DATA COLLECTION ACROSS DIFFERENT TRIALS. SOME OF THAT WORK MIGHT BE RELEVANT FOR THE CONDITIONS YOU'RE TALKING ABOUT.



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JUST WANTED TO PUT THAT OUT THERE.

DR. LEVITT: THANK YOU.

CHAIRMAN GOLDSTEIN: THANK YOU. OTHER QUESTIONS WHILE WE HAVE SETH AND HIS COLLEAGUES BEFORE WE MOVE ON TO THE NEXT TOPIC? IF NOT, SETH, LOVELY PRESENTATION, VERY THOUGHT PROVOKING. AND I THINK WE WILL BE BACK IN TOUCH TO GET SOME HELP IN EVALUATING OUR CURRENT PORTFOLIO. SO THANK YOU, GUYS. APPRECIATE IT.

DR. SEABURY: THANK YOU FOR HAVING US.

CHAIRMAN GOLDSTEIN: ALL RIGHT. NEXT UP WILL BE A SHORT PRESENTATION FROM, I THINK, MARIA MILLAN. THE QUESTION CAME UP IN A PREVIOUS MEETING. WHAT WERE WE DOING TO TRACK OUR EXPENDITURES IN THE NEURO AREA TO BE SURE THAT WE STAYED ON THE CORRECT PATH TO REACH ONE AND A HALF BILLION BY THE END OF THIS TEN-YEAR PERIOD. AND SO MARIA MILLAN AND HER COLLEAGUES AT CIRM HAVE WORKED UP THIS PROBLEM. TURNS OUT TO BE RELATIVELY STRAIGHTFORWARD, BUT, MARIA, WHY DON'T YOU LEAD US THROUGH IT PLEASE.

DR. MILLAN: THANK YOU VERY MUCH. SCOTT OR CLAUDETTE, DO YOU HAVE THE PRESENTATION? THANK YOU SO MUCH.

SO IN RESPONSE TO THE QUESTION, WHAT WE THOUGHT WE'D DO IS JUST PROVIDE WHAT WE HAVE, WHAT



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WE CONTINUE TO COLLECT INTERNALLY, AND THEN ALSO PROVIDE MORE A DETAILED ACCOUNT OF THIS IN SOME OF THE SUBSEQUENT SLIDES, WHICH I WON'T SPECIFICALLY, BUT WILL BE USEFUL PERHAPS FOR REFERENCE. AND WE ARE AVAILABLE FOR QUESTIONS EITHER AT THIS MEETING OR FOLLOWING THIS MEETING.

SO I'LL JUST GO AHEAD AND START. FIRST SLIDE PLEASE. JUST TO EXPLAIN OUR PROCESS, THE PROCESS OF GRANTMAKING AT CIRM. GIL SAMBRANO AND JENNIFER LEWIS HAVE PRESENTED AT PRIOR BOARD MEETINGS KIND OF THE PARAMETERS OF HOW GRANTS COME IN, ARE EVALUATED, AND THEN BROUGHT TO THE ICOC FOR FINAL APPROVAL FOR ANY FUNDING. ONCE THAT OCCURS, THEY'RE IMPORTED INTO OUR GRANTS MANAGEMENT SYSTEM WHICH IS ESSENTIALLY THE WORKHORSE IN TERMS OF CAPTURING EVERYTHING RELATED TO OUR GRANTMAKING PROCESS.

SO THE ICOC APPROVED AWARDS, INCLUDING THE AMOUNTS AND THEIR ASSOCIATED DETAILS, ARE IMPORTED FROM THAT GRANT MANAGEMENT SYSTEM, THE SOURCE OF TRUTH, INTO MONDAY.COM, OUR PROJECT MANAGEMENT TECHNOLOGY THAT WAS PUT INTO PLACE BY THE TEAM PROBABLY ABOUT TWO YEARS AGO AND HAS BEEN SERVING TO REALLY HELP US WITH THE KNOWLEDGE SHARING AND CAPTURE INTERNALLY. SO THAT'S ALLOWED US TO

GENERATE SOME OF THE THINGS YOU'LL SEE TODAY. SO IT'S IMPORTANT TO OUR PROJECT MANAGEMENT SYSTEM.

THE AWARDS ARE CLASSIFIED AND QUALIFIED WITH OUR SCIENCE OFFICERS TO ENSURE THAT THE TYPE OF PROGRAM, THE DISEASE AREA, THE TECHNOLOGY, ET CETERA, ARE APPROPRIATELY TAGGED IN THAT SYSTEM. AND THEN THERE'S A PROCESS BY WHICH THEY'RE THEN INCORPORATED INTO A REPOSITORY OF INFORMATION THAT GET VERIFIED AND CORRECTED ALONG THE WAY.

