

هو المحبوب

1

ملاحظات اخلاقی در کارآزمایی بالینی

ارائه دهنده: دکتر ندا یاوری

استادیار گروه اخلاق پزشکی

Informed consent

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Informed consent is the process by which the treating health care provider **discloses appropriate information** to a **competent patient** so that the patient may make a **voluntary choice** to accept or refuse treatment.

- consent is often viewed as the single most ethically important aspect of medical ethics
 - “all of medical ethics is but a footnote to informed consent” (Mark Kuczewski, 1996)

Historical course

4

An excerpt of the **Hippocratic Oath**
(fifth century B.C.E.):

Conceal most things from the
patient... Give necessary orders
with cheerfulness and serenity...
revealing nothing of the patient's
future or present condition.

- An excerpt of the **Plato Republic**
book:

When a man is ill... to the physician
he must go, and he who wants to
be governed, to him who is able to
govern

Historical course

5

- Medical Ethics codes of American medical Association (1847): The patient **must obey** the doctor's instructions **without delay** and **unconditionally.....**
- Medical Ethics codes of American medical Association (1990): The patient has the **right to decide** on the care that the doctor **recommends**. Based on this, the patient is entitled to **accept** or **reject** the proposed treatment

Why informed consent?

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- *Autonomy*
- Trust
- Protection

Autonomy

7

- Self-ownership/ Personal integrity/ Right to self- determination
- Beauchamp and Childress: “The **autonomous individual** acts freely in accordance with a **self-chosen plan**, analogous to the way an **independent government** manages its territories and establishes its policies”

Autonomy

8

Medicine affects **non-technical** and **controversial** matters of **value** and **faith** on which physicians are not experts

Why informed consent?

9

- *Autonomy*
- Trust
- Protection

Protection

10

- From **investigators' attempts** to promote science and personal careers, even **on participants' backs**
- From **neglectful clinicians** or from **overconfident**, but often wrong, **paternalistic** ones
- O'Neill: IC is best understood as a way to prevent **deception** and **coercion**: it provides reasonable assurance that **the patient or subject has not been deceived or coerced**.
- Informed consent decreases the **knowledge gaps** between physicians and patients or research participants, specially in the **investigational context**

The elements of informed consent

11

1- **Threshold elements** (preconditions)

- Competence
- Voluntariness

2- **Information elements**

- Disclosure
- Recommendation
- Understanding

3- **Consent elements**

- Decision
- Authorization

The elements of informed consent

12

1- **Threshold elements** (preconditions)

- **Competency**

- Voluntariness

2- **Information elements**

- Disclosure
- Recommendation
- Understanding

3- **Consent elements**

- Decision
- Authorization

Consent in special situations

Vulnerable Populations



Children

Prisoners



Pregnant Women
and fetuses

Cognitively
Impaired



Different culture
or language

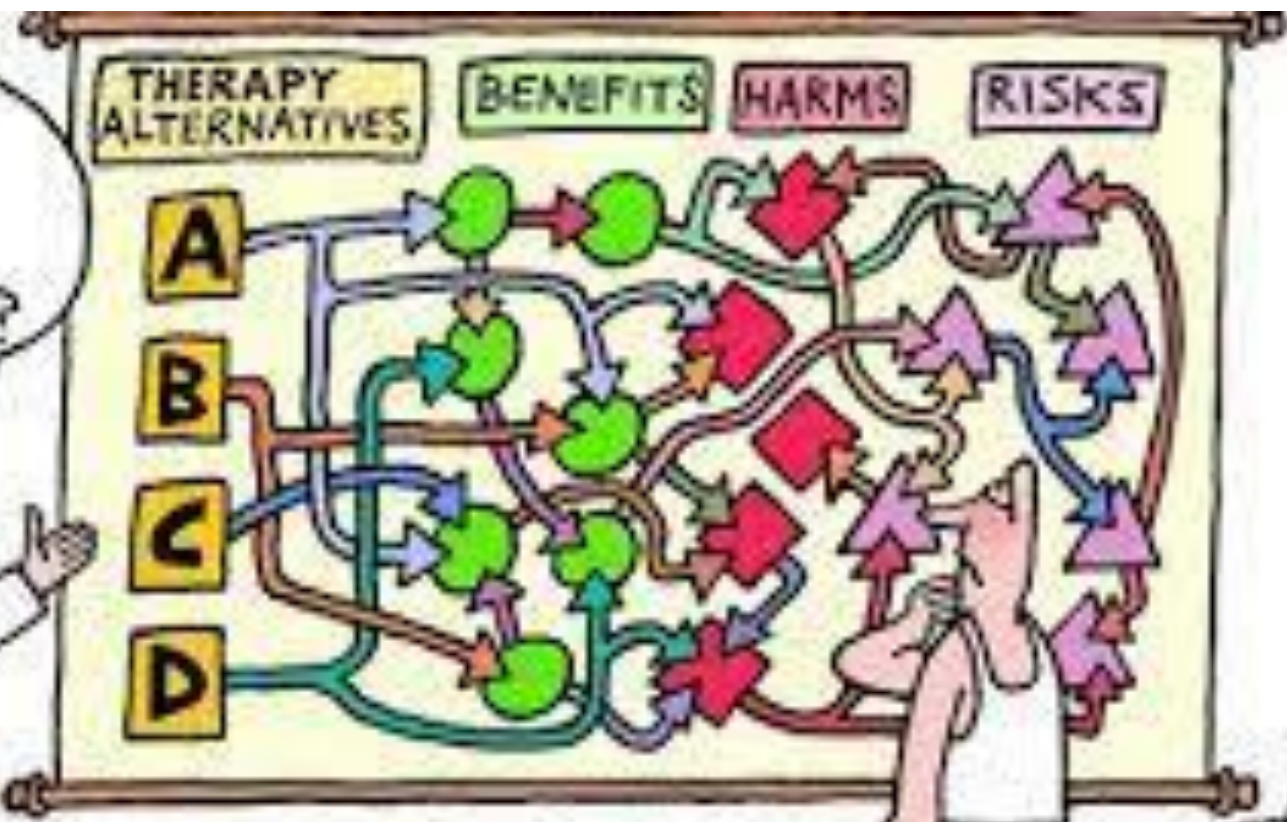


Terminally ill



Financially
impaired

which therapy would you prefer?



