

| BEST PRACTICES FOR SHORT-TERM HEALTHCARE MISSIONS | |
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| Question: Under which (if any) conditions can experimental medications be used in short-term healthcare missions? | |
| Participants in discussion | Background (perspective) |
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| Why is this important? This is an issue of trust, safety and perceptions. | |

Biblical concepts involved

Do unto others as you would have them do unto you

Luke 6:31

Do to **others** as you would have them do to you.

Healing and trust

Proverbs 13:17

A wicked messenger falls into trouble, but a **trustworthy** envoy brings **healing**.

What is the scientific evidence regarding the use of experimental medications?

Pharmaceutical companies have created a large number of safe and effective medications

The pharmaceutical companies in the Western world have compiled an amazing track record for developing life-saving medications. Excellent results for patients with cancer, infectious diseases and transplants are examples of the impact of modern medications. Vaccines have vastly reduced the threat of life-threatening illness for people¹. These successes and many others have led to the perception that there is a medication to cure every ailment – and if there is not, a new experimental medication, which can heal and restore health, is just around the corner. Unchallenged belief in technology leaves little or no room for God in restoring wholeness.

Not all experimental medications are efficacious and safe.

The pharmaceutical industry is in the business of creating new medications which have the potential to make profits for the company. Of 5000 medications which advance to pre-clinical trials, about 5 make reach the market². The United States has chosen not to engage in open access to experimental medications, because people would be exposed to untested and potentially dangerous medications and prospective clinical trials would be less likely to recruit sufficient numbers of patients to determine whether a medication is safe and effective. Therefore, all medications must go through clinical trials which occur in three phases.

Phase I trials evaluate the safety of the medication in 20-80 individuals, mostly healthy volunteers. These studies are geared to determine side effects and the normal pharmacokinetics of the medication. Medications that appear to be safe move on to the next phase.

Phase II trials compare the effect of the medication at different doses for the condition that they are expected to treat. Efficacy and short term adverse effects are evaluated. Occasionally phase II trials will compare the effect of the new medication with the standard therapy.

Phase III trials evaluate the medication efficacy and safety relative to the standard therapy for hundreds if not thousands of patients with the disease of interest. If the medication appears to be safe and efficacious the United States Food and Drug Administration (FDA) will approve it for use.

Unfortunately there have been a number of medications that have been approved by the FDA, which subsequently have been recalled (i.e.: Vioxx) because of unexpected and severe adverse events profiles. Other medications have received “black box” warnings, indicating that they can cause serious life threatening adverse events, years after being introduced (i.e.: erythropoietin). There often is a pattern of enthusiasm for a new medication that is similar to a bell-shaped curve –1) early enthusiasm leads to a marked increase in the use of the medication, 2) as more physicians use the medication previously unreported adverse events become apparent the growth of medication sales stalls, 3) Due to the increasing recognition of the problems with the medication it is abandoned by a large number of physicians, 4) over time, physicians come to realize the medication can be best be used for a subset of patients³.

It is noteworthy that nearly all homeopathic medications do not undergo a clinical trial process because the manufacturers elect to sell them as nutritional supplements which do not have to demonstrate efficacy, only that they cause no harm.

Close relations between the pharmaceutical industry and physicians can impact medication study results

Some of the most revered and respected physicians in medicine receive pharmaceutical industry support to conduct clinical medication studies. A concern has been expressed that these influential physicians may be influenced by their source of financial support. Biases may influence how a medication is presented in the literature. A recent Cochrane review by Jorgensen et al, found that industry-supported studies of new medications are more likely to be biased such

that adverse effects were less likely to be reported⁴. Jorgensen evaluated the differences between industry-supported reviews and those performed by independent investigators, the Cochrane Review. Compared with industry supported reviews and reviews with undeclared support, Cochrane reviews had more often considered the potential for bias in the review. The seven industry supported reviews that had conclusions recommended the experimental drug without reservations, compared with none of the Cochrane reviews.

Perceptions can influence the effectiveness of medications and placebos

The popularity of new medications is often based on the perception that what is new is better. The expectation of benefit from a medication often impacts at least subjective reports of improvement. This improvement in symptoms solely due to the expectation of cure/improvement is called the placebo effect. To assess this effect in randomized medication trials, some patients will receive a pill with no active ingredient, a “sugar pill”. The placebo effect has been shown to be effective in the treatment of diseases⁵⁻⁷. Patients may also experience the “nocebo” effect, which has been defined as “the phenomenon whereby a patient who believes that a treatment will cause harm actually does experience adverse effects”⁵.

