im very excited to introduce the next

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he was the founding chair of the

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he recently served as special advisor on

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dr emanuel received his medical degree

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he is published widely in the area of

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endoflife care in addition he is often

contributing to the new york times

editorial page and cnn

in 0 he received the dan david prize

in the category of bioethics im

confident you will enjoy his lecture

today

whenever i begin talking about the

ethics of clinical research id like to

start with a little history to situate

our thinking about research ethics

because it didnt begin yesterday it

didnt begin with the declaration of

helsinki it didnt begin with nuremberg

one plausible way of starting the

history of research is in the year

william watson who was then a physician

at the foundling hospital in london

sought to test two claims related to

smallpox inoculation

he wanted to know was preparing the

patients with a purgative beneficial to

their getting inoculated and second what

was the best source of the inoculation

was it an early pox or was it a late box

he then conducted several trials the

first trial was he had

0 children treated with mercury and

yallop a very strong laxative and

purgative 0 with senna and syrup of

roses a mild laxative and purgative and

had no medications

all the children at the foundling

hospital had the same diet similar

clothes they played in the same field

and slept in the same dormitories

pus from an early park was used the end

point was the number of pox on each

child because

researchers at that time knew or doctors

at that time knew that the number of

pucks correlated with the severity of

the illness

well watsons experiment had a

deliberate study design he had controls

and matched subjects he controlled the

circumstances and other factors that he

could identify and he had a quantitative

end point

many historians say that clinical

science began in with this

experiment

we can go on and there are many other

experiments that are important

9 was the first placebocontrolled

trial

9 was the first modern randomized

placebo control trial it was

streptomycin for treatment of tb

that is just two or three highlights of

the history of clinical research

simultaneous with the history of

clinical research is the history of

research ethics

the first recorded mention of consent in

a legal case related to medicine occurs

in in a british lawsuit slater a

patient who had broken his

leg had it rebroken by two surgeons and

refixed to get better alignment the two

surgeons were held liable for

rebreaking the leg without consent

because as the judge wrote it appears

from the evidence of the surgeons that

it was improper to disunite the callous

without consent this is the usage and

law of surgeons notice what the judge is

saying at that point that

consent was necessary and that that was

the common practice of

the surgeons and that they had violated

that important need for informed consent

well another important landmark in

research ethics occurs at the end of the

9th century in 9

in the wake of pasteur and koch many

researchers are trying to find bacilli

that are causing

various diseases giuseppe sanorelli an

italian researcher working in latin

america announced that he discovered the

bacillus of yellow fever and produced

yellow fever by infecting five patients

leave aside the fact that yellow fever

is not caused by a bacteria

sir william osler at that time he wasnt

sir william mosler who was merely

chairman of the department of medicine

at johns hopkins but the most important

physician in the entire world got up at

a meeting and condemned sanorelli saying

to deliberately inject a poison of known

high degree of virulency into a human

being unless you obtain that mans

sanction or consent is not ridiculous

its criminal now notice what the most

important physician in the world is

saying at that time that you need

consent to actually administer

a toxin to a person and conduct research

on them

that event heavily influenced her walter

reed when he was appointed head of the yellow fever board by the us military because of that event walter reed decided that his research on yellow fever in cuba had to have certain ethical rules and the rules that he established were first there would be selfexperimentation every person on the yellow fever board would actually have to participate in the research he did not participate because he went back to washington when they were going to conduct it for consultations second there had to be written agreements with the other subjects the cubans who were participating third the cubans who were participating had to get payment in gold and if they died their family would get payment in gold

fourth research was restricted to adult subjects you dont do research on pediatric patients until you do it on adult subjects and so its safe and

fifth he said that every paper had to have the phrase with his full consent in the articles to make sure that everyone