The elements of informed consent

15

1- **Threshold elements** (preconditions)

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The elements of informed consent

16

1- **Threshold elements** (preconditions)

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The elements of informed consent

17

1- **Threshold elements** (preconditions)

- Competence
- Voluntariness

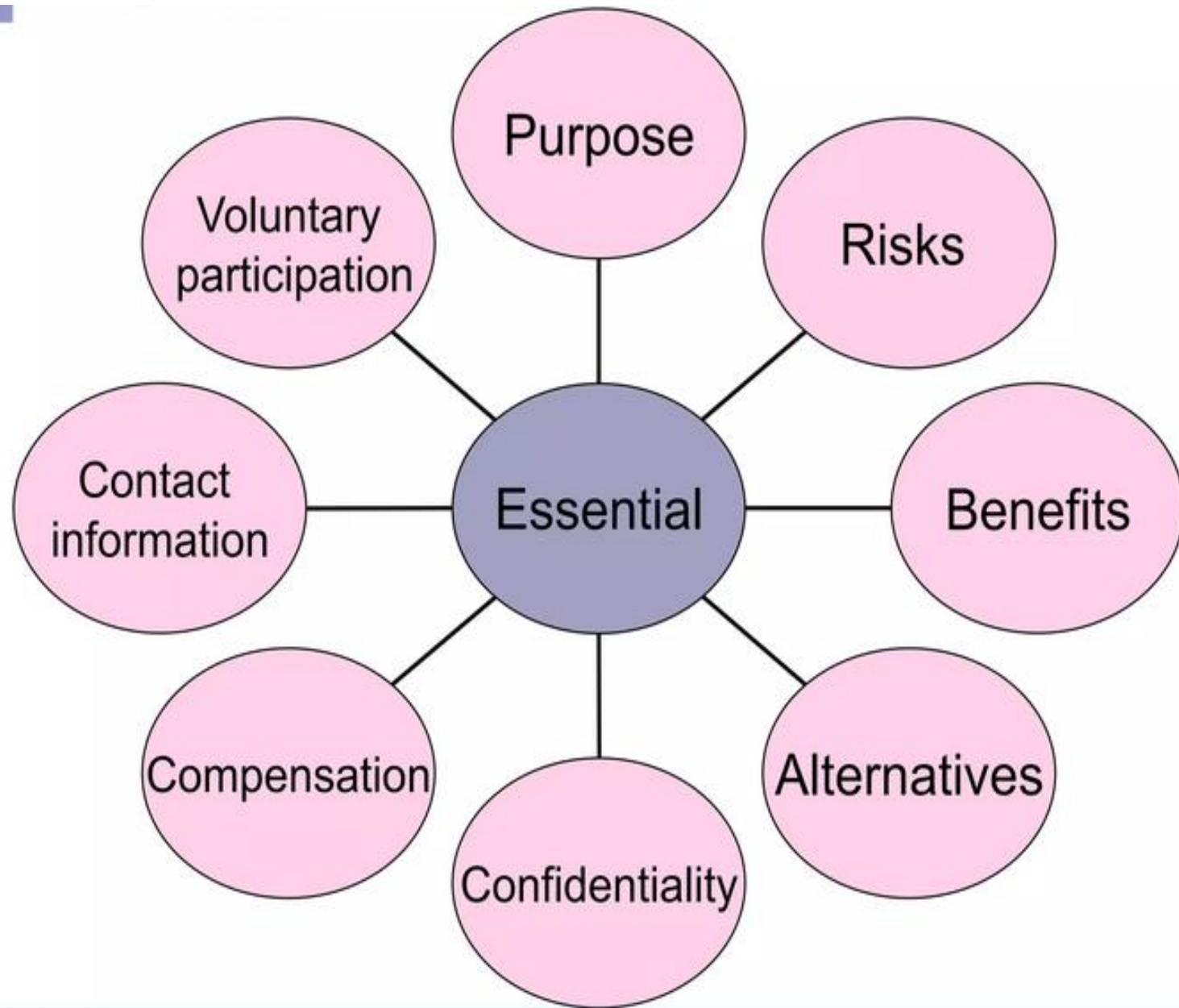
2- **Information elements**

- Disclosure
- Recommendation
- Understanding

3- **Consent elements**

- **Decision**
- **Authorization**





رضایت آگاهانه

19

- ارائه اطلاعات کتبی و شفاهی
- زبان قابل فهم
- امکان پرسیدن سؤالات
- آزادی در تصمیم گیری
- فرصت تصمیم گیری
- اخذ رضایت مکتوب

اجزاء فرم رضایت آگاهانه

20

- ۱- این یک مطالعه تحقیقاتی است.
- ۲- اهداف مورد نظر تحقیق
- ۳- درمانهایی که در این کارآزمایی وجود دارد و اینکه افراد به طور تصادفی به هریک از گروههای درمانی ممکن است وارد میشوند.
- ۴- روشهای پیگیری شامل روشهای تهاجمی و غیرتهاجمی
- ۵- تشریح خطرات قابل پیش بینی مطالعه برای شرکت کنندگان
- ۶- فواید احتمالی مطالعه برای شرکت کنندگان.

اجزاء فرم رضایت آگاهانه

۷- سایر درمانهایی موجود و فواید و خطرات هر یک از آنها.

۸- غرامت و درمان صدماتی که در جریان مطالعه به فرد وارد می شود

۹- بازپرداخت مخارجی که شرکت کننده برای شرکت در مطالعه از جیب خود می پردازد

۱۰- در صورتیکه وجهی در قبال شرکت وی در مطالعه پرداخت میشود میزان و نحوه آن ذکر شود

۱۱- شرکت در مطالعه داوطلبانه است و میتوانند از شرکت امتناع ورزد و یا هر زمان مایل بود از مطالعه خارج

شود بدون آنکه مشمول پرداخت جریمه گردد و یا از خدمات درمانی محروم شود.

اجزاء فرم رضایت آگاهانه

12. نگهداری محرمانه اطلاعات فرد شرکت کننده و اینکه در انتشار نتایج هویت افراد شرکت کننده

محرمانه خواهد ماند

13. فرد شرکت کننده در طول مطالعه از اطلاعاتی که ممکن است بر تصمیم وی در مشارکت در مطالعه

تاثیر بگذارد مطلع خواهند شد.

14. فرد یا افرادی که شرکت کننده برای دانستن حقوق خود، کسب اطلاعات بیشتر و یا در موقع صدمه

از مطالعه میتواند با وی تماس بگیرد.

