

The role of pharmacy in clinical trials it's not just counting pills

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I am currently employed as a Senior Pharmacy Technician working at York Hospital. I work in pharmacy, in the clinical trials department. Just a bit about my background, after school I went to college to do a two year BTEC National Diploma in Health Studies, which I finished in 2004, and after that I decided I wanted to start working so I started working in a community pharmacy and to do that I needed to start studying for an NVQ level 3 in Pharmacy Services. That is a two year course and you are studying for the course whilst you are working, so it is quite hard working full time and studying at the same time, but it is well worth doing because what you are learning you are actually getting to put into practice as well. In 2008, after I had finished my NVQ, I decided I wanted to come here to University so I studied the Medical Physiology degree which I finished in 2011 and I graduate with a 2:1 and then two weeks after leaving here I started working at York Hospital. I was very lucky I actually got the phone call offering me the position whilst I was on the way back to Middlesbrough (which is where I'm from). Whilst I have been working at York Hospital they have been really supportive and they have offered to support me in studying a Postgraduate Certificate in Health Research which I am doing at the University of Leeds and hopefully will be finished in April.

There are various types of clinical trials that are conducted within hospitals and we have currently got the best part of sixty open and they are split between commercial studies, which are run by pharmaceutical companies, and they will be people that you have heard about and read about in the press. We also run non-commercial and academic studies and they're run by NHS Trusts, charities and Universities. These can be a mix of studies, so there is observational studies where you are not dealing with the patients treatment, there's medical device studies, and the type of studies that I support are drug studies which are also known as CTIMP which stands for Clinical Trial of an Investigational Medicinal Product. Investigating a medicinal product, or IMP as it is known, is just the fancy name that is given to a study drug that is being investigated.

I imagine a few of you will be familiar with the different phases of research, but just to run through them in case you are not. There are four phases of research, so new drugs starts of in phase I where you are testing the drug in a group of healthy volunteers; they are often referred to as "first into man" studies. You are involving less than a hundred people and you are testing safety and you are looking for a safe dose range.

After that you are looking at phase II studies and you are moving to 100 to 300 people and you are starting to put that drug that has gone through the phase I study into the diseased population who might benefit from that treatment.

If things are looking good after that you move on to phase III study so you are getting bigger again, with 1000 to 3000 people. So you are putting the new drug into larger groups of people who should hopefully benefit from the treatment. That often involves comparing the drug against the existing gold-standard treatment that is given or comparing it against a placebo. After a drug has been licenced and moved to phase IV research then you are looking for long term safety data, side effects and effectiveness and you are looking at more than 3000 people in those studies.

In order to run clinical trials it is very multidisciplinary and you need to be liaising with lot of people on a daily basis. So we're in touch with sponsors a lot, and the sponsors at the company who are running the clinical trial. They are responsible for helping you set up the study and then conduct it at your site. Then each site will also have a doctor called a Principal Investigator and they are responsible for running the study at your site. They can delegate out their responsibilities to the appropriate teams, so they will delegate out the dispensing to Pharmacy and the lab side of things out to the labs. There are also Research Nurses who support all of us during the set up. They are very much more hands on than we are with patients and they help us during set up and whilst the study is open. We can also go to our Research and Development Team anytime we need advice and they are dealing with the contract side of things, ethics, research governance, more of the paperwork side of things. There are lots of departments in Pharmacy which was something I wasn't particularly aware of when I was working in community, but when I came into hospital pharmacy and was introduced I didn't know there was a clinical trials team, there is a satellite unit that deals specially with chemotherapy, and one unit which we always require the help of is our aseptic unit, so if you are making the dose aseptically I'm not aseptic trained, so I have to request support from our aseptics unit in order to prepare the doses. So I need to consider that whilst I am setting a study up.

As I mentioned earlier we also do phase I studies and we co-sponsor them with the University of York, so we liaise with them a lot as well. We also get inspected every two years by the MHRA.

I won't read all of these out, but here is a list of the specialities that we cover and as you can see there is quite a varied range there. I would say our most research active areas are oncology and haematology and I guess that's just because there is a lot of funding available in cancer research over the other areas recently.

The beauty of this job is that no day is ever the same so there isn't the potential to get bored of it. Whilst the principles of clinical trials all remain the same and we have to adhere to something called Good Clinical Practice, which is the ethics that we have to follow in order to conduct our trials, everything is different and it is brilliant.