THE NUMBERS FROM THIS ARE REPORTED TO YOU IN THE FORMAT OF PRESIDENT'S REPORTS. WHEN I GIVE UPDATES ON OUR PORTFOLIO, OUR STRATEGIC PLAN EXPENDITURES, ET CETERA, AND OUR ANNUAL REPORT IS AN ANNUAL CURATED ACCOUNT OF OUR EXPENDITURES. AND THESE NUMBERS CAN BE EVALUATED AND ANALYZED IN A VARIETY OF WAYS. SO I'M JUST GOING TO GIVE YOU AN IDEA FROM A BIG PICTURE OF HOW, IN RESPONSE TO THE QUESTION FROM THIS TASK FORCE, HOW WE LOOKED AT OUR EXPENDITURES IN NEURO WITH PROP 14 FUNDS TO START WITH. NEXT SLIDE PLEASE.

SO, AGAIN, THESE ARE PROP 14 FUNDS ONLY BETWEEN 2020 AND THE CURRENT TIME. THE TOTAL EXPENDITURES FOR NEURO ACROSS ALL WHAT WE CALL PILLAR PROGRAMS, THE RECURRENT PROGRAM ANNOUNCEMENTS, IS ABOUT $221 MILLION SO FAR OUT OF



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THE $1.5 BILLION SPECIFICALLY EARMARKED UNDER PROP 14.

SO THIS IS BROKEN DOWN BY ANNUAL EXPENDITURES BY PROGRAMS, DISCOVERY, TRANSLATIONAL, AND CLINICAL. AND ACROSS THE BOTTOM YOU WILL SEE WHAT THE TOTAL EXPENDITURES, THE ACCUMULATED EXPENDITURES IN TERMS OF APPROVED BUDGETS FOR THESE AWARDS ARE SHOWN ON THE BOTTOM. IN THE ORANGE ARE THE DOLLAR AMOUNTS, BUT BENEATH IT ARE THE NUMBER OF AWARDS. NEXT SLIDE PLEASE.

IF WE LOOK AT IT -- AGAIN, PROP 14 EXPENDITURES IN NEURO, IF YOU LOOK AT IT ACCORDING TO THE TYPES OF PROGRAMS, DISCOVERY, TRANSLATIONAL, OR CLINICAL PROGRAMS, SHOWN IN THE BAR GRAPH IN ORANGE ARE THE PERCENTAGE OF THE TOTAL AWARDS IN TERMS OF THE GRANTS, THE PERCENTAGE OF GRANTS IN THE DISCOVERY PORTFOLIO, WHICH COMPOSED 42 PERCENT OF THE DISCOVERY AWARDS, ALMOST 30 PERCENT, 27 PERCENT OF TRANSLATIONAL, AND 30 PERCENT OF CLINICAL AWARDS THUS FAR WITH PROP 14 FUNDINGS. ON THE RIGHT ARE THE RAW NUMBERS IN TERMS OF NUMBER OF AWARDS FOR NEURO VERSUS TOTAL FOR EACH CATEGORY. IN GENERAL THE TOTAL IS ABOUT 36 PERCENT OF THE GRANTS ACROSS ALL OF THESE PILLARS WHEN YOU LOOK AT IT WITH RESPECT TO NUMBER OF GRANTS. 36 PERCENT OF THEM ARE



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IN NEURO. NEXT SLIDE PLEASE.

IF YOU LOOK AT IT IN TERMS OF DOLLAR AMOUNTS SIMILARLY REPRESENTED HERE IN THESE BAR GRAPHS ARE THE PERCENT OF DOLLAR EXPENDITURES IN THE DISCOVERY, TRANSLATIONAL, AND CLINICAL PILLARS. YOU WILL SEE THE DOLLAR AMOUNTS ON THE RIGHT SIDE, BUT THAT IN TOTAL IS APPROXIMATELY 33.4 PERCENT OF DOLLAR EXPENDITURES ARE IN NEURO ACROSS THE PILLARS WITH THE BREAKDOWN SHOWN IN THE BAR GRAPH OF PROP 14 FUNDS THUS FAR.

AND BY THE WAY, THIS TRACKS WITH WHAT OUR HISTORICAL AND OUR CUMULATIVE PERFORMANCE HAS BEEN IN NEURO. GENERALLY IT GOES BETWEEN 30 AND 35 PERCENT OF THE RESEARCH DOLLARS HAVE GONE INTO NEURO BETWEEN PROP 14 AND PROP 71. YOU'VE SEEN THIS ANALYSIS PRESENTED EARLY ON IN THE TASK FORCE MEETINGS BY THE TEAM. AND THOSE ARE AVAILABLE AS WELL AS UPDATED NUMBERS IN THIS PARTICULAR SLIDE DECK. NEXT SLIDE PLEASE.

