

Turkish Delight Translating Turkish Clinical Trials

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International Clinical Trials Feb 2011

Clinical trials conducted in emerging regions have expanded to include several countries that were once less dominant in clinical research. Among newly emerging countries, Turkey has shown exponential growth in foreign-sponsored clinical research. There are several factors responsible for this growth, including Turkey's geographic proximity to Europe, the country's extensive regulatory reforms and associate membership status with the EU, as well as successful patient recruitment rates, the presence of highly-skilled scientists, and reduced clinical research costs relative to the west. Presently, Turkey is considered among the top ten countries in terms of potential study subject populations – which consist of the U.S., China, India, Brazil, Russia, Japan, Mexico, Germany, Turkey and Thailand (1).

Most clinical sites in Turkey are located in large cities, where infrastructure is more established and there are a large number of universities and specialized hospitals. These centers offer access to a large pool of eligible subjects which greatly facilitates patient recruitment in the country. Turkey's largest city, Istanbul, has a population of 12.8 million, and is the second largest metropolitan area in Europe (2).

Clinical research in Turkey is conducted in several therapeutic areas, including a number of rare diseases as well as diseases formerly prevalent in more developed countries including cardiovascular diseases, diabetes, obesity, hypercholesterolemia, and several types of cancer. Population growth, increased life expectancy, urbanization, tobacco consumption, and the adoption of western dietary habits have all contributed to a higher incidence of these diseases among the Turkish population.

Despite the advantages offered from outsourcing clinical research to Turkey, several challenges remain. These include regulatory hurdles, and language and cultural barriers that affect clinical research. Additional problems reported by foreign sponsors include an inefficient patient referral network (heavy patient overload), inadequate infrastructure in some centers (logistic, equipment, and data management), and inconsistencies in GCP and local ethics committees (3). For the purposes of this article, the focus will be on linguistic and cultural barriers.

Regulatory Environment

The first clinical trials in Turkey to be conducted according to GCP guidelines were in 1993. In 1995, a Turkish version of GCP guidelines was issued by the Ministry of Health. This was followed by significant reforms to bring Turkish regulatory legislature in line with that of the EU. Between 2008 and 2009, Turkey adopted the EU Directive on implementing GCP guidelines. An increase in GCP training, as well as the adoption of

EU guidelines, has helped eliminate some of the past regulatory issues, and is largely responsible for growth in Turkey's clinical research sector.

More recent efforts to streamline regulatory approval procedures have also facilitated an increase of clinical research in the country. In March of 2010, Turkish requirements for regulatory approval were modified such that a single form is now required for submission to both the National Ministry of Health and the Ethics Committee (4).

Turkey ranks high as a market for counterfeit medicines. However, according to Cengiz Gümüştüs, head of Esfor Security Consultants, it has the fourth highest arrest rate for drug counterfeit production (5). Moreover, the Turkish government has been involved in further efforts to better control and monitor counterfeit drug production. According to a recent interview with Cognex executives by Healthcare Packaging, "Turkey has taken a leading role in addressing fraud in the reimbursement process by mandating new drug traceability processes. These processes also help to control the proliferation of counterfeit drugs." (6)

Translation & Cultural Adaptation

The importance of quality translation and cultural adaptation cannot be over emphasized in international clinical trials. Although good translation products do not assure success, bad ones can cause an otherwise good clinical study to fail by preventing researchers from collecting accurate data or delaying approval from ethics committees. Accuracy and cultural context is especially important in the preparation of patient-related information, where not only the accuracy of the text being translated, but how a message is conveyed is of critical importance.

Experts in translating documents for the pharmaceutical industry use a well established process to ensure that translations are both accurate and culturally sensitive. This process involves numerous steps that are performed systematically by translators who must be fluent in both the source language (the original language in which the study is constructed) and target language (the language in which the study will be conducted). There are several studies involving Turkish patients that have demonstrated the importance of using this translation process. The main goal of these studies is to cultural adapt translated materials to test for comprehensibility among Turkish patients, while also determining whether the information provided to the patients is equivalent in both the source and target languages [(7, 8, & 9)].

In the aforementioned studies, health assessment and quality of life questionnaires (HAQs & QoLQs) were translated, culturally adapted, and linguistically validated. The translation process consisted of forward translation by a team of experts whose native language is Turkish, followed by back translation and review by another team of experts fluent in both languages. Translators in each team agreed upon acceptable phraseology. A comparison of patient comprehension in English (the source language) versus Turkish (the target language) indicated that any language differences were overcome due to successful translation techniques. This was established through discussion between Turkish patients and clinical investigators. Translators also discussed methods and approaches in producing optimal translation products, and translation equivalents were established for terms not commonly used in the Turkish language.

