

Clinical Research and the NRS Biorepository Network

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What is Clinical Research?

- ▶ Clinical Research is the part of healthcare looking at the safety and effectiveness of medication, medical devices, treatments etc intended for human use.
- ▶ It is used to improve patient outcomes in the real world.
- ▶ It is heavily regulated to ensure patient safety and to ensure objectivity of results

Where Did Research Come From?

- ▶ James Lind is thought of as the first doctor to conduct a modern style controlled clinical trial. This was the famous scurvy trial of May 1747.
- ▶ It had been long suspected that citrus fruit would prevent scurvy, but nobody had done anything to prove it, or implement its use.
- ▶ Dr Lind (Royal Naval surgeon) was so concerned about the high mortality rate amongst the sailors on HMS Salisbury, he set out to prove the fruit theory.
- ▶ Twelve of the worst affected were selected and put into pairs. Each pair was given a different treatment. Five suspect treatments, and one fresh fruit treatment
- ▶ After six days, one fruit participant was well enough to return to duty, and the other was able to nurse the remaining patients.
- ▶ Cider, funnily enough, was the next best.
- ▶ As for the rest, well... don't try those at home!

Where Did Research Come From? continued



- ▶ So, if you got oranges and limes, or even cider to an extent, you were saved.
- ▶ If you got brine or vitriol, you still had scurvy, and now you had an upset tummy to add to your misery.
- ▶ The empirical evidence was there, but was it ethical?
- ▶ Did the Participants have a choice?
- ▶ NO!
- ▶ ***But, (whisper it), it was only 1747.***

The Past is a Foreign Country: They do Things Differently There. L.P. Hartley

- ▶ Well, 1747 was a long time ago, surely things updated pretty quickly after that?
- ▶ Let us jump to the 1940s and the Nazi concentration camps. Many were experimented on horribly without any consent. Truth came out at the Nuremberg Trials in 1946.
- ▶ From the horrors that came out at the Trials, the Nuremberg Code was developed as a set of research ethics principles for human experimentation.



Nuremberg Defendants Listen to the trial through translation

Did Nuremberg Solve the Issue?

- ▶ There are 10 points, and they are all still recognisable: -
- ▶ Voluntary consent is at number 1
- ▶ The risk of harm to the participants must be minimised
- ▶ The experiment must only be carried out by suitably qualified scientists
- ▶ The participant must be able to withdraw consent etc...
- ▶ However, this was a code, not law, and did not have to be adhered to



The Immortal Life of Henrietta Lacks

by Rebecca Skloot

Henrietta Lacks as a
young woman



Whose Tissue is it Anyway?

- ▶ Henrietta was poor and black. When unwell she went to Johns Hopkins hospital - the only one to treat the poor and black.
- ▶ On examination she was found to have a cervical mass. Treatment involved putting in radium rods to shrink the mass
- ▶ Tissue was removed without her knowledge and passed on to researchers who successfully grew it as a cell line.
- ▶ It was an immortal line - it grew and grew, and was given away to others for use.
- ▶ Then somebody commodified it and started using it to turn a profit

It Doesn't matter Whose it is, It's What We Do With it That Counts

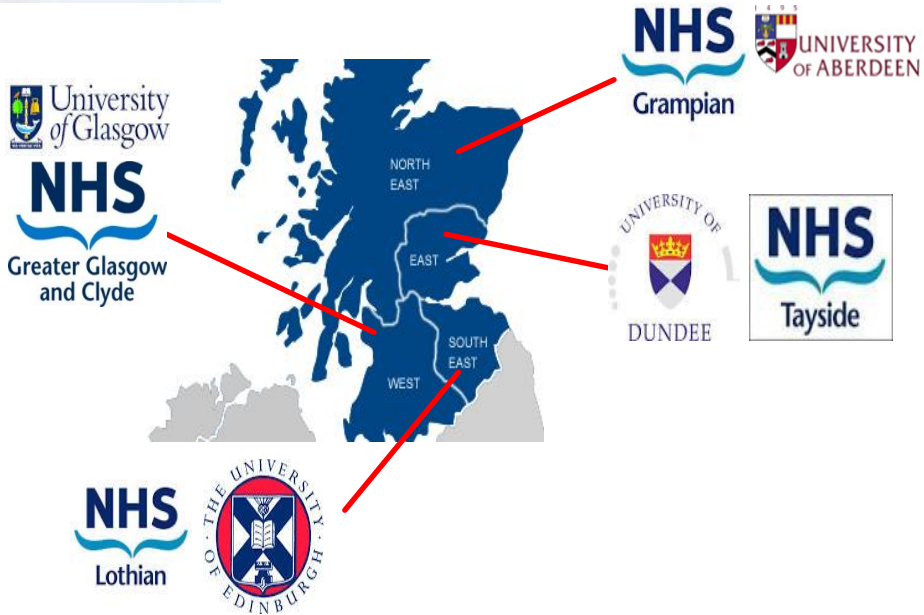
- ▶ Henrietta Lacks Died in 1951, but her cells lived on in research
- ▶ If we remember the Nuremberg Code, the first line says “The voluntary consent of the human subject is absolutely essential”
- ▶ In the 1950s, researchers were injecting patients with “vitamin shots” in reality, HeLa tumour cells. Nobody was told.
- ▶ Most had an immune reaction and fought off the tumour, but some died.
- ▶ The Nuremberg code didn't apply to nice people like. us, just to those nasty people, like the bad Nazis.
- ▶ We might question whether Henrietta needed to know her cells were being used in research, but surely all those who were injected with her cancer cells really did have the right to know