knew they were

the research was done in compliance with

the patients

well

we could go through a lot of history

thinking about what the right ethical

requirements are there were 0

principles in the nuremberg code the

declaration of helsinki initially had

paragraphs but weve proposed that there

are eight distinct ethical requirements

for research to be clinical research to

be ethical first there has to be a

collaborative partnership second the

research has to have social value third

the research has to be done in a

scientifically valid manner fourth there

has to be fair subject selection fifth

there has to be a favorable risk benefit

ratio to this research six there has to

be an independent review of the research

to make sure that its ethical

seventh there has to be informed consent

and eight there has to be respect for

the humans who are participating in the

research after theyve agreed in the

informed consent process now one of the

things i want to emphasize is that those

eight principles are not higgled

higgledy piggledy put together theres

an order you start at the top and work

your way down well what do those eight

principles mean well the first one of

collaborative partnership means that to

be ethical clinical research must

involve the community in which it occurs

it cant be subjected the community

cant be subjected to the research they

have to actually agree this requires

community participation in planning

conducting and overseeing research and

somehow integrating the research results

into the actual health care system

it means avoiding supplanting existing

health care services and the sharing of

the rewards with the actual community

mechanisms to achieve collaborative

partnership can include community

advisory boards patient advocates on

scientific advisory boards even the

advocates urging funding and remember

the community doesnt just have to be a

geographic area it could be a community

of patients with a particular illness

second principle social value to be

ethical clinical research must lead to

improvements in health or advancements

in generalizable knowledge we must

consider how the research will improve

health of the participants in the

research the community in which the

research is conducted and again doesnt

have to only be a geographic community

and the larger

world research which is valueless does

not fulfill this principle is research

that cant be generalizable

me two studies where weve confirmed

some finding three or four or five times

we dont need the sixth study

and very importantly research which is

not disseminated

that has no value because no one can

learn from it so research where the

results are in the bottom drawer theyre

never discussed that is valueless

research that research actually is

unethical third principle scientific

validity research must be conducted in a methodologically rigorous manner that is practically feasible to be ethical the research must produce reliable and valid data that can be interpreted

invalid research includes underpowered studies where you have seven people in one arm and eight and another arm what are you going to conclude studies with biased endpoints biased instruments to assess outcomes or statistical texts that arent appropriate to the study

studies that cant enroll sufficient number of subjects are also not scientifically valid

the fourth principle is fair subject selection

the scientific objectives of a study not the vulnerability and not the privilege of patients should guide inclusion criteria and the populations targeted for enrollment

lowering risk enhancing generalizability these can be considered

convenient groups such as the children in a foundling hospital should not be

selected groups cannot be excluded

without good scientific reasons we dont

just exclude women piggle the piggly we

actually have a reason we might not want

to enroll them higher risk is a valid

reason to exclude groups thats why we

often test a patients renal function to

make sure that its adequate to the

research

and finally we shouldnt select rich or

politically powerful or otherwise

wellconnected people for promising

research studies and here a little

example might be helpful

several decades ago when

antiangiogenesis factors were coming on

to be tested in clinical research the

new york times on a sunday had an

article above the fold on page one

saying that this was going to cure

cancer this was the next best treatment

the next day monday

telephones at the several institutions

that were running that trial were

ringing off the hook people were trying

to contact members of the board of

directors or the head of the institute
trying to get on the trial because it
was so promising it would cure their
cancer well institutions had to actually
have a way of not just selecting those
people who had connections to the most
powerful people in the institution for
the study you have to have fair uh
subject selection and that includes not
only getting those people who are
wellconnected for promising studies
fifth principle favorable risk benefit
ratio this may be the most important
principle
in assessing the risk benefit ratio i
think that theres a fourstep
evaluation process first the risks have
to be identified assessed and minimized
the risks include physical risk were
all familiar with that death or
disability or infection psychological
risk depression anxiety we should also
consider in some research discrimination
social risks economic loss we need to
evaluate the magnitude of those risks
and the likelihood of harm but we