AND THIS IS BROKEN DOWN IN TERMS OF THE CATEGORIES. SO WITHIN NEURO, HERE ARE THE CATEGORIES THAT HAVE BEEN TRACKED BY THE TEAM, PROP 14 FUNDING IN TERMS OF DOLLAR AMOUNTS IN THE VARIOUS CATEGORIES. I WON'T READ THEM OFF. AS YOU CAN SEE, THOSE ARE SHOWN ON THE LEFT SIDE, AND THE CIRM



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FUNDING IN MILLIONS IS SHOWN THROUGH THESE BAR GRAPHS WITH THE CATEGORY OF NEURODEVELOPMENTAL, NEUROTRAUMA, NEURODEGENERATIVE DISEASES BEING SOME OF THE MORE PROMINENT ONES, AND THEN THERE'S SOME SMALLER INVESTMENTS WITH PROP 14 SHOWN BELOW. NEXT SLIDE PLEASE.

AND THIS IS ACCORDING TO THE TRANSLATIONAL R&D INVESTMENTS SO FAR WITH PROP 14 FUNDINGS. NEXT SLIDE PLEASE.

AND ACCORDING TO THE CLINICAL PROGRAMS, THE LARGEST NUMBER OF FUNDING WITH PROP 14 DOLLARS SO FAR HAS BEEN IN ONCOLOGY AND GLIOBLASTOMA, GLIOMAS, OTHER NEURODEVELOPMENTAL, RETINAL DISEASES, ALS AND OTHER MORE NEURO DISEASES, STROKE, AND EPILEPSY, AND SOME IN PARKINSON'S. NEXT SLIDE PLEASE.

AND THEN YOU'LL SEE IN YOUR, NOT BOARD PACKET, BUT YOUR VIRTUAL BOARD PACKET ALSO THE UPDATED NUMBERS FOR THE COMBINED PROP 71 AND PROP 14 EXPENDITURES.

AND JUST FOR SAKE OF ORIENTATION, NEXT SLIDE PLEASE, THE TOTAL EXPENDITURES OR THE TOTAL INVESTMENT IN R&D IN TERMS OF PERCENT OF AWARDS IS APPROXIMATELY 30 PERCENT BY NUMBERS OF GRANTS. NEXT SLIDE PLEASE. AND 32 PERCENT OF DOLLARS AWARDED



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ACROSS ALL OF THE DISCOVERY, TRANSLATIONAL, AND CLINICAL FROM 2007 TO DATE.

I'M GOING TO END THERE BECAUSE A LOT OF IT GOES INTO REAL DETAIL, AND THIS IS -- WE HOPE THIS ANSWERS THE QUESTION OF HOW WE ARE TRACKING THESE EXPENDITURES. AND AS YOU KNOW, IT'S REPORTED OUT IN OUR ANNUAL REPORT AND PRESIDENT'S REPORT; BUT, OF COURSE, THE NEURO TASK FORCE COULD ASK US TO PROVIDE THESE UPDATES WHENEVER IT'S USEFUL. AND WE HAVE THE MEANS -- WE HAVE THE SYSTEMS TO BE ABLE TO DO THAT. SO I JUST WANTED TO GIVE A BROAD OVERVIEW. TEAM MEMBERS ARE ON THIS CALL IN CASE THERE ARE SPECIFIC QUESTIONS RELATED TO THE PORTFOLIO THAT COULD HELP OUT IN TODAY'S DISCUSSION.

SO THAT'S ALL I HAVE FOR NOW, DR. GOLDSTEIN.

CHAIRMAN GOLDSTEIN: GREAT. THANK YOU VERY MUCH, MARIA. THAT'S VERY HELPFUL. THANK YOU TO YOU AND YOUR COLLEAGUES. LOOKS LIKE WE ARE MORE OR LESS ON TRACK, WHICH IS GOOD. I SEE WE HAVE A QUESTION FROM MARV.

DR. SOUTHARD: I WAS JUST WONDERING IF THERE COULD BE A CLEARER CALL-OUT OF THE ZERO EXPENDITURES FOR MENTAL HEALTH DISORDERS IN THIS BECAUSE IF THAT WAS THERE, I MISSED IT.



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DR. MILLAN: YES. IT DEFINITELY WAS A MAJOR FOCUS OF ALL THE PRIOR NEURO TASK FORCE MEETINGS, AND THAT'S THE REASON THAT THE REMIND PROGRAM. I BELIEVE THAT THAT WAS KIND OF THE --

DR. SOUTHARD: THE GENESIS OF THAT.

DR. MILLAN: WELL, IT WAS DEFINITELY A VERY STRONG MESSAGE THAT WE -- THAT THAT IS AN AREA OF NEED IN TERMS OF OUR FUNDING. AND THAT DID LEAD TO THE REMIND CONCEPT APPROVAL THAT JUST OCCURRED IN THE SEPTEMBER BOARD MEETING. SO I DIDN'T CALL IT OUT SPECIFICALLY BECAUSE THAT HAD BEEN DISCUSSED SO EXTENSIVELY.

DR. SOUTHARD: THANK YOU.

CHAIRMAN GOLDSTEIN: FRED.

DR. FISHER: THANKS FOR THAT. AND IT'S ALWAYS HELPFUL TO HAVE THE INFORMATION REFRESHED.