More Modern Times

- ▶ Between 1988 and 1995 there was an unauthorised removal, retention and disposal of human tissue from infants at Alder Hey Children's Hospital, Liverpool, amongst others.
- ▶ The parents of these children were not asked if this was acceptable.
- ▶ This lack of transparency is how trust in research is lost.
- ▶ The public enquiry (Redfern Report into this scandal led to the Human Tissue Act 2004
- ▶ And the Human Tissue (Scotland) Act 2006
- ▶ This sets out the methods by which human tissue may be used, and it is consent based.

So, Where are we now?

The Scottish Biorepository Network



4 Nodes: -

North Node - Based in NHS Grampian with close ties to Aberdeen University

East Node - NHS Tayside and University of Dundee

South East Node - NHS Lothian and University of Edinburgh

West Node - NHS Greater Glasgow and Clyde, and University of Glasgow

- ❖ Chief scientist Office and NHS Research Scotland collaborated to support the Scottish Health Boards by funding a REC approved Research Tissue Bank in each of the main health boards to provide tissue governance oversight across Scotland.
- ❖ Directly responsible to each Health board but also have close collaboration within their corresponding medical schools.
- ❖ All adopt the HTA Codes of Practice as best working conditions.

What do the Biorepositories do?

Collection

- Human Biological Samples
- Within ethical framework

Storage

- Secure
- Retrievable

Distribution

- Safe
- Accurate

Accreditation

- ❖ At the moment we have accreditation through Healthcare Improvement Scotland.
- ❖ Next round of accreditation to be carried out under the auspices of the Central Management Team of the Chief Scientist's Office (Early 2019)
- ❖ Regardless of who offers the accreditation, there is a panel of independent auditors who examine our ability to act as a biorepository and offer laboratory services.

We Must Meet Three Accreditation Criteria: -

- ❖ Consent and Authorisation.
- ❖ Governance.
- ❖ Premises Fit for Purpose.

Accreditation Continued

- ❖ Accreditation offers safeguards
- ❖ Our participants can be assured that their tissue will be logged and handled appropriately.
- ❖ All staff working in the Biorepositories are GCP trained
- ❖ Researchers requesting tissue can be assured that the tissue is ethically sourced and handled such that it can be used in the knowledge that good results can be achieved.
- ❖ Customers accessing our technical and scientific services can know that tests will be carried out in a professional manner using high quality materials and streamlined to meet their requirements in a suitable environment.
- ❖ The same standards are met across the network so regardless of the source of material, the same quality can be met.

Streamlined Pathway

- ❖ One application across Scotland - an approved request in Grampian is an approval for Scotland.
- ❖ We utilise national co-ordinated costs to reflect project requirements.
- ❖ We assess requests using local access groups made up of clinicians, academics and researchers to ensure the project is well planned and of merit. Once satisfied, permission can be given for tissue to be provided.
- ❖ If tissue cannot be sourced at local biorepository, request can be made for tissue around the network. There is an MTA in place to allow biorepository to biorepository transfer without issue.

Limitations

- ❖ We can offer support for projects using our ethics, however, there are obviously limits to what this allows us to do.
- ❖ Tissue released under our ethical approval comes with limited data - nothing that may identify a participant can be released.
- ❖ We cannot collect extra biopsies. Our material is “surplus to diagnostic” and as such comes at the discretion of the relevant pathologist. The clinical diagnosis will always trump your research project.

Future Vision for The Scottish Biorepository Network

- ❖ Roll out of a national NRS Biorepository IT software that will provide a consistent approach for the biorepositories and a unified IT platform to allow us to move forward together.
- ❖ Unified Portal for commercial and non-commercial clinical research studies to access tissue and associated data and further improve the efficiency of how application are approved and circulated across Scotland.
- ❖ Closer collaboration between biorepositories and safe havens across Scotland to enable linkage of existing clinical data sets with human tissue samples so that quality annotation will greatly enhance the identification and characterisation of tissue samples whilst maximising its value across a broad range of disease cohorts that could include data including pathology, imaging and larger data sets that we normally cannot provide

Conclusion

- ❖ Quality and ethics are intertwined within the Biorepository Network
- ❖ We must maintain and work within accreditation and ethics framework.
- ❖ Collection, storage and distribution of human tissues together with clinical trials work and other lab techniques are handled within their written and controlled procedures.
- ❖ One stop shop for researchers - local, national and international - whether small scale and local, or networked and commercial.
- ❖ The network of biorepositories work together to provide assistance from set-up to delivery, working more closely with the network of data safe havens.
- ❖ We rely on local and national teamworking without which we would not be able to provide the service we do.

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