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Practical Operation of Telemedicine for Diagnostic, Therapy and Long Term Observation of Arterial Hypertension

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1. Introduction

Telemedicine increases quality of life dramatically. Patient's autonomy and responsibility are strengthened, that means a significant benefit. Patients realise a better safety with diagnostic and therapy as well as a decrease in therapeutic risks. This leads to a great acceptance of telemetric methods. Improvement of quality of life by telemedicine is demonstrable in heart failure, diabetes mellitus, rhythm disorders, psychiatric diseases and blood pressure. (Schmidt, 2009)
Telemetric medicine can be helpful in wide areas with low density of population like Africa and Asia, but also in rural regions in Europe (like Sweden, Scotland etc.) or North America or Canada with its large rural districts.
Worldwide, hypertension is common (Wolf-Meier et al., 2003) and regarded as a major public health problem. The prevalence of hypertension was found to be 28% in North America and 44 % in western Europe (Wolf-Meier et al., 2003).Though arterial hypertension was thought to be low in Africa in the 70ties and 80ties of the last century newer studies showed a prevalence between 15 % (Nigeria) and 28 % (Ghana) (Cappucio et al., 2004). Altogether patients in underserved rural areas have a higher prevalence of uncontrolled hypertension (Mainous et al., 2004).
Home monitoring can be a valuable tool in all populations. Patients who self-monitor can reach target BP goals with less medication (Verberk et al, 2007). Compared to office monitored patients they used an average of 1 drug or 1 dose less (p<.0001) at a reduced cost of $1124 per 100 patients for 1 month (p<.001) (Verberk et al., 2007).
The effectiveness of home monitoring is enhanced with Internet-based communications by health care providers (Green et al., 2008). A significant higher proportion of patients who received home blood pressure monitoring and Internet-based pharmacist care had controlled blood pressure (56%; 95%CI, 0,49-0,62) compared with those receiving standard care (31%; 95%CI, 0,25-0,37) or home-based care alone (36%; 95%CI 0,30-0,42) (p<.001) (Green et al., 2008)
Experience of safety and autonomy as well as responsibility for the own health is promoted by telemedicine. Numerous studies indicate an improvement of psychosocial factors. A deterioration of patient's psychosocial adaptation to the underlying disease by the used technology was picked up seldom.

Telemonitoring of blood pressure can be integrated into nearly every health care organisation. It can be realized in a regional as well as in a superregional model. Data are available at any place with Internet option. It's application is independent of national health care systems and allows their observation of patients far away from the treating centre. Beyond this every physician involved in the treatment is able to look to the data every time (via patient's password). This is of eminent importance to provide patients in large areas with a small number of physicians. Until now for Germany there are 110 national or superregional concepts integrating telemedicine into daily practise of treatment.

2. WHO Recommendations (Prevention of Cardiovascular Disease: guideline for assessment and management of total cardiovascular risk. WHO 2007)

Raised blood pressure is estimated to cause about 7 million premature deaths throughout the world, and 4.5% of the disease burden (64 million disability-adjusted life years (DALYs)) (World Health Organization, 2005; World Health Organization, 2002.; Lopez et al., 2006). It is a major risk factor for cerebrovascular disease, coronary heart disease, and cardiac and renal failure. Treating raised blood pressure has been associated with a 35–40% reduction in the risk of stroke and at least a 16% reduction in the risk of myocardial infarction (Collins et al., 1990). Raised blood pressure often coexists with other cardiovascular risk factors, such as tobacco use, overweight or obesity, dyslipidaemia and dysglycaemia, which increase the cardiovascular risk attributable to any level of blood pressure. Worldwide, these coexisting risk factors are often inadequately addressed in patients with raised blood pressure, with the result that, even if their blood pressure is lowered, these people still have high cardiovascular morbidity and mortality rates (Godley et al., 2001; Klungel etal., 1998; Trilling and Froom 2000).

Almost all clinical trials have confirmed the benefits of antihypertensive treatment at blood pressure levels of 160 mmHg (systolic) and 100 mmHg (diastolic) and above, regardless of the presence of other cardiovascular risk factors (Collins et al., 1990; Blood Pressure Lowering Treatment Trialists' Collaboration. 2000). Observational data support lowering of these systolic and diastolic thresholds (Van den Hoogen et al., 2000; Vasan et al., 2001).

Several trials in patients at high cardiovascular risk (Heart Outcomes Prevention Evaluation (HOPE) Study Investigators. 2000; PROGRESS Collaborative Group. 2001; PATS Collaborating Group. 1995) have confirmed these observational data, showing reductions in cardiovascular morbidity and mortality in people whose blood pressure is reduced to levels significantly below 160 mmHg systolic and 90 mmHg diastolic. These trials support the view that, in patients at high cardiovascular risk, with blood pressures in the range 140–160 mmHg (systolic) and 90–100 mmHg (diastolic), lowering blood pressure reduces the number of cardiovascular events. These trial results suggest that treatment for such high-risk patients should begin at the lower blood pressure thresholds.

Although women are at lower total risk of cardiovascular disease for a given level of blood pressure, and randomized controlled trials generally include a greater proportion of men than women, the treatment thresholds for systolic and diastolic pressure should be the same in men and women (Gueyffier et al., 1997).

Total risk of cardiovascular disease for any given level of blood pressure rises with age. However, evidence from RCTs is currently limited and inconclusive about the benefits of treating those over 80 years of age. For now, the treatment threshold should be unaffected by age, at least up to 80 years. Thereafter, decisions should be made on an individual basis;

in any case, therapy should not be withdrawn from patients over 80 years of age (Bulpitt et al., 2003; Bulpitt et al., 1999).

3. Targets for blood pressure

In low- and medium-risk patients with elevated blood pressure, the Hypertension Optimal Treatment (HOT) trial found maximal cardiovascular benefit when blood pressure was reduced to 139/83 mmHg (Hansson et al., 1998). Clinic and population-based survey data continue to suggest that the lower the blood pressure achieved, the lower the rate of cardiovascular events (Gamble et al.,1998; Andersson et al., 1998; Liu et al., 2005). In people over 55 years of age, the systolic blood pressure is more important (Kannel 2000), so the primary goal of therapy is to lower systolic blood pressure to 140 mmHg or less. There is no apparent reason to modify this target for women or older patients.

Several trials (Hansson et al., 1998; Brenner et al., 2001; Parving et al., 2001; UKPDS Group. 1998; Zanchetti and Ruilope 2002) have shown that, in patients with diabetes, reduction of diastolic blood pressure to about 80 mmHg and of systolic blood pressure to about 130 mmHg is accompanied by a further reduction in cardiovascular events or diabetes-related microvascular complications, in comparison with patients with less stringent blood pressure control (Hansson et al., 1998; Brenner et al., 2001; Parving et al., 2001; UKPDS Group. 1998; Zanchetti and Ruilope 2002). In patients with high or very high cardiovascular risk, including diabetes or established vascular or renal disease, therefore, blood pressure should be reduced to 130/80 mmHg or less.

4. Methods for blood pressure measurement

Technical progress in blood pressure measurement is impressive in the last 20 years. The greatest advantage was the introduction of ambulatory blood pressure measurement and the telemetric transmission of home measured blood pressure into diagnostic and therapeutic follow up.

The different methods of blood pressure measurement are not competing but compiling. Each of the different techniques in blood pressure measuring contains certain advantages and power as well as disadvantages and weakness.

4.1 Blood pressure measurement (Mancia et al., 2007):

Blood pressure is characterized by large spontaneous variations both during the day and between days, months and seasons. Therefore the diagnosis of hypertension should be based on multiple blood pressure measurements, taken on separate occasions over a period of time. If blood pressure is only slightly elevated, repeated measurements should be obtained over a period of several months to define the patients ‘‘usual’’ blood pressure as accurately as possible. On the other hand, if the patient has a more marked blood pressure elevation, evidence of hypertension-related organ damage or a high or very high cardiovascular risk profile, repeated measurements should be obtained over shorter periods of time (weeks or days). In general, the diagnosis of hypertension should be based on at least 2 blood pressure measurements per visit and at least 2 to 3 visits, although in particularly severe cases the diagnosis can be based on measurements taken at a single visit. Blood pressures can be measured by the doctor or the nurse in the office or in the clinic (office or clinic blood pressure), by the patient or a relative at home, or automatically over 24 h.