TWO THINGS. SO BASED ON THE QUICK MATH FROM SCREEN, OVER THE ENTIRE LIFETIME OF CIRM, IT LOOKS LIKE IN THE NEIGHBORHOOD OF A BILLION DOLLARS HAS BEEN SPENT ON NEURO OVER THE THREE PILLARS. AND NOW WE HAVE 1.5 BILLION THAT WE ARE CHARGED WITH TRACKING. AND I'M WONDERING OVER WHAT PERIOD OF TIME ARE WE GIVING OURSELVES TO EXPEND THAT 1.5 BILLION. AND THEN I HAVE A FOLLOW-UP QUESTION.

DR. MILLAN: THANK YOU SO MUCH. IS THAT



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DIRECTED AT ME, OR WAS THAT FOR THE WHOLE NEURO TASK FORCE?

DR. FISHER: NO. IT'S DIRECTED AT THE PEOPLE WHO KNOW THE ANSWER TO THE QUESTION, WHICH I ASSUME IS YOU.

DR. MILLAN: SO JUST IN RESPONSE TO YOUR QUESTION, I'M GOING TO KIND OF JUST REMIND EVERYBODY THAT WE DON'T HAVE A SPECIFIC, EXCEPT FOR THE REMIND PROGRAM ANNOUNCEMENT THAT WAS JUST APPROVED BY THE BOARD, OUR PROGRAM FOR DISCOVERY, TRANSLATION, AND CLINICAL, THE PROGRAMS THAT I JUST REPORTED ON, ARE BASED ON BRINGING IN ALL APPLICATIONS THAT ARE ELIGIBLE ACCORDING TO SCOPE. AND THE SCOPE IS REGENERATIVE MEDICINE PROGRAMS. YOU'RE AWARE OF -- THIS IS SOMETHING THAT GIL PRESENTED AT EVERY APPLICATION REVIEW SUBCOMMITTEE MEETING AS WELL AS AT THE GWG.

SO THEY COME IN AND THEY ARE JUDGED BASED ON SCIENTIFIC MERIT, IMPACT, AND ALL OF THE REVIEW CRITERIA THAT GIL HAS PRESENTED. SO BASED ON THAT, THE PROGRAMS ARE THEN BROUGHT TO THE BOARD. SO THE RESULTING 30 TO 35 PERCENT IN TERMS OF EXPENDITURES TO NEURO HAS GROWN THROUGH THIS PROCESS. SO IT WASN'T SPECIFICALLY PROGRAMMED THAT WE ARE BUDGETING 30 PERCENT OF OUR RESEARCH BUDGET FOR NEURO. AND SO



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I THINK EVERYBODY -- BUT BASED ON THAT, IF WE WERE TO LOOK AT HISTORICAL PERFORMANCE, IF WE WERE GOING TO CONTINUE TO HAVE THAT 30-PERCENT EXPENDITURE THROUGH THE COURSE OF THE PROP 14 FUNDING LIFE, FOR INSTANCE, WE WOULD BE ON TARGET TO EXPEND THE $1.5 BILLION BECAUSE IT WOULD ESSENTIALLY -- THE 1.5 BILLION OUT OF THE ELIGIBLE 4.8 BILLION OF THE $5.5 BILLION PROP 14 IS APPROXIMATELY 31.25 PERCENT OF THE TOTAL $4.8 BILLION IN TOTAL RESEARCH FUNDS.

SO IF OUR PERFORMANCE AS WE ARE GOING RIGHT NOW CONTINUES TO TRACK AT THE HISTORICAL PERFORMANCE, THEN IT WOULD TRACK ALONG AND BE PROPORTIONALLY EXPENDED TO ABOUT 30, 35 PERCENT. SO THAT MATCHES THAT 31 PERCENT OF THE 4.8 BILLION.

WHETHER IT'S ANOTHER 10 YEARS OR 15 YEARS, THE PROJECTIONS ARE CONTINUALLY BEING UPDATED BASED ON OUR RESEARCH EXPENDITURES AND PROGRAMS THAT ARE BROUGHT TO THE BOARD AND EVOLVING STRATEGY THROUGH THE NEURO TASK FORCE AND SOME OF THE CONVERSATIONS THAT WILL HAPPEN AT THE SCIENCE SUBCOMMITTEE AND THE BOARD.

PLEASE LET ME KNOW IF THAT DIRECTLY ANSWERS YOUR QUESTION. AND IF NOT, I'LL TRY TO FIGURE OUT WHAT OTHER INFORMATION I CAN BRING INTO IT.



