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I’m Peter Schwartz the director of the IU Center for Bioethics and of the bioethics

subject advocacy of the Indiana CTSI and this is

our next installment about bioethics and sorry about translational research ethics applied topics talk series these

are meant to be short 20 to 30 minutes

introduction to a key topic in research ethics often boring on regulations or

researchers for people who have an interest want to go these are our

website through the CTSI on the Senate website what is makes resources for people to

learn always call us or email us at the program be staff as we call it for

consultations we are always very happy to provide so it's my pleasure introduce

Jane our top JD MA she's a fast investigator of this Center that's

actually the longest span no she is

also very importantly the director of the IU Health Department of ethics in

charge and she's also an adjunct

professor in there's a great pleasure - MS Hart saw Esquire who's nothing right

Bob I think counselor arts all right so

so that idea - talk is to discuss an area of research all right how do they

clinically happen and this sort of fuzziness of knowing when and when you

do not need consent of the individual to research sort of arising out of that

interaction and [Music] so just some brief objectives we're

going to review this Oracle context of research treatment distinction within a context of consent and so the

purpose of doing that is mostly to make the argument or at least to excuse how

messy this issue is and why it's so messy then to identify some concerns of

informed consent in individual and combination say so what I mean by that is individual meeting consent in

treatment versus consent in research versus consent in research arising out

of treatment and then to clarify the regulatory values and the requirements

of research in a clinical context and I think I am going to need the video thing on the side to - is there a way to

adjust that you can minimize it okay because oh because I otherwise will not

be able to read my own slides and I need them okay so the reason that I decided

to do this talk was to use it as a deadline to get a handle on an issue

that is coming up right now our Center which is the consent the extensible

consent to research that is contained in our general consent to treatment so when

patients come into clinic or hospital within Indiana University they sign what

is called a general ethical consent to treatment and teaching responsibilities and the first paragraph of that is

entitled authorization for treatment but includes this which is I understand the hospital is a research and teaching

institution and my body looks by parts matter including organs may be used for

teaching and research and so for those

of you who are regularly interacting with patients this paragraph actually

causes a lot of trouble for us you chefs don't like it clinicians don't

know how to respond to their patients objections to it we are unsure why it's

in there and what it actually does and so the concern would be as we certainly

move through this talk that means several concerns but it disrupts the therapeutic relationship because it

makes patients unhappy right at the outset of their of their interaction

that it gives clinicians false comfort in research that they would do leukemia

can rely on this for the research that they do in clinic which they cannot and

and then just the sort of confusion as to what why where did this come from and

why is it here so along that half argument at least for

three categories of consent relevant scenarios the treatment scenario being

non therapeutic research scenario so those would be the sort of more typical

research studies that sort of like advertised on the bus do you have

diabetes come in for your research that sort of thing and then the combined research treatment scenario that now

it's tied largely to bio banking issues of bio banking issues of data collection

biospecimen storage and that sort of thing which is really specimens obtained

during treatment and used in research so that narrow category of not narrow right

as a huge category of research now so I also I got to find some primary in each

of these three categories the these are my own observations based on reading the

literature and the case law sociated with each of these categories that I had to sort of somatically identify the

priority in each of those concern with

consent in treatment scenario of his informativeness whether the person is informed with the rationale being that

they need to be informed in order to calculate the risk benefit analysis of treatment with benefit being the thing

that distinguishes treatment from research generally the most well known

case was a woman who could send it to a

pelvic examination under ether this is occasion like 1915 I think she

can send it to a pelvic exam but explicitly withheld her consent from any

surgical procedure done while she was underneath her and the physician did a

surgical removal of tumor anyway and we sue the hospital

she actually ended up losing because she sued the wrong entities which is relevant the ultimate legal principle

that comes out of this is that you do not obtain so then we have our non

therapeutic research category where the focus is an emphasis on voluntariness

that the person who's there wants to be an increase to the mystery of coercion and the rationale for that being that

they understand in the absence of

voluntary consent is absolutely essential and then our third category

which is really going to be today which is this combined category where the

research is being done either as part of treatment or arising out of clinical

care and my schematic categorization there is that the concern in those cases

is a potential conflict of interest which might disrupt the fiduciary

obligation of the physician to the patient and that your example of that

the prime example the famous warm case of the patient who had hairy cell leukemia and was treated