shouldnt invent the magnitude or

likelihood and when data suggests the

likelihood of harm say psychological

stress from genetic studies which has

been shown not actually to be present we

shouldnt invent those harms

and we should identify mechanisms that

minimize the risk maybe you do a study

thats high risk initially in the

hospital or you observe patients in the

outpatient setting before sending them

home

second identify potential benefits to

individual participants and enhance them

consider the physical psychological

social and economic benefits but you

should consider only benefits from

research interventions not benefits from

added health services say a special

vaccine or payments that are not

necessary to the research goals

third step if the potential benefits to

the individual outweigh the risk to the

individual then you can proceed

but what happens if the risk of the

individual might outweigh the benefits

to that individual

then its important to evaluate the

risks to the individual against the

social benefits or the social value of

the knowledge gained if the social value

is high sometimes we accept higher risk

to individuals

sixth principle independent review

investigators have multiple legitimate

interests they have potential conflicts

of interest independent review of the

research is aimed to minimize these

potential conflicts of interest

independent review also assures society

that it wont be the beneficiary of

unethical research

seventh principle informed consent

informed consent ensures individuals

decide whether they enroll in research

and whether the research fits with their

own values interests or goals for those

who cant consent such as children and

mentally impaired we must ensure that

research fits with their interests

usually through a surrogate decision

maker well what constitutes valid

informed consent

there are four principles that have to

be fulfilled

competence of the subject

disclosure of information to the subject

understanding or comprehension by the

subject and voluntariness they decide to

enroll of their own free will now the

federal regulations require that every

informed consent document have eight

elements

that define the purpose and duration of

the participation the risks the

alternatives the benefits the

confidentiality of records the

compensation if injuries occur if any

doesnt have to be compensation persons

to contact to answer questions about the

protocol and voluntariness and the

patients right to withdraw from the

research

now when i was training many decades ago

i thought well you get the signed

informed consent down document

done thats the end of the ethics of

research that is wrong we need to

respect human subjects who are enrolled

in research and thats the eighth and

final principle the ethical requirements

of research do not end with the signed

informed consent document they also

include monitoring subjects welfare

protecting confidentiality permitting

people to withdraw from the study if

they want providing new information that

might be learned that might affect their

participation and informing the subjects

of what was learned from the research at

the end of the research

so those are the eight ethical

requirements

let me state all eight requirements are

necessary and essential to making

clinical research ethical we cant say i

like one two four and eight

we have to fulfill all eight but we also

should recognize that independent review

can occur in multiple ways irb is just

one of the mechanisms not the only

mechanism similarly informed consent are

per is a procedural requirement and

we dont always have to get a signature

to have valid informed consent in some societies a signature is not the way you demonstrate consent a handshake is or a meal is and so we need to fulfill the principle of informed consent but we should be sensitive to the cultural context in which it occurs such that we dont impose our values on another community

in fulfilling the eight ethical requirements there can be conflicts and this we must recognize whats fair in subject selection could increase risks what enhances scientific validity may also increase risk whats necessary to respect enrolled subjects might compromise scientific validity

theres no simple formula for resolving these kind of conflicts

you have to adjust the design to meet the requirements it sometimes said we balance the principles or we weigh them or we specify the principles the important point is to be clear about what is being done and give reasons why were balancing