4.2 Office blood pressure measurement

Office blood pressure measurement is considered to be the gold standard of blood pressure measurement. Blood pressure can be measured by a mercury sphygmomanometer the various parts of which (rubber tubes, valves, quantity of mercury, etc.) should be kept in proper working order. Other non-invasive devices (auscultatory or oscillometric semiautomatic devices) can also be used and will indeed become increasingly important because of the progressive banning of the medical use of mercury. However, these devices should be validated according to standardized protocols (O'Brien et al., 2001; http://www.dableducational.org), and their accuracy should be checked periodically by comparison with mercury sphygmomanometric values.

4.3 Blood pressure (BP) measurement

When measuring BP, care should be taken to:

1. Allow the patients to sit for several minutes in a quiet room before beginning BP measurements
2. Take at least two measurements spaced by 1–2 minutes, and additional measurements if the first two are quite different
3. Use a standard bladder (12–13 cm long and 35 cm wide) but have a larger and a smaller bladder available for fat and thin arms, respectively. Use the smaller bladder in children
4. Have the cuff at the heart level, whatever the position of the patient
5. Use phase I and V (disappearance) Korotkoff sounds to identify systolic and diastolic BP, respectively
6. Measure BP in both arms at first visit to detect possible differences due to peripheral vascular disease. In this instance, take the higher value as the reference one
7. Measure BP 1 and 5min after assumption of the standing position in elderly subjects, diabetic patients, and in other conditions in which postural hypotension may be frequent or suspected
8. Measure heart rate by pulse palpation (at least 30 sec) after the second measurement in the sitting position

4.4 Ambulatory blood pressure

Several devices (mostly oscillometric) are available for automatic blood pressure measurements in patients allowed to conduct a near normal life. They provide information on 24-hour average blood pressure as well as on mean values over more restricted periods such as the day, night or morning. This information should not be regarded as a substitute for information derived from conventional blood pressure measurements. However, it may be considered of important additional clinical value because cross-sectional and longitudinal studies have shown that office blood pressure has a limited relationship with 24-h blood pressure and thus with that occurring in daily life (Mancia et al., 2001; Mancia et al., 1995; Mancia et al., 2007). These studies have also shown that ambulatory blood pressure

1. correlates with hypertension-related organ damage and its changes by treatment more closely than does office blood pressure (Fagard et al., 1997; Mancia et al., 1997; Fagard et al., 1997; Verdecchia et al., 1990; Mancia et al., 2001; Redon et al., 1996),
2. has a relationship with cardiovascular events that is steeper than that observed for clinic blood pressure, with a prediction of cardiovascular risk greater than, and additional to the prediction provided by office blood pressure values in populations as

well as in untreated and treated hypertensives (Clement Det al., 2003; Sega et al., 2005; Fagard and Celis 2004; Dolan et al., 2005; Fagard et al., 2005; Hansen et al., 2005; Kikuya et al., 2005; Pickering et al., 2006), and

3. measures more accurately than clinic blood pressure the extent of blood pressure reduction induced by treatment, because of a higher reproducibility over time (Coats et al., 1992; Mancia et al., 1994) and an absent or negligible ''white coat'' (Parati et al.,1985) and placebo effect (Mancia et al., 1995; Staessen et al., 1994).

Although some of the above advantages can be obtained by increasing the number of office blood pressure measurements (Fagard RH et al., 1997; Mancia G et al., 1994), 24-hour ambulatory blood pressure monitoring may be useful at the time of diagnosis and at varying intervals during treatment. Effort should be made to extend ambulatory blood pressure monitoring to 24 hours in order to obtain information on both daytime and night time blood pressure profiles, day-night blood pressure difference, morning blood pressure rise and blood pressure variability. Daytime and night-time blood pressure values and changes by treatment are related to each other (Mancia G et al.,1995; Mancia G et al., 2007), but the prognostic value of night time blood pressure has been found to be superior to that of daytime blood pressure (Staessen JA et al., 1999; Sega R et al., 2005; Fagard RH et al., 2004; Dolan E et al., 2005; Fagard RH et al., 2005; Kikuya M et al., 2005). In addition, subjects in whom nocturnal decrease in blood pressure is blunted (non-dippers)(O'Brien E et al., 1988) have been reported to have a greater prevalence of organ damage and a less favourable outcome, although in some studies the prognostic value of this phenomenon was lost when multivariate analysis included 24-h average blood pressure (Staessen JA et al. 1999; Fagard RH et al., 2004; Fagard RH et al., 2005; Hansen et al., 2005; Ohkubo T et al.,2002; Verdecchia P et al.,1994; Metoki H et al., 2006; Hansen TW et al., 2006). Evidence is also available that cardiac and cerebrovascular events have a peak prevalence in the morning (Willich SN et al., 1992; Rocco MB et al.,1987; Muller JE et al., 1985; Elliott WJ. 1998), possibly in relation to the sharp blood pressure rise occurring at awaking from sleep (Millar-Craig MW et al., 1978; Kario K et al., 2003; Mancia G et al.,1980), as well as to an increased platelet aggregability, a reduced fibrinolytic activity and a sympathetic activation. Worsening of organ damage and the incidence of events have also been related to blood pressure variability as quantified by the standard deviation around mean values (Frattola A et al., 1993; Sander D et al., 2000; Verdecchia P et al., 1996). Although in these studies the role of confounding factors was not always excluded, an independent role of blood pressure variability has recently been confirmed by a long-term observational study (Mancia G et al.,2007).

4.5 Ambulatory blood pressure measurement

When measuring 24-hour blood pressure care should be taken to:

1. Use only devices validated by international standardized protocols.
2. Use cuffs of appropriate size and compare the initial values with those from a sphygmomanometer to check that the differences are not greater than ± 5mmHg
3. Set the automatic readings at no more than 30 min intervals to obtain an adequate number of values and have most hours represented if some readings are rejected because of artefact.
4. Automatic deflation of the equipment should be at a rate of no more than 2 mmHg/s.
5. Instruct the patients to engage in normal activities but to refrain from strenuous exercise, and to keep the arm extended and still at the time of cuff inflations.

6. Ask the patient to provide information in a diary on unusual events and on duration and quality of night sleep.
7. Obtain another ambulatory blood pressure if the first examination has less than 70% of the expected number of valid values because of frequent artefacts. Ensure that the proportion of valid values is similar for the day and night periods.
8. Remember that ambulatory blood pressure is usually several mmHg lower than office blood pressure. As shown in Table 5, different population studies indicate that office values of 140/90mmHg correspond to average 24-h values of either 125–130mmHg systolic and 80mmHg diastolic, the corresponding average daytime and night-time values being 130–135/85 and 120/70mmHg. These values may be regarded as approximate threshold values for diagnosing hypertension by ambulatory blood pressure.
9. Clinical judgement should be mainly based on average 24-hour, day and/or night values. Other information derived from ambulatory blood pressure (e.g. morning blood pressure surge and blood pressure standard deviations) is clinically promising, but the field should still be regarded as in the research phase.

4.4 Home blood pressure measurement

Self-measurement of blood pressure at home cannot provide the extensive information on daily life blood pressure values provided by ambulatory blood pressure monitoring. However, it can provide values on different days in a setting close to daily life. When averaged over a period of a few days these values share some of the advantages of ambulatory blood pressure, that is they are free of a significant white coat effect, are more reproducible and predict the presence and progression of organ damage as well as the risk of cardiovascular better than office values (Mancia G et al., 1997; Sega R et al.,2005; Fagard RH et al., 2004; Fagard RH et al., 2005; Sakuma M et al., 1997; Ohkubo T et al., 1998). Therefore, home blood pressure measurements for suitable periods can be recommended before and during treatment also because this relatively cheap procedure may improve patient adherence to treatment (Zarnke KB et al., 1997).