How big is the recurrence risk?

How big is the breast cancer recurrence risk?

Does radiotherapy impact my survival rate?

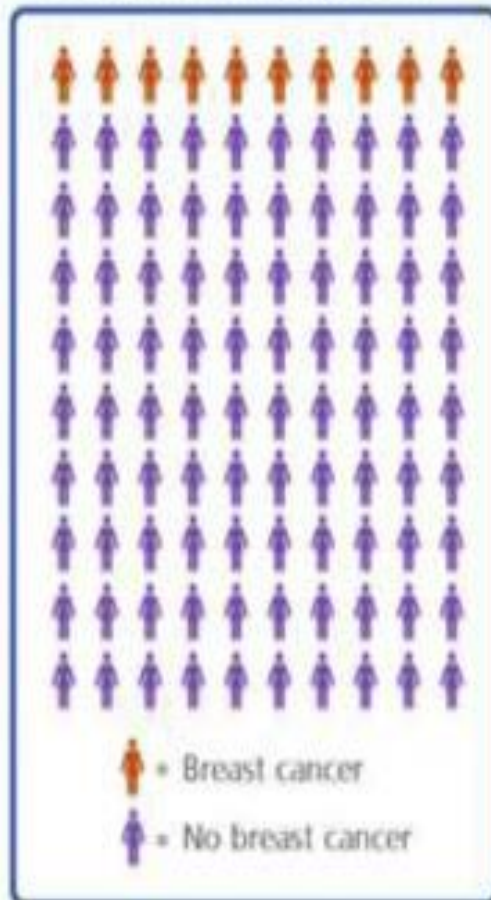
Checkups

What are the options in case of a recurrence?

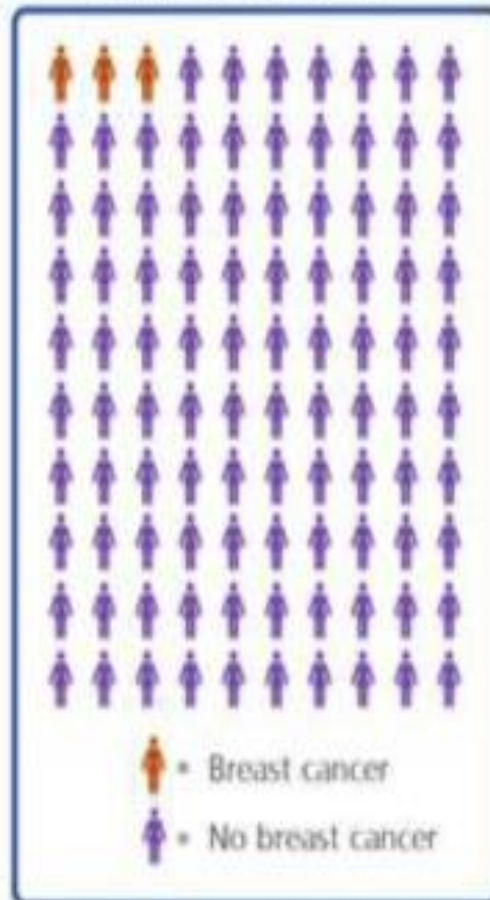
Radiotherapy reduces the local recurrence rate with a factor 3. Click on the image below for more information.



WITHOUT radiotherapy



WITH radiotherapy



Weighing up the potential benefits and harms of the Astra-Zeneca COVID-19 vaccine

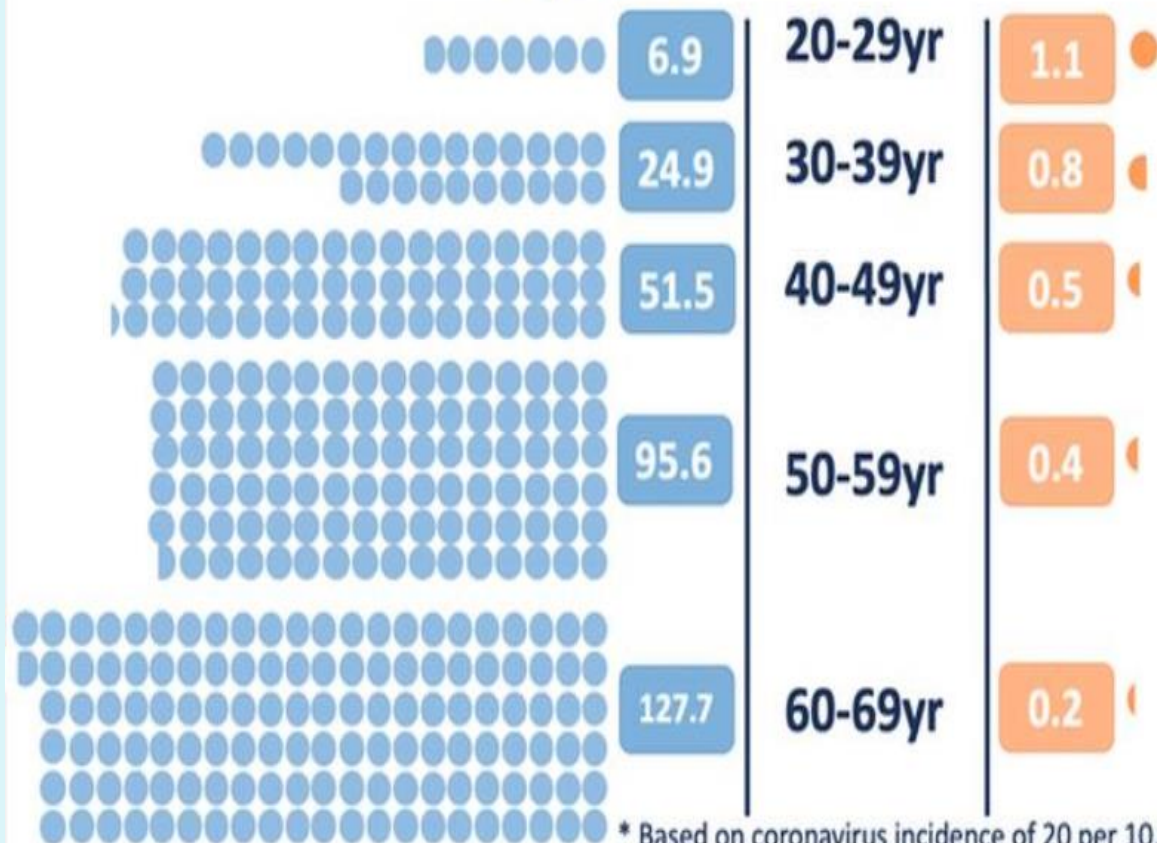
**For 100,000 people
with high exposure risk***