Translation Issues Each language has its own challenges and cultural aspects that must be addressed. This becomes even more critical when translating sensitive documents such as those required for clinical trials. Some of the major challenges in the translation of Turkish documents include important differences between Turkish and other languages such as English or Western European languages. Turkish is a Ural- Altaic language composed of about 90,000 words, whereas English, a member of the Germanic family, is composed of about 350,000 words. As a result, Turkish translations are significantly shorter for the most part than their English equivalents. This alone is an indication that certain words in the source language (English) may not have exact equivalents in the target language (Turkish) [(9)].

Back Translation Back translation works best when the languages and cultures involved are closely related, such as Dutch and German. It is an important part of the translation process as it helps to ensure that the meaning in the original text is not lost in the translation. However, in cases where languages differ significantly, such as English and Turkish, further comparison between the translated and original versions is required. In some cases, word equivalents may not exist at all, and translators must come up with the most acceptable functional equivalents in the target language that best represent words or phrases in the source language.

Cultural Context In addition, cultural references that result in basic language differences must also be taken into account. Even simple everyday items or phrases may have specific differences due to culture. For example, one study aimed at culturally adapting HAQs involving rheumatoid arthritis patients at Ankara University reported that several changes needed to be made to the translated questionnaires to account for cultural differences: “shampoo your hair” needed to be modified to “wash your hair,” because both shampoo and soap were used in Turkey for washing hair at that time, “wash and dry your body” needed to be modified to “wash and dry yourself” to adjust for nuances in the Turkish language, and “do chores such as vacuuming or yard work” needed to be changed to “do the housework such as sweeping the floor or gardening” since there is no equivalent for “chores” in Turkish (8).

These clinical studies focused on Turkish translations further emphasize the importance of using experts in translation. They reinforce that linguistic and cultural barriers can largely be overcome by employing experts who have experience working in clinical research in a particular country. In addition to ensuring accuracy and quality, translation experts also cut down on costs because they help sponsors avoid pitfalls associated with poor translations, and use Translation Memory – a standardized glossary of words and phrases in a particular language that decreases both the time and cost of translation.

Language

As with all international clinical trials, patient-related materials must be translated into the patient’s native language, and regulatory documents must be provided in the country’s official language. Turkey has a single translation requirement which can be attributed to the fact that the country’s official language, Turkish, is spoken by the majority of the population. Although this simplifies the process to some extent, there are other factors that must be considered.

Dialects The majority of the population speaks standard Turkish which is based on the Anatolian dialect of Istanbul. However, there are several other regional spoken dialects which can be divided into two major groups, Eastern and Western Turkish. These two groups have been subdivided by linguists into several other groups. Although Turkish dialects do not greatly differ, and the written language is the same, there are subtle differences in pronunciation and the use of certain vocabulary. Therefore, depending on the location of the clinical site and the specific patient population, these regional differences in the spoken language may need to be addressed by translators. Furthermore, elderly patients may speak a form of Turkish that uses many words borrowed from Arabic and Persian, whereas younger populations use reformed Turkish which has replaced these foreign words with Turkish ones.

Minority Languages Turkish is commonly a second language among ethnic minorities. As a result, there may be specific differences in spoken Turkish that need to be considered and Turkish fluency may vary depending on the level of education of the individual. Therefore, translation into minority languages may sometimes be required. In Turkey there are at least thirty-five non-Turkish ethnic groups, including Turkic minorities who speak different Turkic languages, such as the Uygurs, Kirgiz, Kazaks, Uzbeks, Balkar, and Azerbaijanis. Other minority groups include Kurds, Armenians, Greeks, Circassians, Georgians, Laz, Arabs, Rom (Gypsies), Ossetes, Albanians, Chechens, Persians, Bosnians, and Bulgarians.

Among minority groups in Turkey, Kurds are the largest, with an estimated population of over ten million concentrated primarily in the southeast provinces and Istanbul (10). The next two largest minority groups are: Arabs - about one million concentrated along the Syrian border; and the Laz -about 300,000 living mainly in the Eastern Black Sea coastal region (10). Although these ethnic populations tend to reside in certain regions, urbanization trends have led to their migration into the cities. Thus, patients enrolled in clinical trials may include some ethnic minorities.

Cultural Factors

Each patient's perception of health, disease, and functioning as a result of disease depends on the individual and the society in which they live. It is therefore important for sponsors to account for any differences in cultural perceptions that can affect such things as patient reporting of disease symptoms and adverse events, or interfere with the diagnosis, treatment, and enrollment of patients in clinical trials.

Turkey has a unique culture which is influenced by multiple elements. Despite past efforts to westernize the country and its close cultural affinity with Europe, many aspects of Turkish society today have origins from the Ottoman period. Although this blending of East and West has had a positive influence in many ways, there are cultural aspects of Turkish society that must be considered for their effects on clinical research.