When advising self-measurement of blood pressure at home:

1. Suggest the use of validated devices. Few of the presently available wrist devices for measurement of blood pressure have been validated satisfactorily; should any of these wrist devices be used, the subject should be recommended to keep the arm at heart level during the measurement.
2. Prefer semiautomatic devices rather than a mercury sphygmomanometer to avoid the difficulty posed by having to educate the patient on its use and the error derived from hearing problems in elderly individuals
3. Instruct the patient to make measurements in the sitting position after several minutes rest, preferably in the morning and in the evening. Inform him or her that values may differ between measurements because of spontaneous blood pressure variability.
4. Avoid requesting that an excessive number of values are measured and ensure that those measurements include the period prior to drug intake so as to have information on the duration of treatment effects.
5. Remember that, as for ambulatory blood pressure, normal values are lower for home than for office blood pressure. Take 130–135/85mmHg as the values that approximately correspond to 140/90mmHg measured in the office or clinic (Table 1).
6. Give the patient clear instructions on the need to provide the doctor with proper documentation of the measured values and to avoid self-alterations of the treatment regimens.

4.5 Ambulatory and home BP measurements

Ambulatory BP

1. Although office BP should be used as reference, ambulatory BP may improve prediction of cardiovascular risk in untreated and treated patients
2. Normal values are different for office and ambulatory BP **(Table 1)**
3. 24-h ambulatory BP monitoring should be considered, in particular, when considerable variability of office BP is found over the same or different visits high office BP is measured in subjects otherwise at low total cardiovascular events risk there is a marked discrepancy between BP values measured in the office and at home resistance to drug treatment is suspected hypotensive episodes are suspected, particularly in elderly and diabetic patients office BP is elevated in pregnant women and pre-eclampsia is suspected

Home BP

1. Self-measurement of BP at home is of clinical value and its prognostic significance is now demonstrated. These measurements should be encouraged in order to:
   - provide more information on the BP lowering effect of treatment at trough, and thus on therapeutic coverage throughout the dose-to-dose time interval
   - improve patient's adherence to treatment regimens there are doubts on technical reliability/environmental conditions of ambulatory BP data
2. Self-measurement of BP at home should be discouraged whenever:
   - it causes anxiety to the patient
   - it induces self-modification of the treatment regimen
3. Normal values are different for office and home BP

	SBP	DBP
Office or clinic	140	90
24-hour	125-130	80
Day	130-135	85
Night	120	70
Home	130-135	85
Telemetric	135	85
Diabetes, renal failure, high cardiovascular risk (ESC/ESH 2010), office and clinic	130-139	80-85

Table 1. Blood pressure thresholds (mmHg) for definition of hypertension with different types of measurement. SBP indicates systolic blood pressure, DBP indicates diastolic blood pressure

5. Telemetric blood pressure measurement:

Self home blood pressure measurement has a number of potential advantages. These include avoidance of the "white-coat effect", possibility of multiple blood pressure readings over a long time, blood pressure reading at different times of the day and improvement of patient´s adherence to therapy (Yarows SA et al., 2000; Ogedegbe G and Schoenthaler A. 2006). There are however several difficulties in clinical practice. These include the use of nonvalidated devices, need of patient´s training, the risk of patients becoming neurotically obsessed by the procedure, not infrequently with self-modifications of the prescribed antihypertensive treatment (Imai Y et al., 2004), and the possibility of inaccurate report of home blood pressure values by the patients (Mengden T et al., 1998) as well as the difficulty for the physician to reach appropriate diagnostic conclusions from evaluation of often badly written patient´s blood pressure reports. It has been reported that in 54% of the cases, general practitioners fail to draw any meaningful conclusion out of patients´ blood pressure log books (Krecke HJ et al., 1996). Progress in technology over the last few years has led to the availability of a number of systems for digital storage of HBPM data and their transmission to remote sites (Mengden T et al., 2001).

5.1 Clinical background for the telemetric blood pressure measurement; methodical problems of blood pressure measurement:

In daily practice diagnostic and control of therapy of arterial hypertension are defined by blood pressure measurements at certain points in not exactly defined intervals. Between two office visits important uncertainties and lack of clarity exist in relation to adherence and compliance to therapy. We know, that the direct interaction between physician and patient increase adherence with therapy shortly before and after consultation. Motivation for taking the antihypertensive medication weakens considerably between the visits (Fig. 1). Lack of adherence to therapy ("compliance") is considered as the main factor for not reaching the target blood pressures. Medium therapeutic adherence in antihypertensive treated patients is about 50%. Adherence to therapy and quality of antihypertensive therapy can be increased by measures as increase of office visits, controls at home by ambulatory nurses, behaviour therapy, and specialized antihypertensive training programs. These measures are considerably limited by the available resources of Public Health. Telemedicine offers a promising approach by controlling chronically ills at their homes. The possibilities currently used to optimize the adherence of chronically ill patients are complex and unfortunately not very effective. The difficulties depend on the living and working conditions of our patients, their previous lifestyle (Bobrie G et al., 2007), fears and objections concerning the antihypertensive medication, and their other psychologically conditions like depressions or

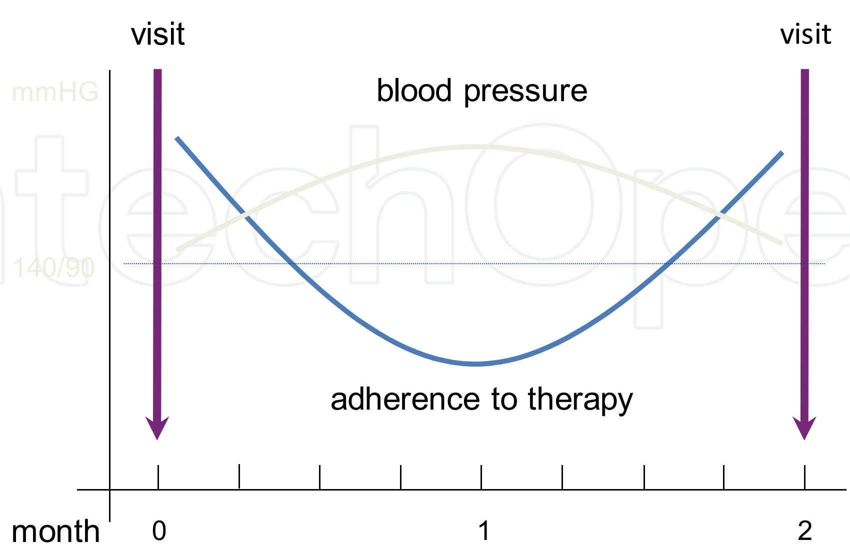

Fig. 1. Blood pressure control in 2 monthly intervals. Decrease of patient's compliance between two visits probably with increase of blood pressure between these visits. The supposed increase of blood pressure can not be recorded by office measurement.

negative emotions (Ashida T et al., 2008; Espinosa R et al., 2008). In addition to this there is the influence of the treating physician (Girerd X et al., 2008), possibly even her or his gender (Ericsson UB et al., 2008); even a specialized care can´t improve the compliance at least in men and older patients (Daghini E et al., 2008).

The assessments of quality of antihypertensive therapy differ between physician and patient (Sichkaruk I et al., 2008): the physician judges his patient better than patients do themselves – on the other hand side overestimates the physician his patient´s adherence (Zeller A et al., 2008).

In addition the physician is confronted with a conflicting problem in his daily practice. On the one site he wants and must have a good attitude to her or his patient, on the other hand site he must try to influence her or his patient´s lifestyle and/or supply them with antihypertensive medication. In this situation it is difficult to get a high amount of correspondence and/or mutuality. To be forced to control (controlling on the physicians side, to be observed on the patient´s side) conflicts with the effort to have a long-lasting good connection with the patients (physician respectively).