Potential benefits

Potential harms

ICU admissions due to COVID-19 prevented every 16 weeks:

Specific blood clots due to the vaccine:



* Based on coronavirus incidence of 20 per 10,000 per day: roughly UK at peak of second wave

Risk of Blood Clots

AstraZeneca Vaccine



4 cases in
1,000,000
Vaccines

0.0004%

Birth Control Pill



500 - 1200 cases in
1,000,000
women

0.05% to 0.12%

Smoking



1,763 cases in
1,000,000
Smokers

0.18%

COVID Infection








165,000 cases in
1,000,000
Cases

16.5%

Maria Leonor Ramos | Médica Interna de Medicina Geral e Familiar

Fontes: Agência Europeia do Medicamento; Suh YJ, Hong H, Dhana H et al. Pulmonary Embolism and Deep Vein Thrombosis in COVID-19: A Systematic Review and Meta-Analysis. Radiology 2021; Cheng, Yun-Jiu & Liu, ZH-Hao & Yao, et al. (2013). Current and Former Smoking and Risk for Venous Thromboembolism: A Systematic Review and Meta-Analysis.

Chance in a million of...		25-year-old	55-year-old
serious harm due to vaccine side-effects		11 in a million	4 in a million
dying with coronavirus		23 in a million	800 in a million
dying due to an accident or injury		110 in a million	180 in a million
dying in a road accident		38 in a million	23 in a million
being hit by lightning this year		1 in a million	1 in a million

How does the risk of serious side-effects from the AstraZenec a vaccine compare with other risks?

Figures show the chance of dying with coronavirus since the start of the pandemic. Figures for accidents and car crash fatalities are for 2018



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INFORMATION SHEET FOR MINORS (<6 YEARS)

BILLY AND HIS HEART



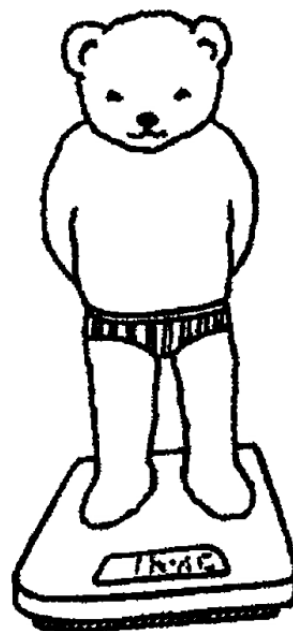
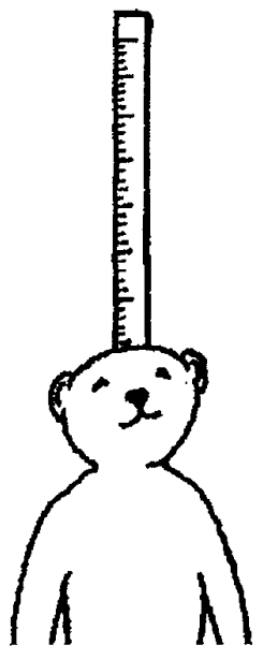


Hello, my name is Billy.

Today I'm going to see a doctor to have a look at my heart. I'm not ill; it's just to see how my heart works.

Would you like to come, too?

I'll show you around. I'm here with my mummy.



The doctor wants to know how big I am.

Stand up straight and tall first.

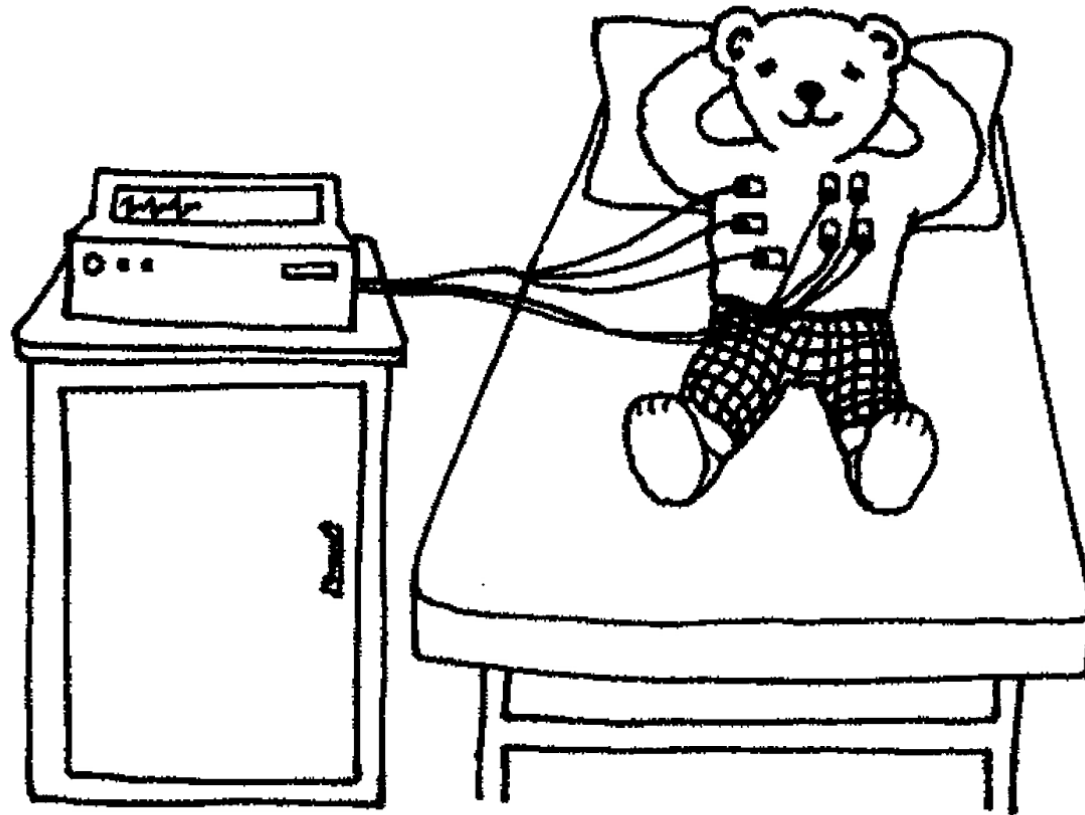
Now hop onto the scales, and wait for the numbers to change.