extensively by a physician who was pursuing actively pursuing a patent on its treatment for that condition and

bringing a number of tests and obtained a number of biospecimen that arguably were not part of treatment at all and

didn't tell the patient did those things weren't necessary for treatment so moving forward just to begin the kinds

of consent forms that we use here at IU Health are pervasive they are used in

almost every academic Health Center to some extent ours seems to be a little bit more explicitly attempting to consent for

research where some of the other ones as you can see here consent consent to be contacted in the future for research we

have been clinic consent to be contacted in future for research and then this is

round universities Medical Center that

things might be removed and there might be quality improvement and scientific

research done as part of the treatment center so I don't need to just pick on our institution this is really pervasive

so where did it come from and they say I think it arises out of the lack of

regulations on them early part of the 20th century middle twentieth century as

well and the resulting lawsuits then that that came because there is no real

regulatory guidance so Henrietta Lacks is the is the sort of famous case of the

person individual whose biospecimens were obtained and used in research but

not her consent for family feeling that they should have been compensated for part of the financial gain as a result

of that research important to understand the did one of the distinction is there

that it matters subsequently the individual who obtained the specimens

Henrietta Lacks dr. Jones was not the individual doing the research so as we

think about our regulatory guidance it's questionable whether the lacs scenario

which we all I think had some initial questions about his act would actually

even be impermissible today it probably would have been permissible under the Commonwealth then we have the famous

article by Henry Beecher from 1966 in

identifying multiple cases of clinical research in the clinical setting where

consent had not been obtained or it not been properly obtained and that being

kind of a watershed paper exposing the issue and then Thomas Moore at our

Thomas More I always do that today is another Catholic school John Moore care

that you received in the late 1970s and the court in his case agrees with him

that he should have been advised of a potential conflict of interest of the physician who was both doing the

research and providing his treatment he's awarded $1 for that nominal damages

which allows the court to identify a new principal legal requirement for consent even in the absence of any real

identifiable damages to the person so

I think what happens here with these with these forms is that in the absence

of any real regulatory authority lawyers

decided that we probably needed to insulate ourselves from research we

needed to provide some kind of insulation for claim similar to Moore's and the way to do that was in that initial treatment consent form so

these forms just kind of emerge over time and they're picked up and used in hospitals

so the question was today in today's contemporary research studies mean

anything or do anything and that answer

is tied to these two big question which is when is informed consent to research required and then in cases where it is

what is required of informed consent or research so to address these are these

are questions that are answered in the common rule and so research consent is

required anytime there is a human subject research defined in a common

rule as research being done on a living individual involving the intervention or

interaction or in which you obtain identifiable specimens or identify

identifiable private information and so you can imagine how many scenarios then

go in in a clinical setting if you have an oncologist for example who is doing

involved in the clinical trial medication on patients whom he or she is

seeing and so they are both the treater

and the private investigator and they

are drawing the blood they know who the patient is there's essentially no no

screen between the researcher another patient or even sort of less formal

things anyway talking to my students that sometimes you know joke about how

how frequently people are involved in research that they don't even necessarily identify as research sort of

and informal thing I'm going to try this communication approach with my patient and see you know if it works and

then if you're planning prospectively to - you know publish that or to offer that

up as actual research it really should have IRB approval less units

so this is so the intervention or interaction the close connection between

the person who is being studied and the person doing the city and if we draw

then the distinction between Moore and Henrietta Lacks you start to see that become so in the last case her

obstetrician was Dr. Jones who obtained a biospecimen from her cervical cancer I

sent it down to a lab where it was de-identified and dr. guy Brigade was

the person who actually did the research and develop the cell line and propagated to someone so there was a distinction

there it set up that sort of students Thomas, John or on the other hand its

musician Dr. Gould was both attempting to develop the patent line and actively

treating the patient for hairy cell leukemia at the same time so he was doing the intervention and interaction

on identifiable specimens so that was

human subjects research I should be clear that the common rules I think is

not promulgated formally until 1991 I think it is it's so this did not

govern that case but those sort of frequency with which those things arose

led to the need for regulations like this so here are some of the definitions

for what an intervention is and when interaction is physical procedures by

which information is gathered manipulations of the subject or the

subjects environment interaction communication or interpersonal contact between the investigator and so there