So my main job is to set up clinical trials from a pharmacy perspective, and because we have the best part of 60 studies open you can't remember the ins and outs of every single one, so it involves keeping a lot of documentation so that you can just go to that file for that study and know exactly what you need to do.

That will cover things like how to order the study drug, how to receive it, how to dispense it, and also how your Pharmacist should be checking it. We do drug accountability so we account for absolutely every drug coming in, getting dispensed and then either getting destroyed at site or getting returned to the sponsor where they can destroy it.

We are also very hot on temperature monitoring. So our fridge lines have to be stored at 2 to 8 degrees celsius and our room temp stock has to be stored at 15 to 25 degrees celcius, and if it goes even point one of a degree above or below that we have to quarantine the stock and go back to the sponsor and report that temperature excursion and they have to assess that and say whether or not the drug is still stable for use, because what we want to be able to confirm is the result that we are seeing in the patient is because of the drug working not because of the temperature excursion.

We also host monitoring visits so I was discussing earlier the sponsors who are responsible for running the study, they come to the site every now and again and they will check your pharmacy files they also check all the investigators files as well, so the doctors and the nurses, they check that all your paperwork is up to date and that all your communications are that you are running the study as you should be. As a general rule of thumb in clinical trials if it isn't written down then it didn't happen.

We also have trial initiation meetings. So just before a study opens we get everybody together because your sponsors provide you with a protocol which is a rather large documents of a couple of hundred pages and it will tell you how they want the study to be run. But it is a document that they will send to hospitals internationally and it is not site-specific. So what you then have to do is make that specific to your site incorporating your local procedures. So at trial initiation we get the doctors, nurses, labs, pharmacy, absolutely everyone together and we discuss how it is going to work at site and it is a really good opportunity to raise any queries before you have got any patients enrolled in the study. As you can imagine all that needs documenting, in standard operating procedures so that we are all following the exact same procedures, so it is a lot of writing.

So you will probably be familiar with the placebo effect and there are various types of blinding in pharmacy in order to maintain the integrity of the research and to hopefully reduce bias. So in open label research everyone knows what treatment the patient is receiving, so say for example we dispense a box of paracetamol everyone can see it is a box of paracetamol. We have a few single-blind studies where the patient doesn't know what they are receiving but everybody else does and then it is really important that you don't accidentally tell the patients what they are having otherwise you are opening the study up to bias. And more popularly is double blind studies where everybody involved doesn't know what treatment the patient has been randomised to receive, so that's your doctor, your research nurse, us in pharmacy, the sponsor. It's actually a computer system that allocates the treatment by a kit number so it is often like a four or five digit number, and that is what we will dispense. So you could always access that computer

system if in an emergency situation you needed to unblind and find out what treatment they are receiving to treat them, but you try not to do that because it might take them off the study.

There is an exception to the double blind rule and it is when pharmacy have to be unblinded for the study to run. We have had studies like this in the past and what we then have to make sure is that when the research nurses collect the drugs from us we have to make sure that we haven't got documentation lying around saying what study treatment they are getting or that we don't actually say to them here is whatever drug it is that we have dispensed.

One of the really rewarding things is seeing things published as you can imagine. So a couple of years ago we ran a Trust-sponsored study and it was called "Crystalloid or colloid for goal-directed fluid therapy in colorectal surgery" and as I was just describing there the pharmacy were the only unblinded team, so the doctors, research nurses and patients and the sponsors were all blinded. The results of it were published in the British Journal of Anaesthesia in 2013 and what they concluded was that the goal directed fluid therapy was possible with either crystalloid or hydroxyethyl starch, which is the colloid, and that there was no benefit of using the colloid over the crystalloid despite its use resulting in lower 24 hours fluid allowance. Now that doesn't make a massive amount of sense to me not being from a surgery background but what it did mean was that in conjunction with a couple of other papers that had just been published from similar trials it has actually changed in practice what is being used by our Trust. So it is really really rewarding to see a change in practice, and obviously a publication as well.

