Author's response to reviews

Title: Home Based Telemedicine Intervention for patients with uncontrolled hypertension: << a real life >> non-randomized study.

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Dear Editor,

Reference: Ms. 1392850474122338 – Home Based Telemedicine Intervention for patients with uncontrolled hypertension: “a real life” non-randomized study

Please find enclosed the revised version of the abovementioned manuscript. We took in due account the suggestions of the Reviewers. An itemised reply to the comments of Reviewer # 1 is attached.

We hope that the current version of the manuscript can be now accepted for publication

Looking forward to hearing from you soon, we send our best regards.

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Response to reviewer 1

Title: Home Based Telemedicine Intervention for patients with uncontrolled hypertension: “a real life” non-randomized study

We have included in the title the phrase "in real life" because we believe best describes the nature of our study.

Major Compulsory Revisions

1. Methods appropriate:

a. Population: The authors state that patients were screened between September 2009 and September 2011. Figure 2 shows 2155 patients were screened and 210 were identified who met this study’s inclusion / exclusion criteria and had an in-home analog phone line. Who were these patients and how were they screened in this study? Were they consecutive outpatients receiving cardiovascular check-ups in a specific GP practice at Fondazione Maugeri, Lumezzane medical center?

In Italy every patient with symptoms or problems initially has to go from their general practitioner who may decide to send for a consultation with a specialist at an outpatient, often located within a hospital.

We substitute the previous text:

“All the patients screened were referred to outpatient hospital for a cardiological check-up by GPs. The patients were from a rural region and were screened between September 2009 and September 2011.”

With:

“All the patients screened between September 2009 and September 2011 arrived consecutively from a rural region to our outpatient (at Fondazione Maugeri, Lumezzane Medical Center) sent by GPs for a cardiological consultation”.

b. Allocation: Figure 2 shows 173 eligible individuals, with 76 assigned to treatment and 97 assigned to control. However, the method for allocating patients to treatment and control groups is not described. This information is needed so that the reader can assess whether the treatment selection method may have served to bias this study’s findings. As an example, if the control patients are those who refused the intervention, this would be problematic as patients refusing new treatments could be assumed to be less interested in their treatments and potentially less adherent.

Sorry, but preparing different versions of the paper we made a mistake in the “cut and paste”. The correct version is:

All the patients involved in the study was from a rural-mountain region, where cellular phone connection problems are quite frequent. First we check the T-Mobile coverage maps of the patient’s zone; than we ask the patient to confirm the situation. For this reason we were obliged to enrol in the Home-Based Telemedicine (HBT) group only patients who could prove to have a good cellular phone connection in their living area, while all the other patients were included in the Usual care (UC) group.
We reported this sentence in the text.

c. Study duration: The method for determining study duration needs further justification. The average study duration in the present study was 80 days for intervention and 82 days for control patients. However, the text states that duration of home follow-up for intervention patients varied from 40 to 120 days and was related to the time required for reaching and sustaining target BP values. This method for determining the follow-up period appears to be designed to achieve the best BP measurements for intervention patients and ignores the possibility of a rebound effect when treatment is discontinued.

What happened when intervention patients did not reach target BP values?

It was impossible, because in the intervention group we stopped the monitoring after being sure that the BP was controlled and after doing ABPM to confirm the result; 120 are the maximum number of days that a patient needed to be controlled.

Was their study duration automatically terminated at 120 days?

No, I have explained above;

If the length of follow-up was based upon the achievement of treatment goals, how was the follow-up period determined for control patients whose BP was not monitored during follow-up?

During the consultation we suggested the patients’ GP to send the patients to execute an ABPM when they thought that BP was controlled; we calculated the follow up in the UC group with the day of the ABPM.

We specified in the text with the following sentence (in red):

“At T1, patients performed an ABPM using a validated Mobil O Graph (I.E.M. GMBH, Stolberg, DE) to confirm the controlled BP values reached. The duration of home follow-up was spread over a minimum of 40 days to a maximum of 120 days. The variability was related to the time required to reach the target value of BP. The BP monitoring was ended after at least 10 days of stable BP target values.”

d. BP change: Please verify that BP measurements used in this study’s primary endpoint were measured at T0 and T1 using the same oscillometric device.

Yes, it is. We have better specified in the text with the following sentence:

During these visits, BP measurements were done always using the same oscillometric device following guidelines [21]. The device measured the BP three times at with intervals and that makes a mean.

What is the purpose of ABPM? ABPM results are not presented in this paper.

The role of ABPM in this “real life” pilot was only to check the right values of BP in 24 hours to confirm our outcome. Unfortunately, we don’t have ABPM before and after for all the patients; for this reason we decided to not present the data. Then we inserted the data only for ABPM measured at T1 and reported in the results. In the method section
2. Data sound

a. Primary endpoint: The authors need to report a combined study result. If the primary endpoint is SBP change, the authors should report the average difference in SBP for patients in the intervention and control groups.

Sorry, what is the meaning of “combined study results” and of “the authors should report the average difference in SPB” because we report this difference and propose the figure 2;

Since this is a non-randomized study, statistical adjustment will be required to account for differences between treatment and control group subjects. While propensity matching is the preferred approach, this study likely does not have sufficient subjects to use this technique. At a minimum, a regression model is needed to perform the required adjustments.

We didn’t do this! We really screened the patients in the outpatient and put them in the different group following the inclusion criteria. We needed to accept the impossibility of a number of patients, living in a rural area, to live without any GPRS connection (real-life study).