Now the doctor listens to my heart with his magic heart tube called a stethoscope.

He also asks mummy some questions.

He writes down some notes in a big folder.

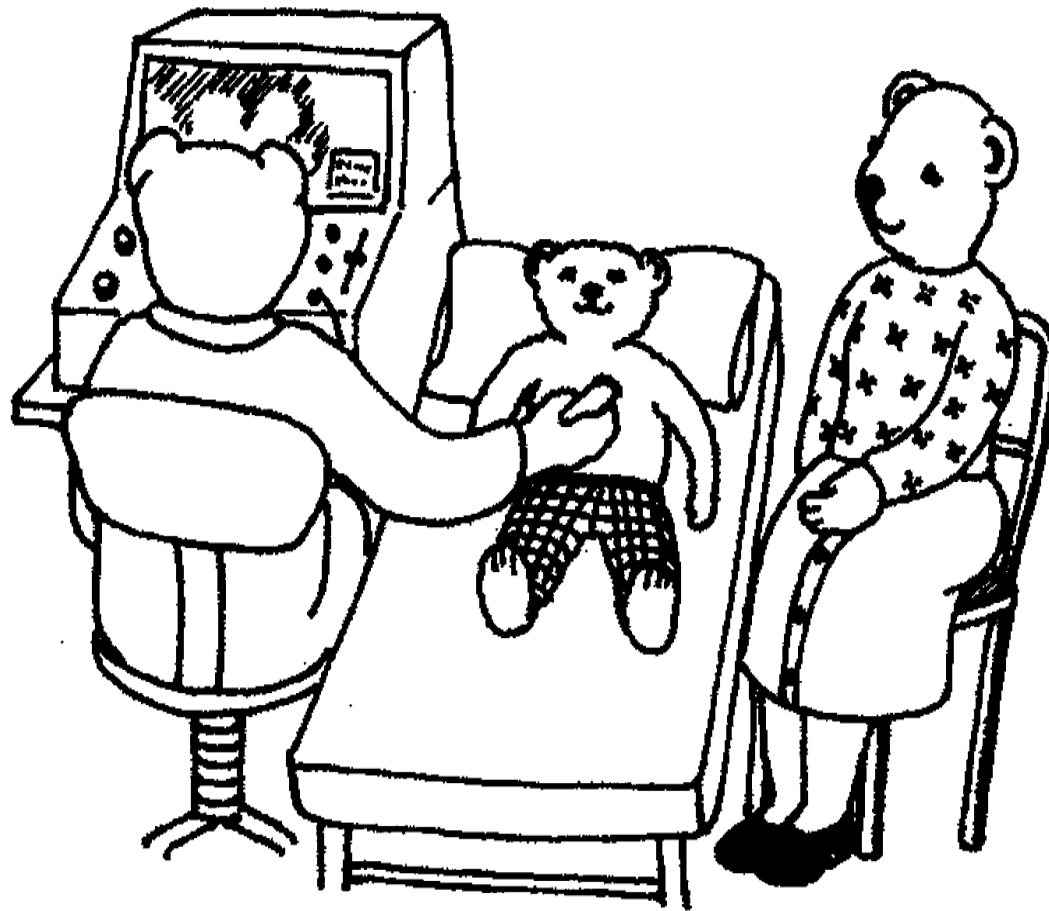


Then I have a test on my heart.

The wires carry messages from my heart to the machine.

The machine draws a squiggly line.

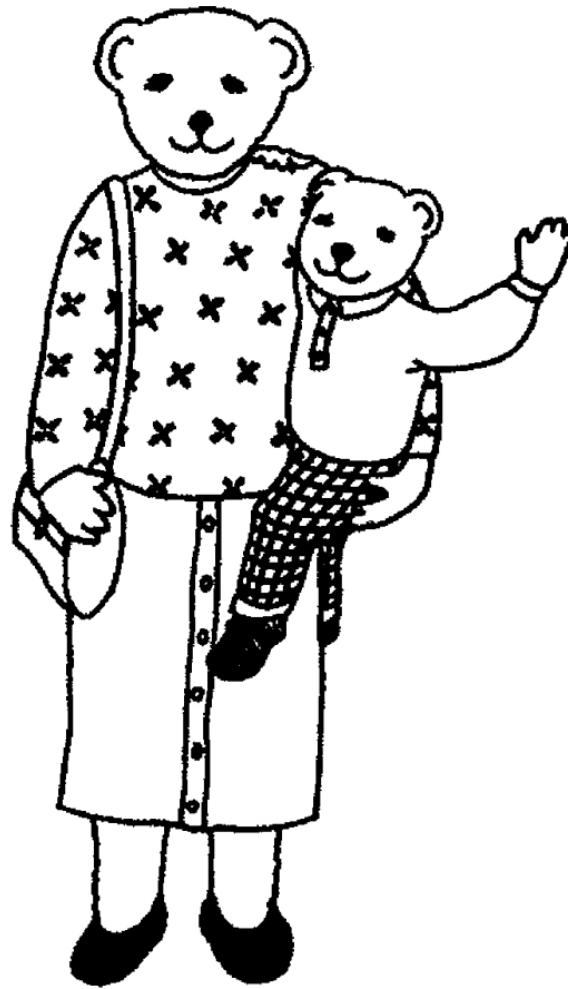
The squiggly line can show the doctor how well my heart is working.



I'm also having a jelly scan.

I'll have to keep very still, even though it tickles a bit!

The machine makes a picture of my heart on a special TV.



Then I get a certificate for taking part.

All finished! Time to go home now.

Goodbye everyone. It was lots of fun!

**Don't forget to colour me in and bring me along
to your visit!**



INFORMATION SHEET FOR MINORS (6-9)

DOES IT MATTER IF MY HEART HAS AN UNUSUAL VALVE?

We are asking whether you and your family would like to take part in a research study.

Before you decide if you would like to join in, it is really important that you understand what the study is about, why the study is being done and what it will mean if you take part. So please read this leaflet carefully with your parents. Also talk to your family, friends, doctor or nurse about it if you want.

If something doesn't make sense or you have more questions you can ask your parents to give us a call and we can discuss it with you and your parents.

