Human Subjects Case Studies

Case Study 1 – Research involving adults with terminal illness

Dr. Abbott, an oncologist at a major teaching hospital, has been asked to put forward a number of her patients for participation in a clinical trial of a new cancer treatment.

Mr. Day is a terminally ill patient with a type of cancer suitable for participation in this trial. Mr. Day is incredibly keen to participate and volunteers at the first opportunity. When asked to explain his eagerness during the recruitment process, he says that God has sent him this opportunity, that the treatment (which he’s “read all about on the internet”) is a “wonder drug”, that it will save his life, and that (if entered into the trial) he expects to be “completely cured” in time for Christmas (less than 6 months away).

Mr. Day’s health carers all think that his views of the trial are extremely over-optimistic. What’s more, his views persist in spite of the fact that he’s been told on a number of occasions that:

1. The experimental treatment isn’t expected to prolong his life by more than a few months (although it may have quality of life benefits too):
2. This expected benefit can’t be predicted with any certainty;
3. The chances of his being “completely cured” by it, or anything else, are close to zero.

When confronted with this information, Mr. Day just says things like “you’re just being cautious and covering your back” or “you lack faith”.

Dr. Abbott thinks that participation in the trial might benefit Mr. Day psychologically, alongside any direct clinical benefits, by sustaining his hopes and expectations, and (conversely) that not permitting him to take part would be psychologically damaging. She also thinks that the fact that he’s very keen to take part should be taken seriously and that not to do so would be a failure to respect his autonomy. But, on the other hand. Dr. Abbott is not sure whether Mr. Day is capable of supplying valid consent, since he appears unable or unwilling o grasp the true nature of his situation and of the trial.

Questions:

1. Is Mr. Day in a position to give valid consent to take part in the trial?
2. Would denying Mr. Day a chance to participate in the trial be a failure to respect his autonomy? What is the relationship between irrational beliefs and autonomous decision-making?
3. Should the fact tat Mr. Day’s seemingly irrational beliefs have a religious basis be a matter for special attention in assessing his vulnerability?
4. Would entering Mr. Day into the trial be exploiting his vulnerability?

Case Study 2 – Research into treatments for behavioral disorders in children

Professor Helsinki, a world-famous psychiatrist specializing in the treatment of children, wants to comparatively evaluate four different treatments for a rare behavioral disorder called RBDC. RBDC, which involves occasional bouts of abusive and violent behavior and episodes of severe paranoia, is most prevalent in children between 11 and 15, but 14% of cases occur in young adults, and a further 6% of cases are in people over 25.

All of the treatments that Professor Helsinki wants to test are ‘standard’ insofar as each has been used in clinical practice in the recent past. However, the evidential basis for each one is minimal (at least specifically in relation to RBDC) and none is proven to work.

In general terms, the options for trial are:

1. A widely used pharmaceutical product;
2. A program of anger management and relaxation exercises;
3. Group therapy;
4. Cognitive behavioral therapy

Professor Helsinki want to enter almost all of his patients with RBDC (all of whom are younger than 16) into the study and to randomly allocate them into one of the above options. He proposes to do this without telling them or their parents/guardians and, hence, without prior consent for participation in the research (although the parents/guardians will be informed after the trial). Consent for the particular therapies offered will be obtained as normal, but the patients and their parents will not be told about the existence of the study or about the randomization process.

Professor Helsinki’s grounds for the non-disclosure policy include:

1. That disclosure to patients or parents would undermine the scientific validity of the study by affecting the behavior and mental states of the research subjects;
2. That disclosure would harm the research subjects by upsetting them and/or exacerbating their paranoia (e.g. the idea of being ‘experimented on’ and ‘watched’ would be highly disturbing to many of these young people);
3. That disclosure would make it impossible to recruit research subjects;
4. That most people with RBDC lack the capacity to validly consent owning to the nature of the illness; that this important research will benefit sufferers from RBDC and may even benefit the research subjects themselves;
5. That his patients could have (‘randomly’) received any of the treatment options in ordinary clinical practice depending on, for example, where thy happen to live, and that Helsinki’s research is just a more systematic and scientifically valuable version of what would have happened anyway.

Questions

1. What are the possible benefits that this research proposal raises?
2. It is ethical to conduct the research without obtaining the consent of either the children participating in the trial or that of their parents/guardians?
3. Do Professor Helsinki’s grounds for non-disclosure justify him carrying out the trial without consent?

Case Study 3 – Recruiting homeless participants to Phase 1 trials

A large pharmaceutical company conducts Phase 1 trials of its products at a specialist trials unit in a major European city. These are trials conducted using ‘healthy volunteer’ subjects and designed to test the safety and pharmacological effects of new drugs, and to establish maximum tolerated does levels. The products being tested have all undergone prior testing on animals, and in some cases there will have been previous trials in humans.