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DR. FISHER: LET ME GIVE YOU MY INTERPRETATION OF THE ANSWER, AND YOU'LL TELL ME IF I'VE UNDERSTOOD IT CORRECTLY. SO WHATEVER PERIOD OF TIME WE ALLOW OURSELVES TO EXPEND 1.5 BILLION, WHICH FROM A RESOURCE ALLOCATION METHODOLOGY, WE WOULD -- MY PRACTICE IS TO FIGURE OUT HOW MANY YEARS DO I HAVE TO SPEND THIS MONEY. AND YOU'RE SAYING THAT WITHIN WHATEVER PARAMETERS EXIST AROUND THE AMOUNT OF TIME WE HAVE TO SPEND THE MONEY, YOU'RE TELLING US THAT WE WILL ACHIEVE THE PROPOSITION'S GOAL OF AT LEAST 1.5 BILLION IN NEURO SPENDING JUST BASED ON WHAT WE ARE CURRENTLY DOING NOW WITHOUT ANY NEW INITIATIVES, ANY ADDITIONAL NEW INITIATIVES NOTWITHSTANDING WHAT THE BOARD JUST APPROVED.

THAT SEEMS IN MY MIND TO ANSWER ONE OF THE FUNDAMENTAL QUESTIONS OF THIS TASK FORCE IN TERMS OF ARE WE ON TRACK TO AND HOW WILL WE INVEST 1.5 BILLION IN NEURO. AND THE ANSWER IS HERE IS HOW. YOUR DATA JUST SHOWED THIS IS THE WAY WE'RE GOING TO GET THERE, AND WE ARE GOING TO GET THERE. SO WE CAN ASSURE THE CITIZENS OF CALIFORNIA AND THE BOARD OF CIRM THAT WE WILL BE IN COMPLIANCE WITH THE CHARGE OF THE PROPOSITION AND ANSWER THE QUESTION THAT THE BOARD HAS ASKED US TO ANSWER. DO I HAVE THAT RIGHT?

DR. MILLAN: YES. WHAT YOU SAID IS IF WE

CONTINUE THE WAY WE ARE AND WE CONTINUE ON THE SAME PATH AS HISTORICAL EXPENDITURES, WE WILL MEET IN TERMS OF DOLLAR AMOUNTS FOR THE GIVEN TIME. WHETHER IT'S 10 YEARS, 15 YEARS, WE WILL BE ABLE TO MEET THE REQUIREMENTS OF INVESTING $1.5 BILLION INTO THE NEURO FIELD.

DR. FISHER: THAT'S REALLY GOOD NEWS ON ONE HAND BECAUSE WE DON'T HAVE TO CONCERN OURSELVES WITH WHETHER OR NOT WE'LL BE IN COMPLIANCE WITH THE EXPECTATIONS OF THE PROPOSITION.

THAT THEN BEGS MY SECOND QUESTION, WHICH IS THERE IS NOTHING RESTRAINING US FROM SPENDING MORE THAN 1.5 BILLION ON NEURO. AND THEN WE GET TO ASK OURSELVES THE QUESTION WHERE ELSE OR WHERE SHOULD WE BE SPENDING MORE MONEY THAN WE ARE CURRENTLY SPENDING? AND IT MAY BE PREMATURE TO ASK YOU AND THE STAFF FOR YOUR RECOMMENDATIONS IN TERMS OF WHAT WE SHOULD BE TURNING OUR ATTENTION TO IN TERMS OF NEURO SPENDING AND HOW THAT PLAYS OUT IN TERMS OF NEURODEGENERATIVE, MORE NEUROPSYCH, MENTAL HEALTH, OR MORE OTHER THINGS.

SO IN TERMS OF WHERE THIS COMMITTEE GOES NEXT, IN MY HEAD I'M CHECKING OFF THE BOXES OF THE CHARGE OF THIS COMMITTEE, AND ANY NEW AND INNOVATIVE INVESTMENT IDEAS, WHETHER THEY'RE IN



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NEURODEGENERATIVE OR NEUROPSYCH OR NEURO ANYTHING ELSE, THERE MIGHT BE NEW AND INNOVATIVE OPPORTUNITIES THAT GROUPS WOULD LIKE TO SEE US INVESTING IN. ALL OF THE EARLY WORK YOU DID WITH THE NEURODEGENERATIVE FOLKS LEADING THEM TO THE EXPECTATION THAT WE WOULD BE SPENDING MORE THAN WE TRADITIONALLY HAD BEEN IN NEURODEGENERATIVE. HOW DO WE RESPOND TO THE EXPECTATION OF THE SCIENTISTS IN VARIOUS COMMUNITIES THAT SEE OPPORTUNITIES FOR EVEN GREATER INVESTMENT? AND WE SHOULD BE A GIVING HEADS-UP TO THE BOARD AT SOME POINT THAT WE ARE ON TRACK TO MEET THAT GOAL, AND NOW WE WANT TO FIGURE OUT WHERE WE SHOULD BE SPENDING MORE MONEY, WHICH IS THE OTHER PART OF OUR CHARGE AND IF STAFF HAVE COME TO ANY CONCLUSIONS AT THIS POINT ABOUT HOW WE SHOULD GO ABOUT THAT.