different principles this has a very

important corollary and that corollary

is we can have two different approaches

to the same research study and both

approaches could be ethical even though

we balance them differently

finally all eight ethical requirements

are universal they dont apply only to

research in the us or europe

no country can say well were different

we have a different value system these

eight ethical requirements apply to

clinical research everywhere and

anywhere its done

all eight ethical requirements must be

adapted however to the local health

economic cultural and technological

circumstances for instance the disease

risk that affects your risk benefit

ratio may be different in different

countries and that will affect how you

evaluate the risks of a research

protocol thats not to say favorable

risk benefit ratio is a principle you

ignore its to say the context really

matters and assessing whats a favorable

risk benefit ratio

so in conclusion let us remember that

there are eight ethical requirements for

ethical clinical research collaborative

partnership social value scientific

validity fair subject selection

favorable risk benefit ratio independent

review informed consent and respect for

human subjects and they need to be

fulfilled in that order when someone

says is a protocol ethical you dont

just jump down to the informed consent

document you go through a systematic

review starting with collaborative

partnership and social value working

your way down to informed consent and

respect for human subjects so those are

the eight ethical requirements that make

clinical research ethical and it should

be applied in every protocol we see

the ethics of phase one oncology

research theres a very commonly highly

controversial area of research i like to

begin with a patient that i once cared

for she was a year old female she had

a right breast mass that was excise a

09 to 0 centimeter mass 0 of of

her lymph nodes were involved with tumor

she had an er0 but a pr of the rest

of the work up was negative she received

radiation but no chemotherapy at that

time

three years later she had her occurrence

in her liver and lungs

she was

initially treated with one chemotherapy

regimen when that stopped working she

was treated with a second chemotherapy

regimen when her cancer progressed

in her liver

she and i began discussing phase one

trials

as she said to me i want to fight my

cancer the first phase one trial failed

after two cycles her tumor continued to

grow she wanted another phase one agent

rather than hospice after a second agent

failed after two cycles uh she be came

into my office and i remember the day

very vividly she had substantial pedal

edema she could barely walk down the

hall to the room but she came to clinic

wanting yet a third phase one agent

now

she wanted that phase one trial a lot of

people would be critical of her getting

the phase one agent

how do we evaluate those phase one

trials she enrolled in were they

actually ethical

remember we defined eight ethical

requirements for clinical research to be

ethical there had to be collaborative

partnership social value to the research

it had to be done in a scientifically

valid way there had to be fair subject

selection there had to be a favorable

risk benefit ratio there had to be

independent review

patients had to voluntarily sign an

informed consent document and the

researchers had to respect the human

subjects who were enrolled in the

research now the main criticism of phase

one oncology research when you actually

boil it down is that it violates two of

those eight principles it violates the

favorable risk benefit ratio principle

and it violates the informed consent

principle

what is it about the risk benefit ratio

well critics say that phase one oncology

research inherently has an unfavorable

risk benefit ratio

phase one research is not intended to

benefit the individual participants

phase one research has some risks to the

individual participants especially in

oncology when they have

toxic drugs and with no benefits but

with some risk the risk benefit ratio is

inherently unfavorable

if the risk benefit assessment is

unfavorable for individual participants

its argued then the research is

conducted only to gain knowledge for

society if the primary beneficiary of

the research is society then individual

patients are exploited for the benefit

of society as one critic put it the fact

that there is no treatment for a

condition does not make any intervention

therapeutic or even quote probably

therapeutic phase one cancer drug

research may not be performed on

terminally ill subjects under these

guidelines because there is no

reasonable probability it will be the

best it will benefit subjects that is

george annis from boston university

criticizing the ethics of phase

research

relying on valid informed consent by the

research participants has been the

response to the possibility of

exploitation of patients in phase one

oncology research

so the belmont report says when the

research involves significant risk of

serious impairment review committees

should be extraordinarily insistent on

the justification of the risk looking

usually to the likelihood of benefit to

the subject or in some rare cases to the

manifest voluntariness of the

participants

well

then critics say but informed consent in

the phase one oncology space is invalid

valid informed consent requires

disclosure of information on the
objectives of the research the benefits
the risks and alternatives understanding
of this information by patients and
third a voluntary uncoerced consent
but the critics say theres a problem
physicians dont provide appropriate or
accurate information to the subjects and
physicians stress and exaggerate the
benefits while minimizing the risks to
research participants so for example
leroy walters another bioethicist said
consent forms are very often deficient
and they over promise they make phase
one studies sound like the cure for your
cancer
so the problems with informed consent
include the fact that
the informed consent documents
exaggerate but also that patients dont
really understand lots of critics will
say because patients are terminally ill
they cant understand the true
objectives the benefits and the risks of
a phase one study their understanding is
clouded by their physical state and