are a whole range of IRB review well let's start with an IRB

review would be required and they're largely contingent on that distinction

the intervention and interaction distinction so prospective collection of

biospecimens for specific research things so you know you're doing research you have a research question your

purpose of interacting with the patient is to obtain data for the research perspective collection and storage of

biospecimens for future use so you know that's why you're collecting them

secondary use of identifiable biospecimens and I think this is a really important distinction for us to

make for clinicians who are doing research or researchers who are relying on clinicians for those

biospecimens there's a whole category of biospecimens that become

available because they are this room waste leftover or refuse of clinical

diagnostic procedures of care so an example of this pregnancy HSG test so a

woman has a home pregnancy test indicating that she may be pregnant she comes in to have confirmation when the

blood tests the blood test indicates that she is pregnant and those wastes of that afterwards is sent to somebody

who's doing research on biomarkers for stress or something knows what it is and

that secondary de-identified use would not fall within this within this

category it would not constitute human subjects research so the

identifiability of the subject becomes the critical issue for a lot of this secondary use of coded biospecimens

investigators access to the secondary use of de-identified biospecimens and

regenerate on the data for the FDA and testing an efficacy of diagnostic

devices using data so examples

kind of talk about this back at all examples of research not requiring IR Group IRB approval so this is your first

category red collection and use of biological specimens obtained through standard of care clinical

so patient who comes in and has a biopsy of their cervical cancer a patient who

comes in has the blood HCG test those kinds of things the waist or remnant of

that specimen can be used in research

secondary use of de-identified coated biospecimens when you don't have a code and they use the biological specimens

from deceased individual Center project for that decay

it's interesting to note in the Henrietta Lacks case this is just a little bit of an aside that there were

concerns about consent even in her case and the autopsy of her case was limited

her head and her brain were not autopsy because the family would not

consent to that so there was some understanding of deaf consent even

within that context which I think is I think my URL at the bottom there is no

longer an active URL so yes what is the

so the FDA is not I don't know I'll be

honest with you maybe if somebody else in the room I understand that the FDA exceptions to this John I think it is

not party to the comment I think that's right but there are 16 agencies that are

[Music]

which kind of biospecimen research can go forward with no consent right and

then I've left out of here the issue of waivers of consent which is a sort of

you know in the interest of time but obviously there would be human subjects research for which you could get a waiver because of the

but really announcer practicability problem with consenting under certain circumstances but it was second bullet

point the first part is de-identified human stuff unit foot samples and it's not human subjects research at all

where's it's a I asked you a question

this is Andrew it so when you say de-identified biospecimens to set what

happens to the medical record that goes with that biospecimen is that part of

the DIA does that have to be removed completely or is it just the identification of the person but other

information that goes with that specimen age and weight or height or disease like

that are those have to be scrubbed as well some of those categories will

identify individuals over the age of

necessarily the other our number but a

general sort of guideline or rule that I particularly kind of like this is that if you can use

the various categories to easily triangulate a single person then that

specimen is identifiable so if you think about something like zip code plus age

plus sex those three things together probably

make that biospecimen identifiable and so the EMR through an entire EMR

traveling with a biospecimen is identified very clear that question of

which bits and pieces of the EMR you attached to a single biospecimen out at being identifiable is a little a little

bit fuzzier some things are automatic social security number for example other things not so much it depends on the

combination exactly yes yeah yes I

that's what I was getting at this complication for particularly so someone who has a particular disease state and

their major sex and they're being seen at a particular clinic even if the name

and other identifying still might be able to triangulate it to offer any from

general rules at all here because I think as we get further into genetic and genomic research we're going to be able

to identify either pathogenic genes or

potentially pathogenic genes that are unique or at least very rare and so

the mere presence of those would seem to make somebody identifiable

and so I see and so that actually was exactly the reason for the proposed new

common rule they proposed that any settlement djr if you have those

resources but that's why they but I

wonder whether discussion but I do wonder whether we're affectionate to the

place where and the example or the

analogy that I might use for that

remember that website so that was the website that people could use to have affairs

somebody hacked it and identify all of the credit card numbers and they were

sophisticated enough that they were then able to create a map where they I think

they triangulated maybe ISP numbers with credit card numbers down to addresses

have pinpointed the addresses of individuals who had attempted to date

through this app so I can see how something like that would easily be able you know in some future dystopian not so

future world happen with DNA well there have to be a database of DNA to prepare yeah well I mean I mean you

go to some DNA that's rather specific and all you need to go with yeah

also just a speculation but you would like just having like you would still

need some kind of yeah unless it's highly specific but there are those

[Music]

something like have to be a research enterprise or specialized ancestry.com

they've been able to people and arrest them based on mellitus yeah so let me

just get through anyway two more slides here basically and then we can kind of these sexier topics and even bottom line