The demonstration of medication benefit is often best shown relative to no or placebo therapy. Despite the good science of such an approach, there are questions as to the morality of offering a randomized portion of the patients *no treatment*. Some investigators have successfully stated their opposition to placebo trials, especially when a potentially life-saving therapy is being withheld⁷⁻¹⁰. De Deyn has suggested that placebo therapy may be offered if: (a) no adequate therapy for the disease should exist and/or (presumed) active therapy should have serious side-effects; (b) placebo treatment should not last too long; (c) placebo treatment should not inflict unacceptable risks, and (d) the experimental subject should be adequately informed and informed consent given⁷.

Subjects often do not understand the risks associated with experimental drug therapy

All experimental medication trials are dependent on obtaining informed consent from the subject. However, studies have shown that many subjects do not understand the basic terms including blinding (neither the patient or physician knew which study medication was given so as to avoid bias in the evaluation of results) randomization (the patient is assigned to a treatment arm by a process similar to the flip of a coin) used by the physicians¹¹. These problems are compounded in psychiatric patients¹² and patients who speak a different language and are from another culture. The literature is replete with studies and opinions regarding informed consent in cross-cultural settings¹³⁻⁶². Issues of international transplantation and gene analysis has made the issue of consent even more contentious^{13,42,44,62-65}. The essential components of a cross-cultural consent process are:

1. Obtain Institutional Review Board approval

2. Arrange for an agreement between the home institution and the host institution.
3. Make sure the patient/subject is capable of understanding and signing the consent.
4. The consent should be translated into the native language
5. Contextualize the consent to the culture. For example may be necessary to engage the potential subject in a story-telling mode (in areas where literacy is low).
6. In societies that are more communal in nature, adapt the consent so that other parties (spouses, family, key community leaders) can also assent to the medication.
7. Don't be in a hurry.
8. Ask questions about what would happen if...

World Health Organization (WHO) Standards for Donated Drugs (Second Edition 1999) - Excerpts

2. All donated drugs or their generic equivalents should be approved for use in the recipient country and appear on the national list of essential drugs, or, if a national list is not available, on the WHO Model List of Essential Drugs, unless specifically requested otherwise by the recipient.

Justification and explanation

This provision is intended to ensure that drug donations comply with national drug policies and essential drugs programmes. It aims at maximizing the positive impact of the donation, and prevents the donation of drugs which are unnecessary and/or unknown in the recipient country.

Possible exceptions

An exception can be made for drugs needed in sudden outbreaks of uncommon or newly emerging diseases, since such drugs may not be approved for use in the recipient country.

Has the experimental medication been approved in the hosting country?

Sender Perspective

Before

Many churches and individuals have received requests for specialized treatment from individuals and missionaries around the world. The church or sending organization should be made aware of the need for the experimental medication and the team leader's intent to provide the medication. The church/sending organization should be fully informed why the experimental treatment is needed. A review of the potential alternatives to experimental medication and a full review of the necessary approvals (receiving hospital, IRB, local governmental approval, etc) is necessary. There should be prayerful consideration of the situation, so as to determine God's will, prior to commitment.

During

If the use of experimental medications is approved, the sender will need frequent updates. The congregation/sending organization should be praying and providing other support for the person receiving experimental medication.

After

The major issue is whether the church/sending organization bears responsibility should the patient die or experience significant adverse effects. Should the use of the experimental medication be successful, then the glory goes to God, not the medication or physicians who provided the medication.

Goer Perspective

Before

Occasionally team members receive a plea (often by e-mail) for help for a person with a serious disease. Beyond praying for a person, it may seem reasonable to use all of the resources that God provides. Often academic physicians are aware of experimental treatment regimens and may consider whether such a treatment would be beneficial.