Volunteers typically spend between a few days and several weeks in the unit. After completing a questionnaire and undergoing initial health checks and baseline measurements, they will receive one or more doses of the product under investigation, while being subject to regular monitoring and assessment. Volunteers are required to report any adverse effects, and medical staff are on hand in case treatment is needed.

Because subjects participating in Phase 1 trials receive no therapeutic benefit it is usual for them to be paid. The unit’s recruitment materials (leaflets and posters, which volunteers are encouraged to take away and distribute) state that “compensation for time and inconvenience” will be paid “according to the length and nature of the trial”. In addition, the leaflets highlight the fact that meals and accommodation are provided free for the duration of the trial, and that entertainment and recreational facilities are provided.

In the past the company has had little difficulty in getting its trials approved by the research ethics committee, and it has a good safety record. However, a new IRB member has questioned the level of payment offer to volunteers and discovered that these are much lower than those typically offered by other pharmaceutical companies. Further investigation reveals that a large proportion of the volunteers are long-term unemployed and homeless (most of the addresses supplied on the initial questionnaire are for local hostels for the homeless or other temporary accommodation). Many are thought to be alcoholics or drug addicts, although they have to declare themselves ‘clean’ at the time of registering for a trial and will be unable to consume alcohol or drugs while in the unit. It is also evident that, despite an absence of high-profile advertising, the unit is widely known, with many volunteers travelling ling distances to participate in trials. Many have participated in trials for this or other companies on several previous occasions, and although the eligibility criteria specify a minimum of three months between trials, there is some evidence of volunteers falsifying their identity to overcome this restriction.

The company is unapologetic about its low payment levels or the socioeconomic groups from which its subjects are drawn. It argues that the ease with which it recruits volunteers demonstrates that the benefits to participants are substantial, and that higher payments might amount to undue inducement. It also points out that the number of participants withdrawing from trials is very low, as is the number of complaints received.

Questions:

1. What advantages does the pharmaceutical company gain by recruiting from a disadvantaged sector of society, and what benefits do the volunteers gain from participation in the trials?
2. What disadvantages or risks does this method of recruitment have for the company and for the volunteers?
3. Are there grounds for considering the company’s recruitment practice to be exploitative? If so, what are they and do you agree that it is exploitative?

Case Study 4: Tuberculosis vaccine research in a developing country

Tuberculosis (TB) is a major cause of morbidity and mortality, with nearly nine million new infections and two million deaths per year worldwide. Incidence of the disease is highest in developing countries, particularly in Africa, but it is also a problem in developed countries, some of which have seen a resurgence of the disease as a result of antibiotic resistance, reduced immune response due to HIV infection and migration from parts of the world in which the disease is rife. The commonly used vaccine against TB is Bacile Calmette-Guérin (BCG). However, while this is effective in young children, its effectiveness is more variable in adolescents and young adults, and it is not recommended for patients with impaired immune systems. In addition to problems of antibiotic resistance, drug treatments have had limited impact in developing countries due to cost and poor compliance.

Development of new, more effective vaccines appears to be the most promising strategy for controlling and eventually eradicating TB. Several potential vaccines have been developed as a result of advances in understanding the genome of the infectious agent. Some of these have undergone Phase 1 testing in Europe, and now European researchers working on a Modified Vaccina Ankara (MVA) vaccine wish to carry out further trials in various countries including Mozambique, a country classified by the United Nations as one of the world’s least developed and with prevalence rates among the highest in the world for HIV and TB.

The proposed trial in Mozambique is designed to test the effectiveness of the new vaccine when used post-infection and in conjunction with BCG. It will run for five years and will involve the following arms:

1. BCG only in adult males not known to have HIV;
2. BCG plus MVA in adult males not known to have HIV;
3. BCG only in adolescent males not known to have HIV;
4. BCG plus MVA (lower dose) in adolescent males not known to have HIV;
5. BCG only in subjects in the early stages of HIV;
6. BCG plus MVA in subjects in the early stages of HIV

Participants will be subject to monthly health checks, which will include monitoring of weight, blood tests, and sputum tests. They will be given advice on healthy eating and where necessary provided with the resources to maintain a healthy diet. Consent will be obtained in the standard way.

Costs will be lower than if the trial was conducted in Europe, and the high prevalence of TB should make recruitment of subjects relatively quick and easy. The researchers argue that it is important to test the vaccine in populations similar to those in which it is intended to be used. However, some members of the research ethics committee question the affordability of the vaccine for a country as impoverished as Mozambique and contend that, while it may be affordable for richer African countries, such as South Africa, the primary use is likely to be in those developed countries that are experiencing an increase in TB infection.

Questions:

1. In what ways might the trial be considered exploitative?
2. Would it be acceptable to include placebo arms in the trial if the region in which it is carried out is one in which BCG is not usually available?
3. Should the trial be allowed to go ahead as it stands? If not, how can it be made ethically acceptable?