[Music]

situations so if your research does

constitute human subjects research the elements of consent that are required are fairly detailed extensive so this is

just a summary this is not verbatim and this is the summary of the requirements for research in the common rules so if

you are doing human subjects research you must obtain a detailed consent they

lose a statement what the study is and foreseeable risks and benefits and alternatives and all this other stuff

and in addition to that if it's going to include a biospecimen you must have

these two additional elements of

indicating of the potential for future research and brief you know not broad

consent so if you are you're going to do use a broad consent or potential for

future research you must have all of the elements of the standard informed consent plus these additional six pieces

of information which include contact information of an individual who can answer questions which I think is really

important let's begin to research on biospecimens people largely don't

understand so the place where I kind

of end up you know back where I began is this this language and the general

consent ubiquitous academic health centers that purports to consent to research in a clinical setting that's

where these folks receive this document right they are not recruited to research and then get this document they are

there for treatment and so my conclusions would be that there are

really two pathways to research and access context one involves human subject research where you have to

comply with regulatory requirements for consent as set forth in the common rule and therefore they sort of Kongo consent

to treatment consent to research forms would not be compliant they would not satisfy those requirements they would

not satisfy the requirements for an incentive the other pathway to research

and in clinical context are arising out of the clinical encounter however you want to think it would be non human subjects or exempt research in which

consent is not required at all so the combo of consent forms aren't necessary

doesn't have to be careful about the intercept because recognizing that

consent is a process is not just a document given that were accredited we do require a record sending process for

this entry search so that way so even knowing that would be fine but this

so where I end up in terms of practical advice to our clinicians or

not and that institution we sort of heat

our patients objections to being confronted with a sort of kind of consent to research when they're there

for treatment pushes the right side

people were surprised when I hear about it my impression people are surprised

when I've seen a research put that in

with be useful in preventing them later oh you're doing research again even for

me so your objection is that well that's not actually but at least it it takes on

it confronts that price so I yes and I

kind of like the language that's used by Northwestern I think this probably it

also it also doesn't cover you can have human subjects research review of

medical records right which they will contact the person that says will

contact you to discuss research opportunity nights that's different than so this is just saying if we're it's

like that in research right you sign up for and then contact you with research

yeah I don't know there's um and I let

the TGA is sitting here that basically you'd like it's a rican centralization

of what it's being it's we don't need

your consent so look at the identified information about you we do that we

don't need your consent to use your left or a sample rate it's trash so it's not

a matter of hey come here there are

things about you that we will do to protect your identity also can access

identifiable information without consent

for research for research Wow when

expedited category and now it now exempt category for secondary research as long

as there's privacy we have prospective

identifiable medical record research so I want to get back to this though this issue though because this becomes

important to meet you so for research that one of the fundamental sort issues is voluntariness and so one

of the questions that I have about this particular form is whether somebody who is there for treatment has to sign a

consent for treatment that includes a consent for research can be said to be voluntarily agreeing to that research I

think there's some questions about whether these forms which include a lot

of information our voluntary has to any of it but certainly if we prioritize

voluntariness and research there's

there's something similar I think in this instance to like the ACMG

controversy

said that you had to return if you were going to do a large-scale genetic test you were as researcher within clinical

settings you were required to return specific genetic information and the

original statement said that there was no option if you are going to get a

large-scale test you had to also receive information that wasn't and then there's

a huge backlash to that then ended up with them sort of rescinding that

recommendation and I think there's something really resonant with hearsay

now with if you're going to if you're bringing someone into the ER and saying

do you want to receive treatment if you do yeah there's a there's I mean so the

language in in law would be these are if adhesion contract with the bargaining power is so uneven and the need is so

great for whatever is that you're seeking that the contract could effectively say anything and you would sign it and so those are generally

frowned upon so and then there's an

interesting and I'm getting to it here either there's an interesting history to treatment consent forms specifically