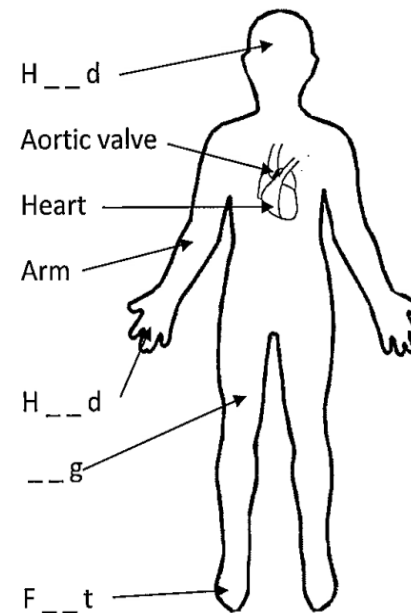
Thank you for reading this.

INFORMATION SHEET

What is research? Why is this project being done?

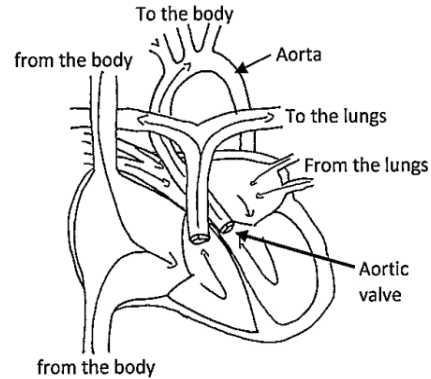
Research is a way we try to find out the answers to questions.

This research is being done to look at one of the valves in your heart where the blood flows through.



Can you fill in the missing letters?

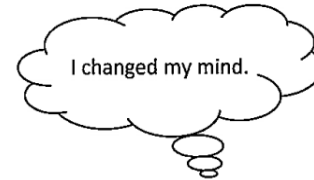
Your heart pumps blood all the way through your body. To make sure it all goes in the right direction the heart has 4 valves. In our research study we are looking at one of them, the aortic valve. Most people have a valve with 3 parts but in some people it only has 2 parts.



We also know that other people in the family can have a valve with two parts as well. That is why we are asking your family to take part in the study, too.

Why have I been asked to take part?

You have been asked to take part because you or someone in your family has an unusual valve in your heart.



Did anyone else check the study is OK to do?

Before any research is allowed to go ahead it has to be checked by a group of people to make sure that the research is fair.



Do I have to take part?

No, you don't. It is your choice whether you want to take part and you can always change your mind.

What will happen to me if I take part?

We have to ask you not to have any breakfast that morning. But you can drink water and we'll have breakfast for you during your visit.

Once we have checked that you and your parents are happy for you to take part we will invite you to the clinic in Oxford.



Then you and your parents can ask any questions you have.



Then we will:

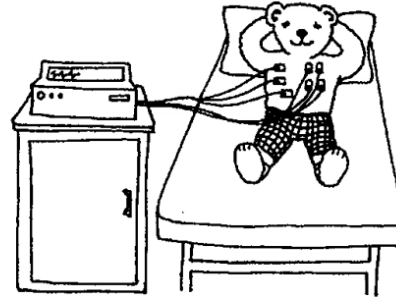
Ask your parents some questions.



Measure how tall and how heavy you are, take your blood pressure and listen to your heart.



Take a trace of your heart (ECG) where a machine draws squiggly lines of your heart on a piece of paper. This shows how well your heart is working.



Do a jelly scan (Ultrasound scan) of your heart and arm while you can find "where's Wally", Winnie the Pooh, Thomas, Nemo or Princesses if you want to.



Give you a certificate for taking part.



When you are older in a few years time we will also ask you to come back for another visit just like this one. This is to see whether anything changed.

Will anything about the research upset me?

All measurements we choose are safe. The jelly scan might tickle a bit and during the heart trace you need to lie still. The blood pressure cuff will give your arm a gentle squeeze.

Will taking part help me?

The study will not help you right now. But it will help us to know more about people having an unusual valve in their heart.

What happens when the research study stops?

The research will be talked about and written down but no one will know that you took part.

What if something goes wrong?

If there is a problem you can talk to your parents or any of the researchers.

Will my information be kept private? Will anyone else know that I am taking part?

All your information will be kept private. We will only tell your parents and your GP.

What do I do if I don't want to take part in the research anymore?

Just tell your parents and the researchers that you don't want to take part anymore. You don't have to give any reason. It is **YOUR** choice.

What happens if I find out that I have an unusual valve I did not know about?

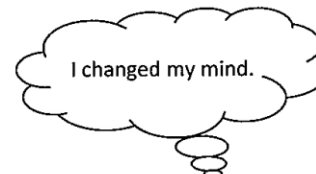
Just like the person in your family (brother, sister, mum or dad) who already knows that they have an unusual valve in their heart you would see a heart doctor in outpatient clinic every few years.

Special thanks to the charity HeartLine and Sheila Barns for giving us permission to use the drawings from their leaflet "Growly Bill and the Outpatients Clinic".

Z D Y R M H E M I E Y S
S X H B O P T R A E H A
V A L V E T A V I R P J
E Y C H O I C E Z M V E
S P N H P L I O S E S L
N P E C G W F R D A T L
K A M A C H I N E S S Y
L H S N O I T S E U Q S
U I T Y N A R T J R D N
M J W M T A E C N E E B
R E S E A R C H E R P E
L E G I G O O S B I F G

Find all 14 words hidden in the puzzle:

ECG	Valve
Heart	Choice
Researcher	Machine
Jelly	Questions
Private	Happy
Scan	Certificate
Doctor	Measure



Summary

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- Physicians need to participate in the **informed consent process** to provide patients with the **best treatment available** by sharing decision-making.
- There is **no single prototype** that meets the elements of the standard of care for informed consent that **applies to all patients**.

**Informed Consent Form Template for
Clinical Studies****Introduction**

Briefly state who you are and explain that you are inviting them to participate in the research you are doing. Inform them that they may talk to anyone they feel comfortable talking with about the research and that they can take time to reflect on whether they want to participate or not. Assure the participant that if they do not understand some of the words or concepts, that you will take time to explain them as you go along and that they can ask questions now or later.

(Example: I am X, working for the Y Research Institute. We are doing research on... Z disease, which is very common in this country. I am going to give you information and invite you to be part of this research. You do not have to decide today whether or not you will participate in the research. Before you decide, you can talk to anyone you feel comfortable with about the research.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.)