These difficulties and the need of medical care in wide areas with low density of population like Africa or Asia, but also in rural regions in Europe (like Sweden, Scotland etc.) North America or Canada with its large rural districts justify the development of new technical devices. Telemetric blood pressure measurements allow new dimensions for the cooperation between patients, physicians and public care. The assumption for a continuously therapeutic effort in cooperation between physician and patient is a therapeutic agreement with a clear definition of the target blood pressure. Randomized small studies show significant better blood pressure adjustment with telemetric monitoring compared to usual care (overview: Mengden T et al., 2001). The comparison shows a more intensive adaptation of antihypertensive medication in telemetric controlled patients. Beyond this the compliance of telemetric controlled patients increased significantly **(Tab. 2).**

6. Problems in home blood pressure measurement

Home blood pressure measurements are an effective and very helpful tool to support adherence to antihypertensive therapy (Mengden T et al., 2001). It can compensate partly the failing supervision by the treating general practitioner in diagnostic and therapy of arterial hypertension. It is helpful with "white coat hypertension", has a better correlation to the damage of target organs, improves the adherence to medical treatment, and allows a better control of long term treatment (Friedman RH et al., 1996 [Fig. 8]; Mengden T et al., 1998).

The acceptance of home blood pressure measurement by physicians is controversy. Less than 50% use it for diagnostic or therapeutic conclusions in their daily practice (Krecke HJ et al., 1996). The physicians justify this with:

- Uncertainty with the accuracy of the blood pressure measurement devices used
- Patient's insufficient training in the technique of home blood pressure measurement.
- Mistakes with documentation of home measured blood pressure.

Therefore automatically storing devices are recommended (Rogers MAM et al., 2001).

7. Telemetric blood pressure measurement in general praxis:

Telemetric blood pressure measurement is based on home blood pressure measurement. The blood pressure readings measured by the patient are send via handy (or an modem

literature	patients	design, duration	datarecord	data transfer	feedback to patients	Patient needs PC	results
Friedman 1996	267 uncontrolled hypertensive patients	UC vs. TM 6 months	patients protocoll	manuelly, weekly, public telefone network	yes, weekly	no	better blood pressure control with TM, especially if the compliance was bad
Rogers 2001	121 patients with arterial hypertension	UC vs. TM 8 weeks	device with storage, automatically	automatically, weekly, public telefone network	yes, weekly report of findings	no	significantly reduction of blood pressure (TM vs. UC)
Artinian 2007	387 uncontrolled hypertensive patients	UC vs. TM [b] 12 months	device with storage, automatically	manuelly, , public telefone network	yes, social health nurse- in TM	no	more decrease of systolic blood pressure (TM vs. UC)
Parati 2007	298 patients with grade I-II arterial hypertension	UC (I) vs. TM (II) vs. TM including feedback [a] (III)	device with storage, automatically	automatically, , public telefone network	yes, group III with memory-function	no	better blood pressure control in group II and III
Madsen 2008	236 patients with arterial hypertension	UC vs. TM 6 Monate	device with storage, automatically	automatically, PDA, Web-based	no	PDA	no difference between UC and TM
Green 2008	730 patients with arterial hyper-tension grade I - II	UC (I) vs. TM (II) vs. TM incuding feedback [b] (III)	device with storage, automatically	automatically, Web-based	yes, in II and III (WEB based)	yes	better blood pressure control in group III

abbrevations: UC - Usual Care TM – Telemonitoring
[a] automatically feedback including memory-function
[b] individualized telephone consultation by health care professional

Table 2. Randomised controlled studies comparing telemonitoring with standard care. Rogers (2001) and Parati (2007) showed moderate to missing effects in their studies. It can be summarised that telemonitoring is superior to usual care only with additional individualised interventions.

internet connection as well) to a data memory connected with a professional data base ("electronic post office"). The data are stored there and can be use by the treating physician and the patient. They are protected by a password and available wherever an internet connection is possible – even on smart phones (e.g. if the patient visits another physician). An alert system is part of the technique: information about exceeding of preliminary target values can be send automatically to the treating physician and/or if wished so) to the patient via e-mail, fax or SMS. The number of divergent blood pressures leading to alert can be selected freely. Alert is programmable concerning missing measurements in a given time interval as well. These technical features lead to a "virtually clinic for arterial hypertension" (Fig. 2), where visits of the patients are possible at any time and attention is attracted for those patients, needing a therapeutic intervention or those with poor compliance or adherence.

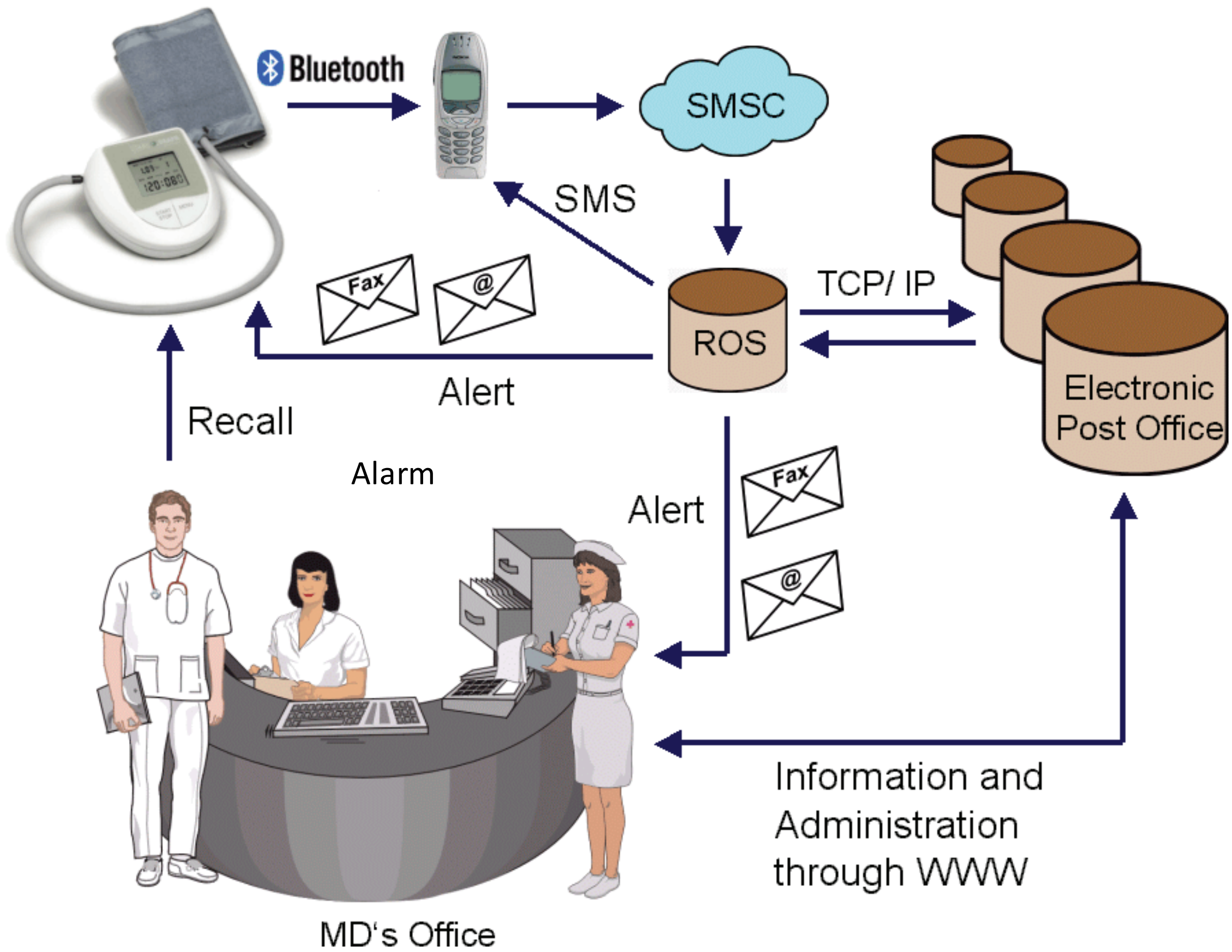

Fig. 2. Virtually clinic for hypertension. Home measured blood pressure is sent via "blue tooth" technique to a modem or handy. This generates a SMS-message to a national centre (ROS), which prompts them into a database. The patient and his physician are able to look to the data after logging in with their passwords. An additional alert-function informs the physician (and patient if she or he wishes so) if adjusted values are exceeded.