So this presentation has been around the role of pharmacy in research but there are a lot of other jobs outside of pharmacy. To just touch upon them, we do have Pharmacy Assistants that support us, they have NVQ level 2s usually or level 3s and they do a lot of our dispensing. Research teams have Clinical Trials Assistants and that is sometimes a degree-level position in which you are supporting the research team. Sponsors also employ Clinical Research Associates and a lot of them have degrees too. They are the people who come to monitor you and check that you are doing things right. It does involve a lot of travelling and you may only have a couple of trials that you are responsible for but you might have twenty sites that you have to look after. They are there to help you set the study up and run it and also help to close out the study at the end. There are Research Nurses who I discussed earlier which is a very hands on role with the patients and Principle Investigator for anybody who is interested in and if you are going on to medicine you might want to be a Principle Investigator. The more paperwork side of it there is Trial Co-ordinator, data administrator and data management jobs. It is worth knowing that a lot of those jobs aren't just based in the hospital so there is a lot in Universities too. A lot of Universities have trials units and run clinical trials.

Questions

Q. You have clearly got some additional qualifications that you did before the degree, in your particular case. The list you had the, you picked out a couple of roles that you said someone with a degree could do, presumably some of those other ones presumably having a biosciences degree will open up opportunities for those?

A. Definitely. The Pharmacy Assistant is an NVQ position but we do have training positions within our Trust where people can come and do the NVQ and learn about that role of pharmacy at the same time, so that is always open to people. Clinical Trial Assistant is usually degree level so you would be able to go straight into that. Clinical Research Associates, some of them have masters, some of them have nursing backgrounds, there is a real range, and you would be best going to say a pharmaceutical company or even if you were to pop it into a search engine then it will tell you a bit more about that role and what specifications they look for nowadays, but I have definitely seen some with degrees. Research Nurses is a standard nursing degree but I think you can do a quicker nursing degree after you have done a bioscience degree, can't you, that's two years instead of three? And Principal Investigators being your doctors so for anyone who is interested in graduate entry medicine a four year course or even a five year course research is always something that people are looking for when they are looking for future doctors. Trial Co-ordinator, Data Management and Trial Administrator could be degree-level jobs.

Chris Willmott: Yes we have had several people go on and do that actually. So pretty much the majority of these roles could be, albeit with some additional training, could be directions that people could head towards.

Q. You said you have some stuff that was published from your work, did you actually get included as an author?

A. Pharmacy got an acknowledgement; if you read the publication because we were responsible for blinding the bags. So what happened was there was two bags for the study, there were colloid and there were crystalloid bags and we had to blind the bags in pharmacy. We also had to randomise the patients in pharmacy and then we had to hand them over to the Research Nurses and the Principal Investigators running the study, so we had quite a hands on role for that study which had about 250 patients in it over a couple of years. But whilst the publication was actually in the surgeons' names and the people who had written the paper pharmacy got a mention, but it wasn't by name.

Q. In terms of the blinding, sometimes you are blinded to that as well? So who knows what is what at the stage when you are involved?

A. Just the computer system. A computer system called an IVRS and there is a web based version of that as well. When the Principal Investigator is wanting to randomise the patient, because that is usually their responsibility, they will log onto that system, they will check that the patient meets all the criteria to go into clinical trial and then the computer system will randomise the patient and keep the randomisation secret

and then allocate kit numbers that are to be dispensed at every visit. It is then our job just to dispense the correct kit numbers. So you need a real keen eye for detail when you are dispensing just because obviously if you were one digit out you might be giving the placebo instead of the active and then you are affecting the results of the study. So you can access the IVRS system if your patient comes into A&E at 3am in the morning if you need to unblind them to find out what they are on you can access that system to do it, but they try to avoid doing so if they at all can because it usually means that person has to be taken off the study.

Chris Willmott: I was a participant in a clinical trial last year, and it was to do with eyes. So rather than calling it “single-blind” they called it “single-masked” because, I think, the concept of single-blind to do with eyes was a bit near the knuckle.

Q. So what would you say was the best thing about your job?

A. I love that I supervise a few people so there are people that assist me to do my jobs. Every day is different. We also go to Research Nurse meetings. Communicating with a wide range of people is brilliant; I never thought I would be speaking to doctors on a day to day basis. The best thing is that I am never doing the same thing. I could be dispensing one morning and I could be setting up a clinical trial in the afternoon, dealing with queries from sponsors, hosting the monitoring visits - it is the variety that I love.

The worst part is probably trying to balance the quantity of trials because they are all very different fields as you can see from the slide. Knowing all of them inside out is quite difficult to do, but that is why we write our standard operating procedures so that you can just go straight to it. But it is quite a challenge just to remember the ins and outs of all of them.