***Informed Consent Form Template for
Clinical Studies*****Purpose of the research**

Explain in lay terms why you are doing the research. The language used should clarify rather than confuse. Use local and simplified terms for a disease, e.g. local name of disease instead of malaria, mosquito instead of anopheles, “mosquitoes help in spreading the disease” rather than “mosquitoes are the vectors”. Avoid using terms like pathogenesis, indicators, determinants, equitable etc. There are guides on the internet to help you find substitutes for words which are overly scientific or are professional jargon.

(Example: Malaria is one of the most common and dangerous diseases in this region. The drugs that are currently used to help people with malaria are not as good as we would like them to be. In fact, only 40 out of every 100 people given the malaria drug XYZ are completely cured. There is a new drug which may work better. The reason we are doing this research is to find out if the new drug ABX is better than drug XYZ which is currently being used.)

راهنمای اخلاقی اختصاصی کار آزمایشی های بالینی

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- فرم رضایت‌نامه‌ی آگاهانه و سایر اطلاعات مکتوبی که در اختیار نمونه‌ها قرار می‌گیرد باید هر زمان که اطلاعات جدیدی که ممکن است به اجازه‌ی نمونه‌ها ارتباط پیدا کند بدست آید، مورد بازبینی قرار گیرد.
- هر فرم رضایت‌نامه‌ی آگاهانه‌ی و سایر اطلاعات مکتوب بازبینی شده باید قبل از استفاده، تایید یا نظر موافق کمیته‌ی اخلاقی را دریافت کند.
- در صورت بدست آمدن اطلاعات جدیدی که ممکن است تمایل نمونه‌ها به ادامه‌ی مشارکت در مطالعه را تحت تأثیر قرار دهد، نمونه‌ها یا نمایندگان قانونی ایشان باید به موقع از آنها اطلاع پیدا کنند و انتقال این اطلاعات باید مستند شود.

راهنمای اخلاقی اختصاصی کار آزمایی های بالینی

- در زمان دریافت رضایت نامه ، باید احتیاط شود که شرکت کنندگان رضایت خود را تحت محظوریت و به علت وابستگی درمانی ، اداری و ... به فرد گیرنده رضایت نداده باشند.
- در این گونه موارد رضایت نامه ی آگاهانه باید توسط فرد دیگری که اطلاع کافی از مطالعه داشته و در عین حال جزو پژوهش گران نباشد و در چنین رابطه ای با مورد نباشد ، کسب شود.

راهنمای اخلاقی اختصاصی کارآزمایی های بالینی

قبل از مشارکت در کارآزمایی ، شرکت کنندگان یا نمایندگان قانونی آنها باید يك نسخه از رضایت نامه هاي امضاء شده و داراي تاريخ و ساير مستندات مكتوب را دریافت نمایند و چنانچه در طول اجراي کارآزمایی فرمهاي رضایت نامه تغييراتي نماید باید يك نسخه از فرمهاي امضاء شده و داراي تاريخ جديد نیز به آنها ارائه گردد.

چنانچه در يك کارآزمایی (درماني يا غيردرماني) ، شرکت کنندگان افرادي باشند که فقط از نمایندگان قانونی آنها رضایت اخذ شده باشد (کودکان ، بیماران با زوال عقلي شديد و ...) باید شرکت کنندگان تا حد ممکن و قابل فهم از کارآزمایی اطلاع حاصل نموده و در صورت امکان فرمهاي رضایت نامه را امضاء نموده و تاريخ را ثبت نمایند.

راهنمای اخلاقی اختصاصی کارآزمایی های بالینی

- در موارد کارآزمایی که به منظور بررسی روش درمانی یا تشخیص در موارد اورژانس طراحی شده و امکان پیش‌بینی روشی برای اخذ رضایت آگاهانه از نمونه‌ها قبل از بروز شرایط اورژانس وجود ندارد، لازم است در دستورالعمل، تمهیدات لازم جهت حداکثر تلاش برای اخذ رضایت آگاهانه از نمایندگان قانونی ایشان در فرصت ممکن تا انجام مداخله درمانی یا تشخیصی مورد کارآزمایی دیده شود.
- در صورتیکه نماینده قانونی شرکت کننده در دسترس نباشد، ورود افراد به مطالعه منوط به رعایت تمهیدات ذکر شده در دستورالعمل برای اخذ رضایت و نیز تأییدیه کمیته اخلاق می‌باشد.

پرداخت **غرامت** در کارآزمایی های بالینی

پرداخت غرامت در کارآزمایی بالینی

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- چه زمانی باید غرامت پرداخت شود؟

صدمه‌ای که بر اساس احتمالات، قابل انتساب به مداخله تحت کارآزمایی یا هر مداخله بالینی که در طی کارآزمایی انجام می‌شود، باشد به نحوی که اگر فرد وارد مطالعه نمی‌شد چنین اتفاقی برای وی رخ نمی‌داد.

- چه کسی مسئول پرداخت غرامت است؟

- ✦ شرکت داروسازی بانی کارآزمایی‌هایی.

- ✦ پژوهشگر و موسسه مربوطه.

در دستورالعمل کارآزمایی باید مشخص شود که مسئول پرداخت غرامت چه فرد یا سازمانی می‌باشد

پرداخت غرامت در کار آزمایي باليني

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● مواردیکه شرکت سازنده دارو مسؤل پرداخت غرامت نیست:

✦ شرکت سازنده باني مطالعه نیست.

✦ داروي داراي مجوز تجویز است.

✦ آسیب به وسیله پزشکی ایجاد شده باشد که پروتکل را رعایت نکرده است.

✦ پزشك به طور مناسبی از پس واکنش ناخواسته دارو برنیامده است.

پرداخت غرامت در کار آزمایي باليني

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- لازم نیست بیمار ثابت کند که صدمه ناشی از پژوهش بوده است.
- بیمه بی کم و کاست (No fault):
 - ✦ پوشش کامل
 - ✦ چه در اثر سهل انگاری باشد یا خیر
 - ✦ عدم نیاز به شکایت
- صرف نظر از اینکه به شرکت کننده قبلا هشدار داده شده است یا از وي رضایتنامه اخذ شده است.