There are certain demands for a "virtually clinic for arterial hypertension":

1. A highly, clinically validated accuracy of measurement for the used blood pressure monitor devices according to the e.g. ESH protocol (Stegiou GS et al., 2010; O´Brien E et al., 2010) or one of the national protocols (see http://www.hochdruckliga.de, http://www.dableducational.org or http://www.bhs.soc.org).
2. Oscillometric measurement devices using the upper arm according to the ESC-guidelines (Mancia G et al. 2007).
3. Automatic data storing with a capacity of at minimum of 250-300 readings.
4. Acoustic and/or visual help remembering for blood pressure measurement and intake of medication.
5. Automatic periodically telemetric data transfer (fixed or mobile line network) to a service centre.

6. Standardised reports including statistical evaluations (mean, minimum and maximum), as well as trend plots for weeks and months.
7. Transfer of blood pressure reports to the patient and her/his general physician via letter, fax or web based e-mail.
8. Control function by general physician and/or a medical service centre.
9. Possibilities of intervention if adherence with the therapy is bad or blood pressure adjustment is insufficient.
10. Data protection and confidence.

Up to date there is no comparative assessment of the different technological possibilities for a virtually "Clinic of Hypertension". Our own experience show that systems with automatically data transfer from patient to a service centre via mobile communications seems advantageously. Fixed line network based as well as PC based solutions have their limitations by installation problems especially in elder patients.

8. Application of telemetric blood pressure measurement in the daily routine of an office for internal medicine

We use telemetric blood pressure measurement in our routine daily care of hypertensive patients in an office for internal medicine. We make use of a validated (Westhoff TH et al., 2006) oszillometric blood pressure measurement device measuring at the upper arm. This devise has a Bluetooth interface and sends its data via Bluetooth-handy to a Regional Organisation System (ROS). From there the data are pushed forward to a database, analysed and stored there. If the measured blood pressure exceeds preliminary settings an alert is sent via ROS by e-mail, fax or letter to the treating physician and/or to the patient. The advantage of this system compared with other systems is that the patient can´t suppress measured blood pressures to endeavour to communicate optimal blood pressure values to his doctor. A small amount of technical solutions have been tested in a number of application studies (Mengden T et al., 2001). The virtually Clinic of Hypertension was tested successfully in several pharmacological studies (Ewald S et al., 2006; Mengden T et al., 2004; Möckel V et al., 2009). In all these studies telemetric blood pressure measurement was proved as practicable and was well accepted by the majority of the treated patients.

8.1 Methods

We used 36 telemetric blood pressure measuring devices (Stabilo-Graph i.e.m., Stolberg, Germany) in following indications:

- Making sure the diagnosis "arterial hypertension"
- First treatment of a newly discovered and to date untreated blood pressure
- Control and modification of a pre-existing antihypertensive treatment

We treated more than 400 patients with telemetric self blood pressure measurement until today. The assessment of the self measured blood pressure values was made in a weekly setting and in addition if there was an automatically alert by the system (we use e-mail and fax only to the doctor, not to the patient).

The patients are trained by a "hypertension assistant" (DHL®). After training the method of home blood pressure measurement according to the ESH guidelines the telemetric blood pressure measurement device is demonstrated and the use of the equipment is trained. According to the ESH guidelines (Parati G et al., 2004) measurements should be done at least between 06:00 and 09:00 hours in the morning before taking the antihypertensive

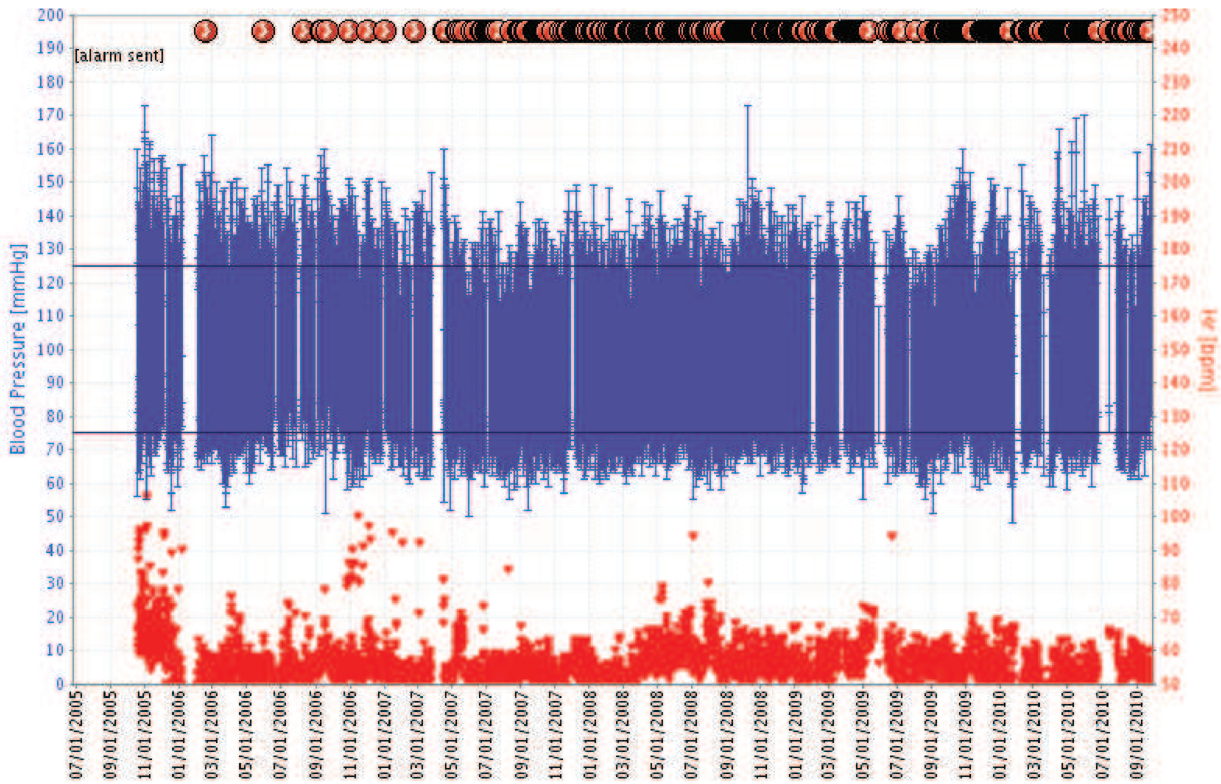

Fig. 3. High long-term adherence with telemetric blood pressure measurement in a type 2 NIDDM patient: 17,7 measurements per week from 10/18/2005 to 09/25/2010

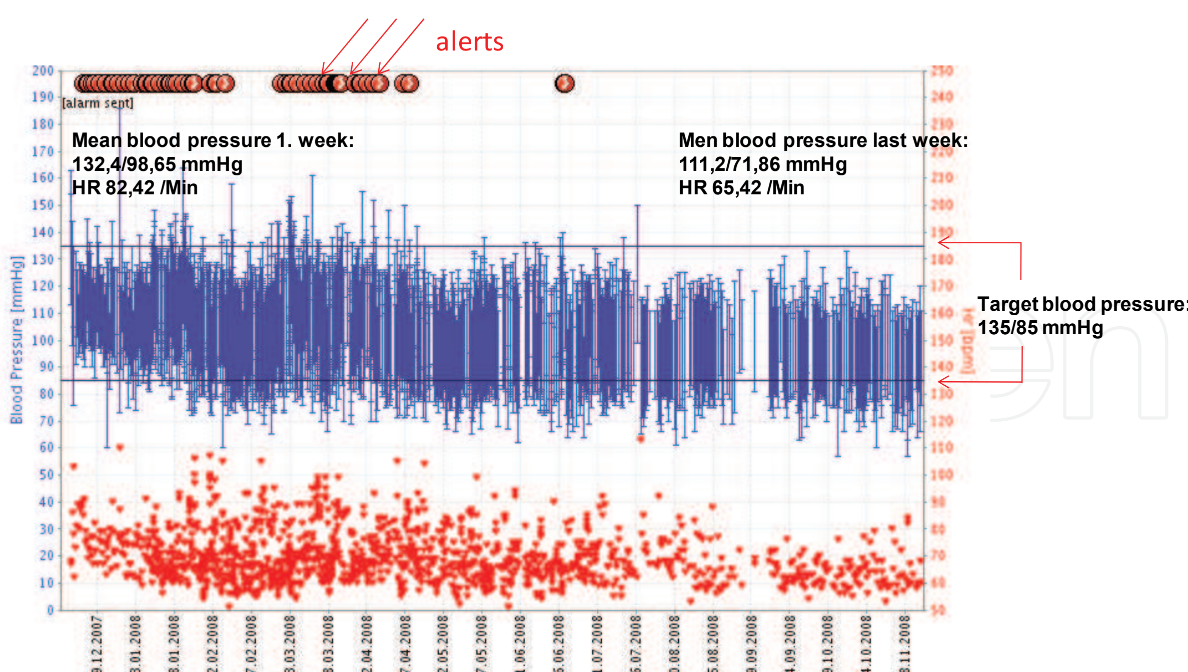

Fig. 4. Typical development of blood pressure under telemetric observation: high alert intervals at the beginning with corresponding mean weekly blood pressure and satisfactory blood pressure after 6 months.