CHAIRMAN GOLDSTEIN: SO I THINK THAT'S A FAIR SUMMARY, FRED. WE ARE ON TRACK. I'LL POINT OUT THAT AT THE MOMENT, THE WAY RELATIVE PRIORITY DECISIONS AMONG DISEASES AND TECHNOLOGIES ARE BEING MADE IS THAT IT'S A COMBINATION OF WHAT GRANT APPLICANTS THINK IS IMPORTANT, SO THAT'S WHAT THEY SUBMIT. AND THEN THE GRANT REVIEW GROUP, GWG, IS THE GROUP THAT ENDS UP DECIDING THE FINAL RELATIVE PRIORITIES FOR WHAT MONEY IS GOING TO BE SPENT ON.



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IT SEEMS TO ME, AT LEAST, THAT ONE WAY WE WANT TO EVALUATE WHERE WE ARE IS, A FEW WAYS, IS TO LOOK AT THE UNIQUENESS OF APPROACHES THAT ARE CURRENTLY BEING USED TO ASSESS MECHANISM AND THERAPY DEVELOPMENT. THE SECOND IS DISEASE IMPACT, WHICH WE JUST HEARD ABOUT. ARE WE ADDRESSING DISEASE IMPACT IN A WAY THAT'S APPROPRIATE, OR ARE THERE PLACES WE COULD SPUR ADDITIONAL INVESTMENT, AS YOU POINT OUT, TO TRY TO MAKE A DIFFERENCE FASTER.

AND THE THIRD ISSUE THAT REALLY HASN'T COME UP YET, BUT I THINK IS RELEVANT IS TO ASK WHETHER THERE ARE PLATFORM TECHNOLOGIES THAT ARE BEING DEVELOPED THAT WOULD HAVE IMPACT IN MORE THAN ONE DISEASE. I'VE MENTIONED DON KOHN'S APPROACH A NUMBER OF TIMES. THERE ARE HINTS IN THE LITERATURE AND SOME OF THE EXPERIMENTS BEING DONE THAT THERE MAY BE SITUATIONS WHERE THAT APPROACH, WHICH IS A PLATFORM TECHNOLOGY, HAS AN IMPACT IN THE BRAIN FOR REASONS THAT ARE MAYBE NOT SO CLEAR, BUT MAYBE RELEVANT.

SO, FRED, I SEE YOU HAVE YOUR HAND UP AGAIN. WHAT WOULD YOU LIKE TO --

DR. FISHER: SO I'D LIKE TO REQUEST THAT, GIVEN THAT THIS COMMITTEE WAS FORMED AFTER THE CIRM TEAM BROUGHT TOGETHER THE NEURODEGENERATIVE DISEASE



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RESEARCH COMMUNITY, LOOSELY DEFINED, TO GET THEIR INPUT IN THE FORMULATION OF THE $1.5 BILLION GOAL, I THINK WE SHOULD BE HEARING FROM THAT COMMUNITY ABOUT THEIR ENTHUSIASM FOR THE OPPORTUNITY TO -- FOR ADDITIONAL INVESTMENT AND WHAT THOSE ARE.

I'D LIKE TO SEE US TURN AWAY FROM ISSUES OF DISEASE IMPACT AND QUALITY OF LIFE AND COST ISSUES. I'D LIKE TO HEAR FROM THE SCIENTIFIC COMMUNITY ABOUT WHERE THEY SEE THE OPPORTUNITY. AND SINCE THE NEURODEGENERATIVE DISEASE COMMUNITY HAD A LOT TO SAY ABOUT THAT, THAT YIELDED THE GOAL OF 1.5 BILLION, AS WE ARE CONTEMPLATING NEW INVESTMENT OPPORTUNITIES, I THINK IT'S TIME, GIVEN WHAT WE SPENT OUR TIME ON SO FAR, I THINK IT'S TIME WE HEAR FROM THE NEURODEGENERATIVE DISEASE COMMUNITY THAT INFORMED THE CREATION OF THAT GOAL NOW THAT WE ARE IN A POSITION TO ACTUALLY ACT ON THE OPPORTUNITY. WE SHOULD HEAR FROM THEM ABOUT WHAT THEY THINK WE SHOULD BE SPENDING MORE MONEY ON.

CHAIRMAN GOLDSTEIN: YEAH. I AGREE WITH THAT, FRED. I THINK THAT'S A GOOD THING FOR US TO DO. I WOULD ADD THAT PROBABLY WE WANT TO HEAR FROM MORE THAN JUST THE NEURODEGENERATIVE COMMUNITY BECAUSE THERE'S A NEURO-INJURY COMMUNITY, PEOPLE WHO WORK ON STROKE AND OTHER, TBI AND OTHER PROBLEMS.



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THEY'RE A PART OF WHAT WE DO, AND THEIR INPUT WOULD BE USEFUL TO US AS WELL, I THINK.