Pain Studies Culture must be factored into the interpretation of patient data in order to ensure consistency and accuracy. Ethnic differences in the perception of pain, for example, have been demonstrated in several cancer studies. One study involving Turkish cancer patients reported patient-related barriers in pain management were in part due to cultural factors. More specifically, because of cultural perceptions associated

with pain medication and side effects or addiction, Turkish patients were more likely to underreport pain (11).

Aging & Dementia The cultural belief that one should accept the aging process has been shown to interfere with the diagnosis and treatment of elderly dementia patients in Turkey. In one study results indicated that access to diagnosis and care for people with dementia is “hampered by cultural barriers” (12). This was further reinforced by a study conducted in Istanbul (composed of people age 70 and over without dementia) which revealed that dementia was not generally considered a medical problem by the elderly Turkish population. Rather, it was associated with aging, and therefore individuals did not seek medical care. (13).

Mental Health Another cultural aspect which may interfere with the diagnosis and treatment of patients in Turkey is the belief that support for mental health problems should be provided by family members and friends, not professionals. Results from one study involving immigrants living in the Netherlands showed that immigrants from Turkey were reported to have a higher threshold for seeking professional help for mental health problems. Despite a higher prevalence of serious problems such as depression among the Turkish immigrant population, including a higher risk of attempting suicide among Turkish women, they were significantly less likely to seek professional care largely due to cultural taboos. As a result did not benefit from new therapies (14).

Religion & Gender Cultural factors associated with religious traditions should also be considered for their effect on clinical research in Turkey. Ninety nine percent of the Turkish population is Muslim, composed primarily of Sunni Muslims. During the Islamic religious holiday of Ramadan, many people in Turkey observe a period of fasting. In order to ensure accuracy, such changes in diet must be accounted for in the interpretation of data, and if possible, studies should be planned accordingly. In addition, gender roles in Turkish society may influence the decision of women to participate in clinical trials. For example, senior male members tend to make medical decisions for other family members such as women. Although roles are changing, especially in urban areas, remnants of a male-dominated society remain (10).

Differences in cultural attitudes among Turkish women have been shown to play a role, along with socio-economic factors, even within different regions of Turkey. Although the incidence rate and prevalence of breast cancer have increased three fold in last decades in Turkey in general, there are big differences regarding stage at diagnosis and effective treatments between the eastern and western parts of Turkey – the incidence of breast cancer in eastern Turkey is more than two times that of the western part due to changing attitudes and a more westernized life style in the later. The poorer survival rate of women in the eastern region was found to be primarily due to limited resources, as well as social, cultural, and educational factors (15).

Minority Status In addition, because of negative cultural attitudes towards certain minority groups in Turkey (particularly Kurds and Armenians) these groups may have limited access to health care. As a result, they may remain undiagnosed and not be well represented in Turkish clinical trials. Statistics for these minority groups are not accurate, and human rights violations in the past have been a common problem. More recent efforts to improve the status and situation of these minority groups have helped to some extent (16).

Conclusions & Recommendations

Global clinical trials are exponentially rising as the number of Western pharmaceutical companies outsourcing to newly emerging countries continues to increase. Turkey is fast becoming a desirable clinical trial location due to several factors including its geographic proximity to Europe, as well as successful recruitment of eligible subjects and regulatory reforms. During 2008 alone, the number of clinical trials conducted by innovative pharmaceutical companies in Turkey is reported to have risen by 30 to 40 % (17). As the regulatory environment in Turkey improves, sponsors must make an effort to properly address language barriers and cultural factors that effect clinical research.

Language barriers can best be overcome by employing experts that have experience conducting clinical trials in the country. In this manner, sponsors are able to ensure that translations are at the level of accuracy and quality demanded of clinical trial documents. Especially in the case of languages that are not closely related, such as Turkish and English, translation quality will depend to a higher degree on the experience and expertise of the translator(s). In addition, incorporating cultural context is a crucial element in the translation of clinical trial documents. Professional translators are native speakers, and are aware of linguistic and cultural differences that need to be considered. Furthermore, these experts are best equipped to define functional translation equivalents and provide appropriate cultural references.

Cultural attitudes and perceptions can also affect clinical research if not taken into consideration. In Turkey, cultural attitudes may affect clinical research by interfering with the interpretation of patient data or reporting of adverse events. In addition, a patient's access to medical care and seeking medical treatment may be determined by cultural factors. By acquiring a greater awareness of cultural differences, foreign sponsors can better ensure that cultural barriers to clinical research are overcome.

In summary, if the linguistic and cultural factors, discussed above are properly addressed, foreign sponsors can fully benefit from the many advantages of conducting clinical trials in Turkey.

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