medication. The alert limit is 135/85 mmHg in absence of other risk factors with adaptation of the target blood pressure according to the additional risks (diabetes mellitus or renal failure for instance) (Figure 3 and 4).

8.2 Statistic methods

We analysed the blood pressure of 147 patients. For that purpose all measurements at start of the telemetric home blood pressure measurement were set to a jointly zero point. The mean weekly blood pressure was calculated for every patient. We studied the hypothesis that telemetric blood pressure measurement would positively influence the quality of treatment by increase of adherence to the therapy. 95% confidence intervals (CI) of blood pressure were calculated.

An additional calculation was done for the dependence of blood pressure to the duration of an interruption of telemetric blood pressure measurement by an analysis of regression calculating the development of blood pressure in dependence to the interval of interruption of telemetric measurement. The increase of blood pressure over the time of interruption was calculated.

The acceptance of telemetric blood pressure measurement and management was analysed by a questionnaire. This was created together with 4 patients. 41 out of 71 questionnaires were answered and analysed.

8.3 Results

Mean age of the 147 patients (53 women) was 55,9 ± 11,6 years (women 56,5 ± 1,7 years, men 55,6 ± 11,6 years). A total of 30.217 single measurements were analysed, per patient 163 ± 172 measurements (median 106 ± 18 measurements). Mean measurements per week were 11,1 ± 5,2 (median 10,9; 1,7 – 26,8). There was no influence of the patient´s age on the frequency of measurements.

In the first measurement interval patients had an optimal adherence (i.e. ≥ 14 measurements a week) to the demanded number of measurements only in the first and second week of examination with 19,8 and 15,2 measurements per week. The frequency of blood pressure measurement fulfilled the criteria for a sufficient judgement until week 16 (i.e. a minimum of five measurements per week (Krecke HJ et al., 1996). This time was long enough to get 95% of the treated patients into their target blood pressure (< 135/85 mmHg). If a second measurement interval was carried out for control, the patients didn´t even reach the "optimal measurement frequency" (i.e. 14 measurements/week) at begin of this period – the minimally necessary number of 5 measurements per week was realized only until week 6 of the second interval (Figure 5).

The duration of measurement periods was between 3 and more than 52 weeks. Only patients with a minimal measurement period of 4 weeks were analysed.

9. Blood pressure under telemetric observation

At the begin (week 0) of a new or changed therapy mean systolic blood pressure was 136,8 mmHg (95%-CI 136,1 – 137,4 mmHg), and mean diastolic blood pressure 85,2 mmHg (95%-CI 84,5 – 85,2 mmHg). Under therapy mean blood pressure decreased to systolic 134,1 mmHg (95%-CI 133,4 – 134,9 mmHg) and diastolic 81,95 mmHg (95%-CI 81,4-82,5 mmHg) after 4 weeks, that means below the target blood pressure of 135/85 mmHg. This reduction remained constant over the observational time of maximal 51 weeks (134,2 mmHg [95%-CI 133,4-134,9 mmHg]/81,95 mmHg [95%-CI 81,4-82,6 mmHg], (Fig. 6).

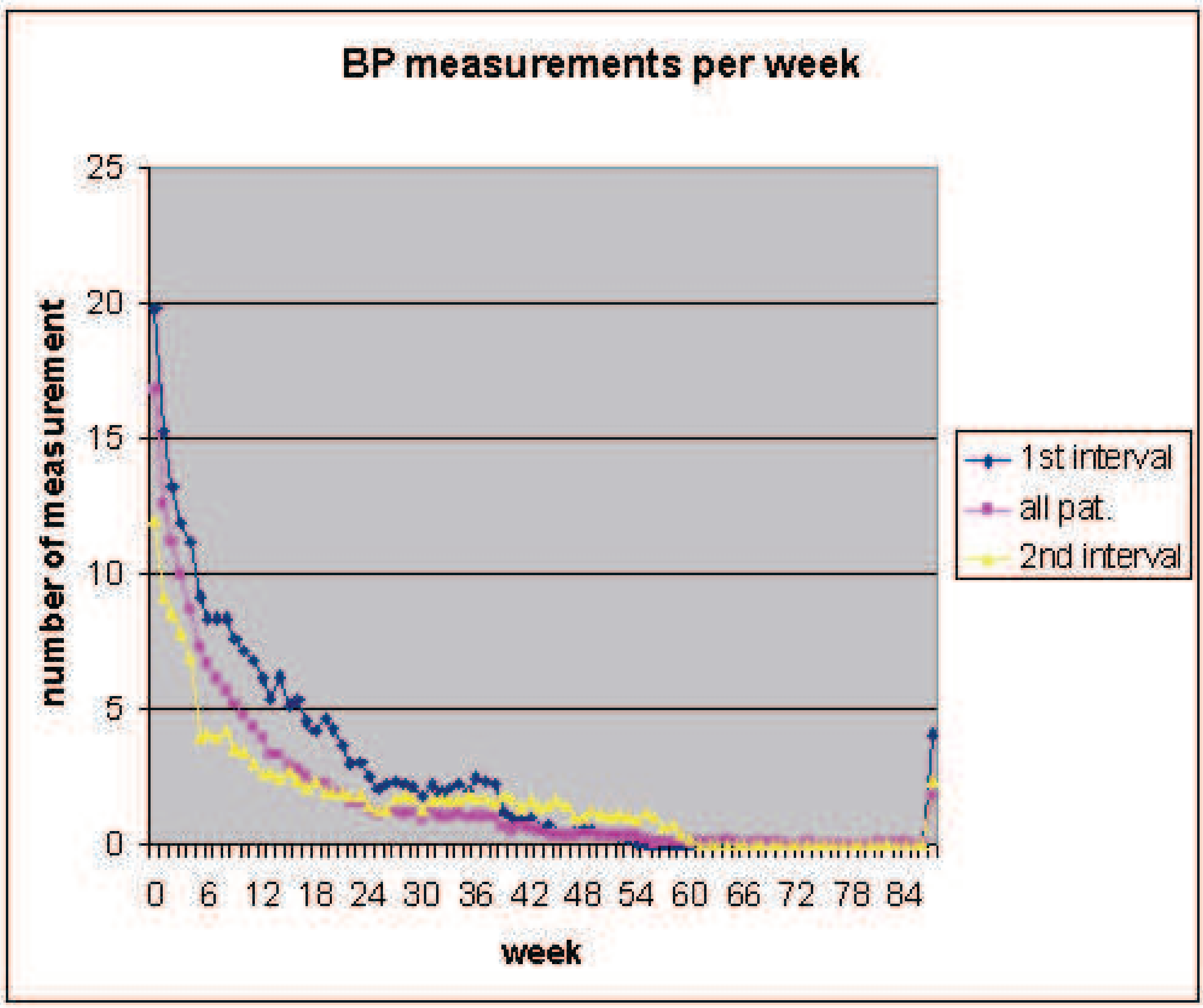

Fig. 5. Number of measurements per week for all patients, patients in first and second measurement interval

10. Does this success remain only under continuously telemetric observation?

32 patients had a telemetric blood pressure control for documentation of the quality of their therapy and to clarify, if the therapeutic success is influenced by the interruption interval due to deterioration of compliance or adherence. In these patients blood pressure decreased from 137/85 mmHg to 131/81 mmHg in the first therapy interval (Fig. 6). Blood pressure at begin of the second telemetric measurement interval continuously was in the target range of <135/85 mmHg measuring 132/81 mmHg. During the second observation interval blood pressure decreased slightly to 130/80 mmHg. The regression analysis showed an blood pressure increase of systolic 0,01242 mmHg (r=0,36) and diastolic 0,007374 mmHg (r= 0,54) per day without telemetric monitoring of blood pressure. That means: The adherence with an antihypertensive therapy started under telemetric observation is very strong. An increase of blood pressure by systolic 1 mmHg is expected not until 12 weeks, and by diastolic 1 mmHg even not until 19,4 weeks.