DR. FISHER: THE CIRM TEAM SPENT TIME TALKING TO SCIENTISTS IN THE FORMULATION OF THIS. AND SO THEY KNOW WHO THEY SPOKE TO AND WHAT THEY TALKED ABOUT. AND I'M CERTAINLY NOT SUGGESTING THAT NEURODEGENERATIVE MIGHT NOT BE THE ONLY AREA WHERE WE FOCUS; BUT GIVEN THE AMOUNT OF TIME WE HAVE GIVEN NEUROPSYCH AND, AGAIN, SPENT MOST OF TODAY HEARING ABOUT MENTAL HEALTH, I'D LIKE TO SUGGEST THAT WE TURN OUR ATTENTION AND INVITE THE NEURODEGENERATIVE DISEASE COMMUNITY TO COME IN AND TELL US WHERE THEY THINK WE SHOULD BE SPENDING MORE MONEY. AND THEN WE CAN HEAR THAT AND MAYBE THAT CREATES A NEW PROGRAM INITIATIVE, MAYBE IT DOESN'T. AND THEN MAYBE WE TURN OUR ATTENTION TO STROKE AND MAYBE WE TURN OUR ATTENTION TO BRAIN INJURY. WE CAN TURN OUR ATTENTION TO LOTS OF DIFFERENT THINGS. AND THE CIRM TEAM CAN TELL US WHAT GROUPS OF SCIENTISTS THEY SPOKE WITH. AND I PARTICULARLY WANT TO HEAR FROM THE GROUPS OF SCIENTISTS THEY SPOKE WITH SO THAT THAT CAN INFORM OUR THINKING AS WE STRATEGIZE HOW WE'RE GOING TO GO FORWARD.

SORRY, MARIA, FOR TAKING MORE OF YOUR TIME.

VICE CHAIR BONNEVILLE: I WAS JUST GOING TO COMMENT THAT IT DOES SEEM LIKE WE NEED AN UNDERSTANDING OF JUST HOW THIS COMMITTEE IS GOING MOVE FORWARD AND HOW THEY'RE GOING TO TAKE UP THE DIFFERENT SUBJECTS. IN ADDITION TO THAT, WE'VE HAD A PASSIVE APPROACH TO WHAT WE FUND IN THE SENSE THAT THERE HASN'T BEEN ANYTHING DIRECTED OUTSIDE OF SICKLE CELL AND NOW NEUROPSYCH WHERE THE TEAM UNDERSTANDS THAT THERE IS A SET AMOUNT OF MONEY FOR A SPECIFIC PROJECT, AND THE WHOLE BOARD HAS AGREED THIS IS WHAT WE HAVE TO DO.

SO, IN OTHER WORDS, IF THERE ARE GOOD NEURO CLIN PROJECTS THAT HAPPEN TO COMMIT OR THAT THE TEAM HEARS ABOUT AND THEY BRING IN, IT GOES TO THE GWG, IT'S MERITORIOUS, IT GETS FUNDED. IF IT DOESN'T, IT DOESN'T. THE GWG DOES NOT COMMENT ON HOW MUCH MONEY WE'VE SPENT IN OTHER DISEASE AREAS. THAT'S NOT THEIR JOB. THAT'S THE BOARD'S JOB. SO THEY JUST DECIDE IS IT MERITORIOUS OR IS IT NOT.

SO A DIRECTED STRATEGY I THINK IS IMPORTANT. THAT'S WHY WE ARE ALL HERE. SO WHAT THAT IS AND HOW IT COMES TO PASS, I THINK, IS WHAT WE NEED TO DETERMINE.

CHAIRMAN GOLDSTEIN: GREAT. IT'S A GREAT POINT. OTHER COMMENTS OR QUESTIONS FROM THE GROUP?



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I THINK HEARING FROM THE NEURODEGENERATIVE FOLKS WILL ALSO HELP US IDENTIFY WHETHER WE ARE UNDERINVESTED IN AN IMPORTANT AREA WHERE USEFUL TECHNOLOGY HAS RECENTLY EVOLVED OR WHERE UNDERSTANDING OF DISEASE HAS BECOME MORE DETAILED AND USEFUL.

SO, MARIA MILLAN, SOMEBODY ON YOUR STAFF, NO DOUBT, CAN PROVIDE US WITH A LIST OF THE FOLKS WE'VE ABOUT FROM THE NEURODEGENERATIVE COMMUNITY IN PAST MEETINGS. SO --

DR. MILLAN: ABSOLUTELY. I JUST WANTED TO -- I THINK THAT WAS MENTIONED. IN 2019, BEFORE THE PASSAGE OF -- BEFORE THE PROPOSITION WAS EVEN ON THE BALLOT, CIRM ASSEMBLED A MEETING CALLED "BRAINSTORMING NEURODEGENERATION." AND THERE WERE SCIENTISTS, MULTIPLE STAKEHOLDERS, OTHER FOUNDATIONS IN THIS SPACE OF NEURODEGENERATION. AND THAT'S WHAT DIRECTOR FISHER IS REFERRING TO. IT WAS A VERY ROBUST MEETING IN TERMS OF THE OPPORTUNITIES FOR CREATING CONSORTIUM APPROACHES, WHICH, AGAIN, INFORMED WHAT THE GENERAL FORMAT UPON WHICH THE REMIND PROGRAM WAS BUILT FOR NEUROPSYCH.