their hope for a cure what clear

thinking patient after all will apt to

take a toxic drug rather than receive

palliative care and comfort measures

when they have just a few months to go

because terminally ill patients cant

give proper informed consent

because they cannot understand the

information theyre given and because

theyre vulnerable they cant provide

valid informed consent

vulnerable populations cannot provide

informed consent and are protected

through special safeguards these

safeguards preclude research that

provides no benefits to patient it all

also includes greater than minimal risk

or marginal increment or minimal risk to

be present

so how do we respond or analyze these

critics

is it ethical to conduct phase one

research when there are no expected

benefits to enrolled subject

what types of phase one research is

being done and what are the actual risks

and benefits of that phase one research

so

first we have to recognize it can be

ethical to conduct research without

benefits to patients if the knowledge to

risk ratio that is the social value of

the research compared to the risk to

patients is reasonable a favorable

knowledge to risk ratio requires that

the knowledge gain is really socially

valuable and greatly exceeds the risk to

individual participants

conducting early phase oncology research

in which the drug doses are too low may

not be socially valuable in terms of the

knowledge about safety and toxicity to

be gained ironically having a favorable

risk knowledge ratio may require more

risk because only then is knowledge

gained about the actual drugs

this thinking argues for the use of more

innovative phase one design such as

intra patient dose escalations

accelerating dose escalation requiring

one patient rather than three at very

low doses of the drug

similarly we actually have to actually

look at the data on the

risks of phase one research how risky is

phase one research

the past is not prolonged so lets look

at the data

so a recent review of phase one studies

from the national cancer institute

covering years from 99 to 00

showed that the research has changed

only percent of phase trials are

with single chemotherapeutic agents

percent are there

single investigational agents of any

kind

and percent of these trials had

multiple investigational agents

of phase trials actually had

a proven drug in as part of that trial

so its hard to say that they might not

offer benefit uh similarly a review of

older trials showed that

about point seven percent of patients on

phase one trials got a complete response

and got a partial response so there

may be some benefits to these phase one

trials other studies have shown similar

data

the ctep database from 99 to 00

involved more than 0 000 patients for

assess for response and more than

almost 000 patients assessed for

toxicity and they showed that in fact

there were complete responses uh studies

that had an approved and an

investigational chemotherapeutic agent

actually had a complete response rate of

percent and in some cases what

youre looking for is stable disease and

had almost a percent stable disease

rate overall

those studies showed that 0 percent

of the patients had a 0 uh partial

response and percent had a complete

response with a third of them having

stable disease so there are some

benefits well

how bad were the toxicities 0 percent

of patients actually ended up dying in

the research protocol

and

fourteen percent had a grade four

toxicity so there are some serious risks

with phase one trials

overall we have to assess what the risk

benefit ratio was and whether thats

favorable or not

there are however also we need to keep

in mind some remarkable therapeutic

benefits in phase one oncology trials

early in the night or late in the 90s

when platinum was tried uh it had

greater than 0 response rate in

testicular cancer on the phase one trial

and percent longterm survival

so occasionally chemotherapeutic agents

do actually have in phase one do

actually have benefit similarly gleevac

had a greater than ninety percent

response rate in cml when initially

tested in the phase one

and some data suggest that enrolling in

phase one research is beneficial to the

quality of life of patients patients in

phase one had stable quality of life and

performance status over one course of

therapy where similar patients receiving

just supportive care had their quality

of life lowered so it may be that there

are some actual physical benefits and

maybe even psychological benefits

so what can we ex conclude risks arent

as bad as

many people think in phase one trials

only fourteen percent of patients had a

grade four toxicity the risk of death is

about point five to point seven percent

for terminally ill patients that may not

be a very high number and it would be

good to have more data especially with

the change in research to more

antibodies and more biologics

there may be benefits also to the

research many phase one drugs now have

greater than response rate and that

there have been several notable cases

where substantial therapeutic responses

even cures have been seen on phase one

trials

and quality of life may be better on a

phase one trial than with supportive

care

so on the risk benefit ratio i think

many people assess the risks of phase

one trial more than they actually are