which arises out of surgery and the inherent risks and dangers of

surgery compared to if you start but if you needed surgery you must be in really

bad shape right so you desperately need it the oldest consent form that we have

record of is a consent form from the Ottoman Empire in the 15th century

indicating that somebody will have their kidney stones removed in if it goes poorly they won't sue so I think that

you know failure of healing it's

not the responsibility of the which seems right yeah which does so

you're right to say that we won't defend

this disclosure and the continued requirement there to receive care you

will be something just kind of research interactions is that everything will be

very well treated right so it's like using your data it's not to say that because you want to come in to get you

for your cancer we will put you on whatever we want for research purposes not even for the careful and you can't

say no to that but the same we will look at your data

protecting privacy tremendously in cases where everything there's no risk to you well we use the leftover samples in

those cases I think you said look I make it automatic treatment that's violating voluntariness I think I would say

well of course we would of course we can do a voluntary about that that's what we're talking about we say we leave

we're defenders of voluntariness research we mean when you take on risk to help other people you know some other

in this case it's just a byproduct of your hair there's no risk to you as part

of the deal yeah well you mean so you know my approach to research anyway like I

agree that the public has a an ethical obligation to participate in research

whether we can impose that upon them through the treatment context and I

think your example that you give of this sort of like hey you know you come in for treatment we treat you really well you're on an academic health center that

to me has echoes of sort of exploitative history of autopsy medicine the idea

that the impoverish will come into the university affiliated hospital and our physicians will work on you through

autopsy which is you know led obviously to enormous discoveries using the same

language in two different contexts because no Research Institute with

institution with treats learning something like that as not it's there

but it but it never is a standalone consent whenever research is

taking place so the pressure this is what purpose does the hospital have in St. us

that's exactly my question it doesn't

seem to operate in any real protective or affirmative or informed way I mean I think there may be some

research that maybe some research that takes place if our the your medical

records and leftover specimens for which we won't be but there's still a

review process with those

and these are single paragraphs pulled out of longer documents so there's I say

but to say if there is a defense of this

sort of language purpose of is to help

people understand something about how this hospital not to get to ask

permission

wouldn't make a difference that all the

sudden we included this type of information in the HIPAA form not in the

agreement to treat for working with

critics that's when they put in even

created a privacy statement and included it there and the absence of including it

there might have precluded the ability to use the medical records without yeah

I remember when I came into being too because they're frustrated our ability

to get medical records and it shouldn't have but people didn't know how to use

it you know in those context and I do I do recall I mean it was pretty specific

about like the information that specifically

two points of historical you know what is the what was during the physical

foundation were cervix which was then sent most of not sure exactly HeLa cells

came from that sound yeah but then when she died was asked for an autopsy with

consent to research use for tissue her husband initially said no and a cousin got him to say yes not actually

was sent but in all the drawbacks of standard consent we didn't use pressure

yeah so again as you say some concerns across that's not a form in this case you perform without use him because sort

of quintessential example you have to

identify if you any commercialization or not you see one that says so my students

hate it but I do agree with the courts analysis and more as to the policy reasons to not compensate participants

courage research in herself researching with naked two people objected better to

the teaching they know I mean not as disruptively

or as aggressively as I think people

maybe have a I don't know maybe I'm reading too much into it I think people have a general sense of what a teaching

hospital is or they get it after they've been here for a while all right and then it was painted

it's some sort Johnson set I don't it still doesn't return yesterday

I don't think we'll really understand how extensive and pervasive researches

here and every single level of interaction with the patient they just

can't even two things one in direct

response to today's question I there are

there is frustration also at issues oh yeah that side of it - I would agree

with that I just don't I haven't seen much of it at the sort of intake process for sure and I also I mean to your point

out that I can remember when my daughter was delivered and you know she has a congenital heart defect and there was a

resident who just kept coming into the room kept going like mouth now now like

just so excited to see this kid so I

think part of that can be mitigated whereas I don't know what you do now

helping people understand the research

yeah I mean I think

other people observing that is also

whether patients know that there may be training okay I will take this one of

our other truths of talks which is on our website to a very area research

across the center on learning healthcare systems in India you've actually promote

the idea that say learning healthcare system it's not just about your care it's about collecting data and moving forward right

it's almost like absence the PR people are you helped me say we should be

champion and you're a part of research enterprise that's why you should come

here you're part of this great institution that's moving towards actually your rights and taking care of you but also I race and run