SO ESSENTIALLY I THINK THE MAJOR MESSAGING WE GOT FROM OUR SCIENTIFIC STRATEGY ADVISORY PANEL, FROM SUBSEQUENT GATHERINGS OR WORKSHOPS THAT ROSA



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AVILES PUT TOGETHER WITH HER TEAM WHEN SHE SAME ON BOARD. ROSA WAS RECRUITED WITH THIS IN MIND BECAUSE SHE'S BEEN INVOLVED IN CONSORTIA, IN FORMATION OF CONSORTIA IN OTHER FORMATS AT THE FOUNDATION FOR NIH. SO THIS IS SOMETHING THAT THE TEAM IS VERY PASSIONATE ABOUT IS HOW DO WE FOSTER COMMUNITIES TO CREATE INNOVATIVE APPROACHES THAT CAPITALIZE ON KNOWLEDGE THAT CAN BE APPLIED BROADLY AND THEN ALSO PURSUED IN A COLLABORATIVE FASHION.

SO I DO THINK WE ARE VERY EXCITED ABOUT BRINGING THAT TO THE NEURO TASK FORCE. AND WE DO HAVE A VERY SOLID STARTING POINT FROM THE VARIOUS WORKSHOPS. AND IN HER PRESENTATIONS, ROSA ACTUALLY OUTLINED THE VARIOUS MEETINGS THAT HAVE TAKEN PLACE EVEN SINCE THE "BRAINSTORMING NEURODEGENERATION" IN TERMS OF VARIOUS COMPONENTS OF THIS, DATA SHARING AND THOSE FORMATS AS WELL AS OTHER TYPES OF COLLABORATIVE FORMATS.

AND THEN, OF COURSE, THERE'S THE CLINICAL ASPECT, AND ABLA CREASEY AND TEAM HAVE BEEN VERY INVOLVED WITH INVESTIGATORS WHO HAVE BEEN INVOLVED IN OTHER INITIATIVES AND WITH OPPORTUNITIES FOR THAT SUCH AS THE ANSWER ALS INITIATIVE AS WELL AS THE NEURONEXT TRIALS AND THINGS LIKE THAT. SO THERE'S SO MANY DIFFERENT LEARNINGS FROM THOSE EXPERIENCES



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THAT I THINK WOULD BE REALLY NICE TO BE ABLE TO BRING THAT TO THE NEURO TASK FORCE.

CHAIRMAN GOLDSTEIN: GREAT. THAT WOULD BE VERY HELPFUL. IF WE CAN GET THOSE SOON, THAT WOULD HELP US PLAN FOR HOW WE WANT TO PROCEED FOR THE NEXT FEW MEETINGS AND, I GUESS, INFORM WHETHER WE WANT TO HAVE SORT OF A SIMILAR MEETING NOW FOR 23 OR 24 THAT MIRRORS WHAT WAS DONE IN 19 BECAUSE THE FIELDS HAVE CERTAINLY MOVED AHEAD. AND SO WE SHOULD GET CURRENT ON WHAT'S WORKING, WHAT ISN'T WORKING, AND WHERE WE ARE.

OTHER COMMENTS OR QUESTIONS? I SENSE A CERTAIN LASSITUDE OVERTAKING THE GROUP. PUBLIC COMMENT IS UP NEXT.

MR. TOCHER: THERE DOESN'T APPEAR TO BE ANY, LARRY. NOPE. I THINK WE ARE GOOD TO GO.

CHAIRMAN GOLDSTEIN: NO PUBLIC COMMENT. THEN I SUGGEST THAT WE ADJOURN. USEFUL MEETING TODAY. THANK YOU ALL FOR YOUR TIME AND PARTICIPATION. WE'LL GET BACK TO YOU WITH INFORMATION ABOUT THE 2019 MEETING SHORTLY OR MEETINGS.

(THE MEETING WAS THEN CONCLUDED.)



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REPORTER'S CERTIFICATE

I, BETH C. DRAIN, A CERTIFIED SHORTHAND REPORTER IN AND FOR THE STATE OF CALIFORNIA, HEREBY CERTIFY THAT THE FOREGOING TRANSCRIPT OF THE VIRTUAL PROCEEDINGS BEFORE THE TASK FORCE ON NEUROSCIENCE AND MEDICINE OF THE INDEPENDENT CITIZEN'S OVERSIGHT COMMITTEE OF THE CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE IN THE MATTER OF ITS REGULAR MEETING HELD ON OCTOBER 18, 2023, WAS HELD AS HEREIN APPEARS AND THAT THIS IS THE ORIGINAL TRANSCRIPT THEREOF AND THAT THE STATEMENTS THAT APPEAR IN THIS TRANSCRIPT WERE REPORTED STENOGRAPHICALLY BY ME AND TRANSCRIBED BY ME. I ALSO CERTIFY THAT THIS TRANSCRIPT IS A TRUE AND ACCURATE RECORD OF THE PROCEEDING.

BETH C. DRAIN, CA CSR 7152
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