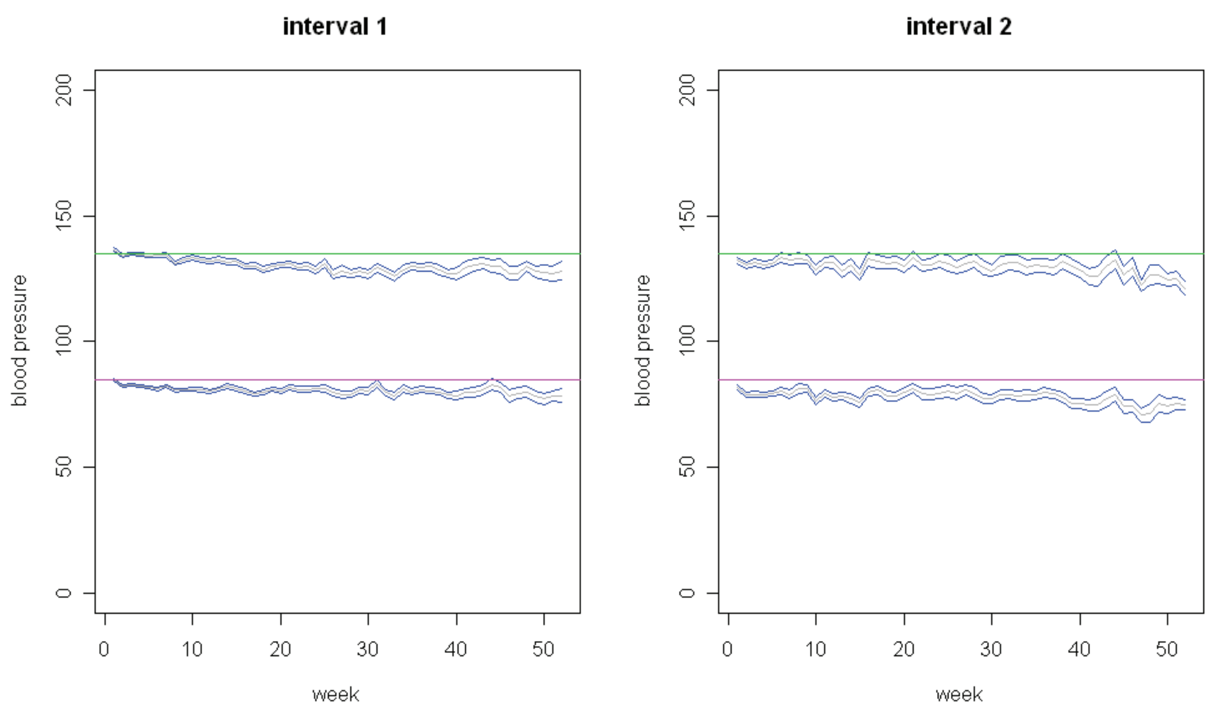

Fig. 6. BP during first interval and during recurrent measurement (interval 2) in 32 patient

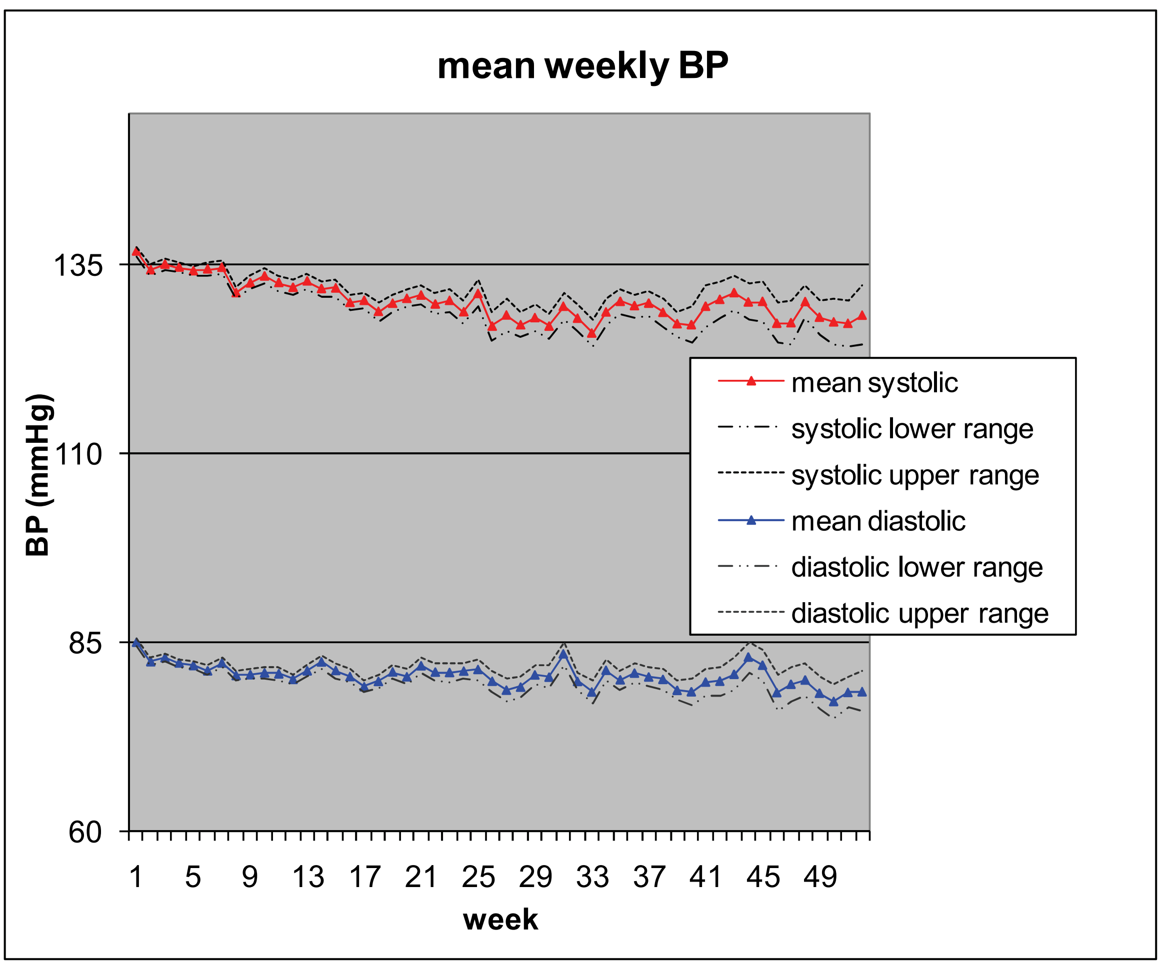

Fig. 7. First interval of telemetric blood pressure measurement (n=147)

11. Acceptance of telemetric blood pressure monitoring

15 out of 39 patients asked in a survey had no objections against the publication of personal data in the internet; no objections (less than a quarter) were existent against publication of blood pressure, diagnoses, and informations on therapy in the internet. Their own blood pressure history was observed in 18% periodically, seldom, and 47% never. Two thirds of the telemetric observed and treated patients wished a possibility for interaction with their physician via internet. Particularly if they would have special causes (62%) or problems with the therapy (i.e. side effects etc.) they would like to contact their physician and communicate directly with him in the internet.
The opportunity to be alarmed automatically by the Telemonitoring system was judged very different: 67% considered alerts as necessary, 22% as desirable, and 17% felt insure by alerts. In her/his daily life no one patient wished to be disturbed or made unsure by automatically generated alerts. On the other side the patients felt reassured upon the information that their physician gets an alert in the case of violation of adjusted target values.
Three quarters of the patients were willing to pay for the hardware of telemetric blood pressure measurement (about 90 €) fully or in part. Two thirds of the patients were willing to pay full or in part even the monthly costs for the database (about 10 €).