and dont include or assess the benefits

that actually result from the trial even

though the trials arent intended to

give benefit doesnt mean that they

cant be beneficial both physically and

psychologically to patients what about

informed consent can terminally ill

patients provide informed consent

so do physicians misinform patients

a old study from 99 actually recorded

informed consent interactions between

the patient and the doctor qualitative

analysis indicated that the three major

information points were communicated in

eighty percent or more of cases the use

of indirect patient response however and

request for additional information

wasnt so good

doherty at the university of chicago

looked at phase one oncologist he has

sensed

their view of research 0

uh of those doctors thought that they

would add one or two months to survival

that percent uh complete respond or

partial response and that a complete

response would be one percent what this

suggests actually is that doctors who uh

administer phase one trials actually

underestimate the benefits uh of

research in addition they actually

dramatically overestimated the risks

they thought that there was a five

percent death rate on phase one style

studies rather than the 0 to 0

which actually exists so even phase

one oncologist at the university of

chicago overemphasized the risk and

underemphasize the benefits that

patients could get

other studies have shown that you know

most physicians

discuss possible side effects possible

risks possible benefits with patients

where theres a discord between

physicians and patients is on the

expected uh change in the length of life

most patients twothirds of them thought

doctors did not discuss a change in the

length of life

physicians generally think that benefits

from the experimental therapy are about

adverse events about 0 percent and

that is uh

different than the actual data

underestimates the actual data limited

data suggests physicians do not

misinform patients and if they do

misinform they tend to overestimate the

risk underestimate the benefits what

about phase one consent forms

misinforming patients

here

we assessed data from phase one

informed consent documents from 999

only 9 of all phase one oncology trials

involved a previously untested drug 0

of these phase one trials had a

therapeutic element to them that is they

had a known drug with therapeutic

efficacy

of those forms 9 percent mentioned

safety dose determination or toxicity as

the purpose of the trial 99 mentioned

that the study is research or an

experiment with most of these being

prominent or highly prominent in the

informed consent document thats in the

first five lines six percent explicitly

mentioned that research is not

therapeutic 9

refer to the chemotherapy agent as

treatment or therapy without any mother

modifier such as experimental

when we looked at the risk section the

risk section on average was lines and

the benefits section on average was four

lines its very hard to say that they

overemphasize the benefits and

underemphasize the risks in addition

of these informed consent documents

mention death as a possible risk

percent mention death more than once

again very hard to say that these

informed consent documents arent giving

an accurate view

possible benefits five only five percent

mentioned cure 0 percent mentioned life

prolongation

mentioned tumor shrinkage most of them

twothirds of them mention generalizable

knowledge as the benefit

ninetysix percent of these informed

consent document had a separate

alternative section percent mentioned

a palliative care is an alternative

percent mentioned standard treatment and

twothirds of the mention no treatment

as a potential alternative

while the documents arent perfect its

very hard to say that the informed

consent documents overpromise benefits

and minimize risk disguise the nature of

the research trial or that its research

and very few even mention cure much less

promised cure well do terminally ill

patients misunderstand the information

theyre given even if its accurate

study from many years ago showed that 9

percent of patients on phase trials

had a prior therapy most had

chemotherapy some had chemotherapy and

radiation therapy

darity looked at these patients and they

were not particularly vulnerable were

male were caucasian the median age

was 0 and had some college or more

suggesting that theyre very educated

other studies looking at education also

so showed that almost twothirds of the

patients had some college education and

almost 90 percent were white again not

the typical view of a vulnerable

population

when talking to patients 00 percent

recalled signing a consent document 9

recall that there was an explanation of

the study as research

ninetyseven percent call recalled the

explanation of risk and suicide and side

effects and 00 could recall at least

one specific side effect

almost all the patients 9 percent felt

well informed before they enrolled in

the phase one trial again very hard to

say that these patients werent well

informed

a survey of 0 patients some of whom

enrolled in phase trials

showed the following had read the

consent form carefully had enough

time to learn about the trial 9

said they had sufficient time to ask

questions and consulted some outside

physician again not exactly the case