We thought that already ANOVA evaluate and take in account the variability of the two groups.

3. Standards adherence

a. Figure 2 should be redrafted to comply with CONSORT statement guidance.

We redrafted the Figure 2.

Discretionary Revisions

1. Research question:

a. The study aim, evaluate effectiveness, is incomplete. The authors should state how they propose to evaluate effectiveness (primary endpoint). They also should introduce their research question with a sentence stating the knowledge gap their study addresses.

We completed the aim in the following way:

The aim of the current non randomized “real life” study was to evaluate the effectiveness of a structured physician-nurse approach supported by remote BP telemonitoring, in patients with uncontrolled hypertension. The effectiveness will evaluated with the reduction in BP values confirmed by ABPM. The data were compared with those collected in patients being followed in usual care conditions during the same period.

The rationale for the present study is not clear from the background material.

As reported in the introduction:

“Many epidemiological studies have shown that the treatment and control of blood pressure (BP) is inadequate in more than 50% of hypertensive patients in spite of availability of several classes of well
tolerated and effective antihypertensive drugs [1,2]. Several factors including the use of suboptimal doses of drugs, inadequate or ineffective treatments and poor drug compliance may be the reason for this phenomenon [3,4]."

The principal problem of a correct follow-up for patients with uncontrolled hypertension is related to therapy. For this reason our service has as a gold standard “Reaching and maintaining the target value of blood pressure, the adherence to therapy, the reporting of the drug side effects and the change of lifestyle condition to reduce cardiovascular risk factors are the gold standard of our Home Based Telemedicine (HBT). Service.”

So we thought that both rationale and gold standard are present in the introduction.

2. Methods appropriate:

a. Primary outcome: This study enrolled patients with uncontrolled hypertension. The authors should consider changing their primary outcome to the percent of patients with uncontrolled hypertension. This is the outcome of most interest to health policy makers. Changes in SBP and DBP could be secondary outcomes.

We report the percentage of the patients, with uncontrolled hypertension at the beginning and at the end of the study, both in intervention and in control group; (see the text in results);

In our opinion, changing the primary outcome with the percent of patients with uncontrolled hypertension could be interesting (and for this reason we report the data) but is not correct in this case because we did not define a clear time (1 months, 2 months etc..) to use telemonitoring and the same for the control group; being a real life study we preferred trying to control BP in all the patients in the intervention group to understand what is the mean time that we need to control a patients in the real life (we cannot abandoned a patient because the study is finished if the BP is not controlled).

For that reason at the end of telemonitoring we performed the ABPM to check if the BP was really controlled (remembering that in the guideline, the normal value for ABPM are very low in comparison with that recorded at home or in office)

b. BP measurements: What prompted variation in the frequency of intervention group BP measurements?

The patients were motivated by the nurse to measure the pressure every day, several times per day. In case of pressure values high or too low and in correspondence to therapy changes the nurse counseled to the patients to intensify the measurements. The patients were phoned after three days if the measurements didn’t arrive.

Did subjects receive instructions as to their desired frequency?

Yes they did, from their nurse tutor during the first educational personal meeting and during all contacts.;

3. Data sound:
a. Adherence: Since medication regimen compliance is a primary factor contributing to uncontrolled hypertension, it would be good to report some measure of anti-hypertension medication adherence in this study's results.

In the HBT group the adherence of therapy was monitored at every contact by nurse. The nurse checked the therapy each time making report the drug name and dosage, thereby verifying in real time the assigned therapy on “personal health record”, the times of administration and if there were adverse effects; finally the nurse verified any discrepancies compared to the previous control. On the contrary in the usual care group, the measurement were done only at the end of the study compared the data collected at the beginning. Then we didn’t performed any measurement of adherence.

This would get at the issue of why BP management improved in the treatment group.

Yes. One of the nurse duty was to check the BP data all days on the personal health record for all patients and in case of uncontrolled values to speak in a very short time (within few hours and, in any case, in the same day) with specialist for deciding an eventually therapy change.

b. Medical costs: The cost comparison should be assessed by treatment strategy. The authors only present costs for their intervention. No attempt is made to determine whether other medical costs (e.g., medication costs) differed between the two groups.

We don’t have data about this because the study was not planned to do this; we decided only to collect data on cost of the intervention group to understand if the intervention has a feasible cost applied in a real life intervention to a great number of patients.

Discussion and conclusions supported:

a. The discussion states that this study seems, “to confirm the importance of a much higher level of compliance.” Compliance results should be reported.

See you the reply above

In the discussion we reported “This leads to re-evaluation of drug compliance or drug therapy. Moreover, when the patients realize that their adherence is constantly and carefully checked, they acquire a feeling of greater control and consequently higher compliance which contributes to positive effects that can be observed in the first few weeks”

b. The conclusion is weak. The authors could be more explicit and say their intervention will decrease the percent of uncontrolled hypertension patients or give the absolute BP improvement (treatment – control).

Done

5. Limitations: Limitations should include a statement that this is a single site study and its results may not be transferred easily to other settings.
Sorry, but we are not completely agree that “its results may not be transferred easily to other settings”.

The model is quite complex but the telemonitoring used is more or less the same used in all the other publication. When someone need to choose a service we think as Roccaforte and al. (2005) that the final choice will rest on a careful evaluation of the characteristics of the local health services, patient population, barriers to the access to optimal medical care, human and financial resources.

6. Acknowledge previous work: Previous work is acknowledged.

7. Title and abstract accurate: Title and abstract are accurate.

8. Writing acceptable: Writing is clear.