پرداخت غرامت در کار آزمایي باليني

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● محدودیتهاي پرداخت غرامت:

✦ درد یا ناراحتیهاي مختصر یا شکایات جزئي و قابل درمان

✦ بي اثر بودن مداخله پژوهشی

✦ وخیم شدن بیماری در حین دریافت دارونما

✦ آسیب به دلیل سهل انگاري تعمدي بیمار رخ داده باشد

پرداخت غرامت در کار آزمایي باليني

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- دریافت برائت نامه به همراه رضایت نامه آگاهانه ممنوع است و پژوهشگر یا موسسه‌های پژوهش را مبرا از مسؤلیت پرداخت غرامت نمی‌کند.





روایت‌هایی از پزشک و بیمار

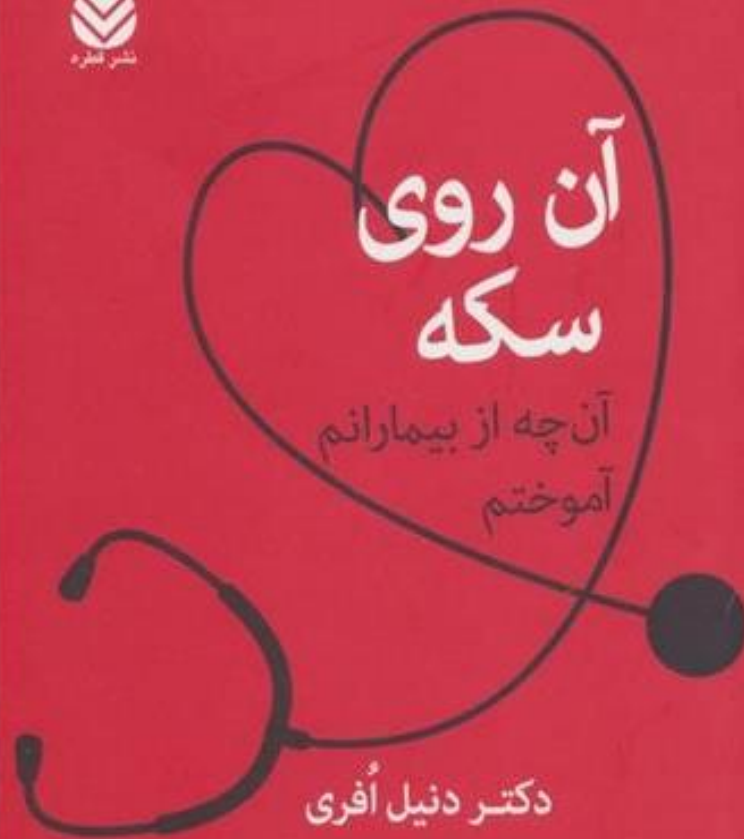
دکتر دنیل اُفری

دکتر افروز معتمد



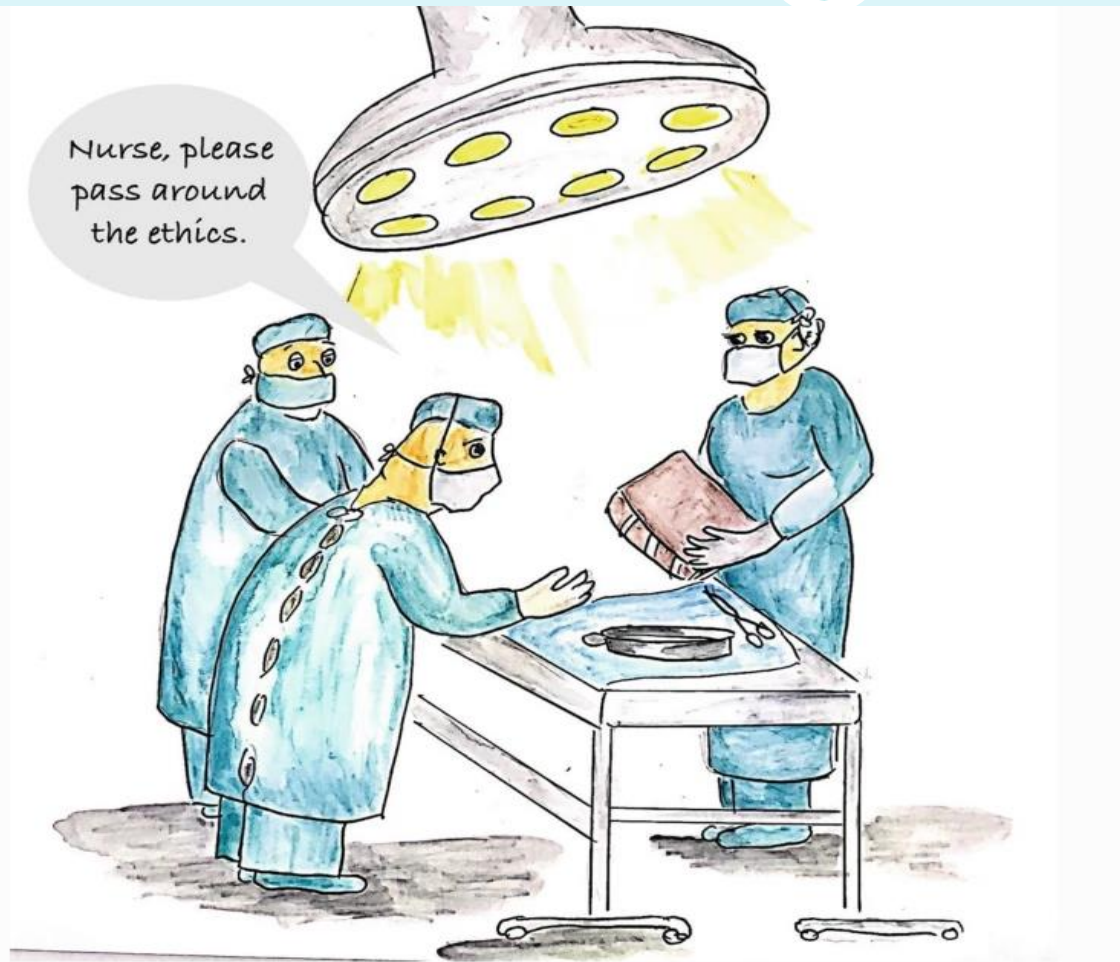
آن روی سکه

آن چه از بیمارانم
آموختم



دکتر دنیل اُفری

دکتر افروز معتمد



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