of patients who feel ill informed indeed

almost all the studies show that ninety

percent or more of patients who enroll

in phase one stop studies feel well

informed before they enroll

so do terminally ill patients have a

therapeutic misconception about phase

one thinking theyre going to get the

cure rather than a study looking for the

maximum tolerated dose

what were the reasons for people

enrolling in trial 0 said they wanted

to get the best care 9 thought theyd

get some medical benefit

in another study 0 thought theyd get

some medical benefit

but

wanted an antitumor response

knew that the trial was a toxicity

determination

so one of the things we know is that

many people

think that they might actually get a

therapeutic response and that actually

is important theyre thinking theyre

going to get a therapeutic response may

not be maybe the rationale for why they

get on but they may actually understand

that the main reason for the trial was

to improve

the care of future patients indeed jaffe

conducted a study that showed that

percent of patients on phase one thought

that the main reason for the trial was

to improve care for

other patients and 0 percent of the

enrollees thought there may not be a

direct

medical benefit to them nonetheless

patients can hope that theyll be the

ones who are bene are going to benefit

weve already reviewed the data on

whether the patients are are vulnerable

one of the things thats pointed out is

they really dont fit the quintessential

qualifications of vulnerable patients

theyre not mentally incapacitated their

physical environment such as prison does

not coerce them and theyre not a group

that has been historically discriminated

against they tend to be white and well

educated its hard to say these people

are a vulnerable population

so why are terminally ill patients

enrolling in phase one studies well

they deny or refuse to acknowledge death

they want to go out fighting they know

their options and nothing would preclude

them from enrolling

so

we looked at

phase one patients in a variety of

centers we surveyed on the day they made

a decision

and what we found is that most patients

really want to go out fighting we who

are struggling to escape cancer do not

obviously want to die of it we do prefer

death to the struggle of life under

cancers on tender rule

the enemy is not pain or even death

which will come for us in any

eventuality the enemy is cancer and we

want to defeat and destroy it that was

one patient from the university of

chicago phase one trial

would a side effect deter patients from

actually enrolling losing their hair

only five percent that would deter them

from enrolling gaining 0

pounds only six percent said that they

would be deterred from enrolling drugs

that temporarily undermine their ability

to think

said that would uh prevent them from

enrolling

there does seem to be one major problem

with the phase one informed consent

process communication about life

expectancy only percent of patients

discuss life expectancy with their

oncologist a moderate amount or a lot

and only percent were told a specific

time frame

this was problematic for many patients a

lot of patients said something like he

wouldnt answer the question i asked

about survival or i tried to discuss

life expectancy but he would not tell me

obviously discussing life expectancy for

someone who has less than a year to live

is not easy or pleasant we all really

want to avoid it but its clearly

necessary for many patients who are
going to enroll in phase one oncology
trials ironically it might actually
increase enrollment at phase one trial
since people are enrolling even when
they think they have long life
expectancies
so remember there are eight principles
for ethical research collaborative
partnership social value scientific
validity fair subject selection fair
favorable risk benefit ratio independent
review informed consent and
respect for patients who are enrolled
the challenge the ethical challenge to
phase one oncology trials are that its
unethical because risk benefit ratio is
unfavorable and informed consent is
invalid studies of the risk benefit
ratio and informed consent suggest these
worries are not as serious as critics
suggest the risk benefit ratio for phase
one trials has changed because of the
type of phase one trials have changed
and they actually have some benefits a
low death rate and a low

grade four toxicity rate and they
substantially improve social knowledge
in addition patients whove enrolled
have sufficient information theyre
satisfied by the amount of disclosure
they have they understand most of the
information they get and they want to go
out fighting and they understand the
issue
like geraldine patients who enroll and
face on trial want to fight their cancer
and almost nothing will dissuade them
from it oncologists need better training
to provide better information about life
expectancy but this may only increase
enrollment in phase one trials what we
can conclude is that phase one oncology
trials tend to actually comply with the
eight principles for ethical clinical
research
they are not invalid because of high
risk benefit ratios or invalid informed
consent thank you and remember keep the
eight principles of clinical ethical
research
and systematically evaluate any trial

whether its phase one oncology trial or

any other trial