Altruism should be a pivotal motive. There should never be a desire to cut-corners or recruit larger number of patients for experimental therapy because of the relatively lower consent requirements in other countries. It is important to remember that there are number of confounding variables which can impact the effect of the medication. A good understanding of anthropology and the diverse physiology is important prior to designing any trial. While the desire to help may be great, it is important to try to understand how God might think about the situation. We trust that God can bringing a believer back to wholeness, even if it involves death. Nevertheless, I believe that God can work through experimental medications to achieve healing. To that end, an appropriately motivated team leader can bring honor to God by working through all of the hurdles necessary to legally use the medication in another country. It is extremely important that mission partners are fully brought into the decision making process.

Situations where only a limited amount of medication is available for a (too) large population of needy people creates a rationing situation. This places the Christian physician in a very difficult situation. The criteria for receiving the medication should be stated in advance.

Success can create a problem similar to that encountered by Jesus – word of a cure spreads rapidly. It would be important to think about one's strategy beforehand. Is this a one-time only offering?

Preparing people for both success and failure is critical. If a medication works, will everyone give the credit to God? What other conclusions can people draw? They may be grateful to “the god of technology”, “the Western medicine god”, etc. – and in terms of God's Kingdom we may be worse off than when we started.

During

Team leaders or team members who provide experimental medications in cross-cultural settings need to be available to provide oversight and guidance for the use of experimental medications. In obtaining the consent it is important to make sure that there is no coercion or unrealistic expectations for the patient. The use of experimental medications as part of a study can be very difficult to explain to people from another culture. Uncertainty lies at the heart of the issues. The effects of experimental medications are *unknown*. No matter how much we think that we know about these medications, our experience with them is too early in the “bell curve” to determine if the medication is inherently useful and good. What do we tell people about long-term effects, say in 20 years?

There are number of cross-cultural situations where one’s motives can be misunderstood by other healthcare professionals. It will also be necessary to contextualize the use of an experimental medication to other healthcare professionals who might think that other motivators (greed, enhancement of position, simple curiosity) may be operative.

After

Obviously one can bask in the satisfaction of knowing that a person was helped by God through the use of an experimental medication. However, should a poor outcome occur, the team leader/ team member is likely to have problems with the recipients and senders.

Recipient Perspective

Before

The motivation for people in need of healing, but have failed traditional therapy, is largely that of desiring to be healed/restored to health. Like other people, there may be unrealistic expectations of the effect of the medication and even an unconscious de-linking of the medication and God’s provision.

During

The patient can have a variety of different outcomes – completely healed, healed but with adverse effects of the medication, much improved but disease remains active, or worse/dead.

After

If the medication is successful, there may be a great deal of gratitude to God and to the people who were responsible for bringing the medication. If the medication does not have the intended consequence, it will be important to make sure that the team leader/team member and/or church provides for the consequences. People may be angry, hostile, sad or frustrated.

CONSENSUS STATEMENT

The use of experimental medications in short term healthcare missions is likely to be extremely rare. Given the unknown risks to the patient, senders and goes, it seems wise to avoid their use entirely. The even more rare use of

experimental medications, for the glory of God's kingdom, will require all parties to insure that due diligence has been exercised.

BEST: DO NOT USE EXPERIMENTAL MEDICATIONS

BETTER: FIND A WAY TO ENROLL PATIENT IN ACTIVE INTERNATIONAL EXPERIMENTAL MEDICATION STUDY

GOOD: ONLY USE EXPERIMENTAL MEDICATIONS IF THE FOLLOWING CONDITIONS HAVE BEEN MET:

1. PHASE THREE STUDY MEDICATION (OR GREATER)
2. INSTITUTIONAL REVIEW BOARD HAS APPROVED INTERNATIONAL STUDY
3. APPROVED INSTITUTIONAL AGREEMENT WITH LOCAL INSTITUTION WHICH PROVIDES CARE FOR PATIENT
4. FOLLOW-UP OF SUBJECT HAS BEEN ARRANGED. THIS IS TO INCLUDE PROVIDING CARE FOR ANY EXPECTED OR UNEPECTED ADVERSE EVENTS
5. THE SHORT TERM MISSIONS TEAM LEADER/INVESTIGATOR WILL CONTINUE TO MONITOR THE PATIENT'S STATUS.
6. LANGUAGE- AND CULTURALLY- RELEVANT CONSENT OBTAINED
7. LOCAL GOVERNMENTAL APPROVAL
8. CHURCH APPROVAL, IN WRITING

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