12. Discussion

Friedman et al. (Friedman RH et al.,1996) studied 267 patients for 6 months in a randomized trial. Telemetric controlled patients showed an additional decrease of systolic 11,5 mmHg and diastolic 5,5 mmHg as compared to usual care (Figure 8). The adherence to therapy was increased by 36% with Telemonitoring. This improvement with Telemonitoring was the crucial predictor for the improvement of blood pressure. In this study the blood pressure data were transferred by a call centre to the general physicians. This was judged as a helpful additional information for therapeutic decisions in > 85%. In Friedman´s study from 1996 an interactive computer based telecommunication system was used weekly telephone calls. The blood pressure data were transferred to the database by the patients themselves assisted by a standardized automatically working telephone interview system. In such a system communication mistakes are possible and the documentation of the blood pressure data is not patient independent.
Another study (Rogers MAM et al., 2001) compared a Telemonitoring interventional group with usual care treated patients. The blood pressure readings were transferred automatically and regularly to a medical centre of competence. The treating physicians as well as the patients of the intervention group were informed weekly about the quality of blood pressure adjustment. The telemetric intervention group showed a significant reduction of mean arterial pressure by 2,8 mmHg whereas the control group had a increase of 1,3 mmHg. Even patients without adaptation of their medication had superior blood pressure reduction in the telemetric treated group. This indicates that the telemetric measurement promoted the adherence with their therapy.
Friedman et al. (Friedman RH et al., 1996) discuss if solely the telemetric blood pressure transfer improve the blood pressure adjustment, or if the specific intervention on basis of the telemetric measurements is decisively. For this discussion there are interesting data generated by an internet based long term study using Telemonitoring (Tab. 2, Green BB et al., 2008; page 10) in three arms:

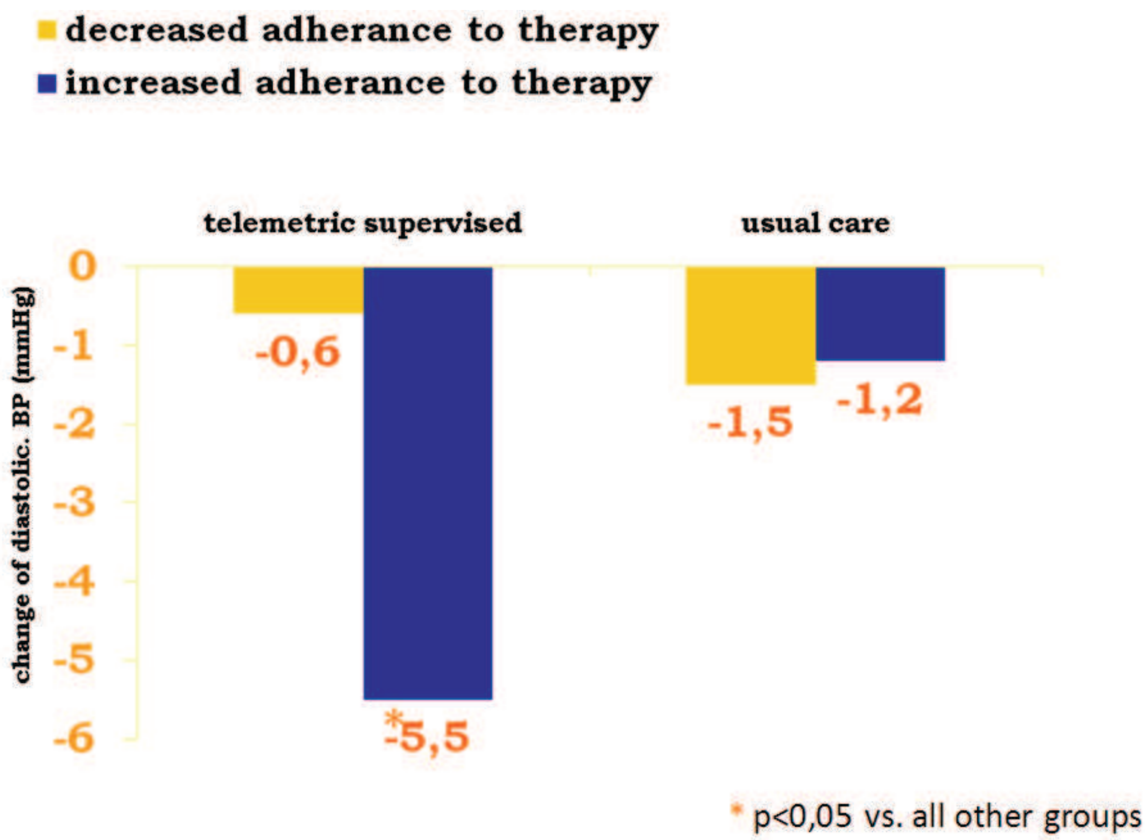

Fig. 8. Blood pressure decreased in 267 randomized patients by systolic 11,5 mmG and diastolic 5,5 mmHg in they were controlled telemetrically with an improvement of adherence by 36%. Friedman RI et al. (1996)

1. Blood pressure adjustment by general physicians ("usual care")
2. Home blood pressure measurement plus internet based training and blood pressure evaluation
3. Home blood pressure measurement plus internet based training and blood pressure evaluation plus phone intervention by a pharmacist

The target blood pressure in group 2 and 3 was <135/<85 mmHg as for home blood pressure measurement. Phone intervention in group 3 was carried out every two weeks by a specially trained pharmacist until target blood pressure was reached. Just the group 3 had a significant improvement of blood pressure compared to group 1 (Tab. 2).

Without an additional intervention other studies showed only a moderate (Rogers MAM et al., 2001; Sehnert W and Maiwald G. 2008) to absent (Madsen LB et al., 2008) effect of Telemonitoring. It can be concluded, that telemetric blood pressure monitoring has a better effect compared to a usual therapy only if there is an additional individualized intervention.

Telemetric blood pressure monitoring may have a big potential in hypertension in pregnancy due to the dynamic of blood pressure in this state (Mengden T et al., 2001; 19: 71suppl 2). Blood pressure changes may be very quick in pregnancy and it is important to realize even small increases of blood pressure.

Further investigations should be done in high risk populations in future. These are hypertensives with coronary artery disease, heart failure ok cerebrovascular problems. A prognostic benefit from such a telemetric observation can be expected in these high risk groups.

Patients' adherence to therapy is the biggest problem in the therapy of high blood pressure. Hypertension is a chronically illness requiring a maximum of understanding from our patients. They are involved in a therapy with possible side effects without substantial symptoms, which mean a therapy causes no symptomatic benefit for the patient. The classic "traditionally authoritarian" relation between patient and physician must be changed from into a dynamic model. In this the patient gets an active part. Home blood pressure monitoring is recommended by the ESH as a sensitive toll for therapy adjustment. Telemonitoring with alert system presents innovative possibilities to improve adherence to therapy by patients and physicians. It improves the patient´s relation to her/his disease – and thereby improves the basis of therapy.
Telemonitoring helps to control the adherence and compliance of an patients without time limits. We observed some of our patients now more than 4 years (Figure 3). A "severe deterioration" of adherence "after 6 months of therapy" (Osterberg L and Blaschke T. 2005) could not be proved with telemetric blood pressure monitoring. We could not observe therapy failure – caused in 50% by insufficient up-titration of the antihypertensive medication (Mengden T et al., 2001) – in our telemetric controlled patients.
Telemonitoring of blood pressure can be integrated into nearly every health care organization. It can be realized in a regional as well as in a superregional model. Data are available at any place with internet option. It´s application is independent of national health care systems and allows the observation of patients far away from the treating center. Beyond this every physician involved in the treatment is able to look at the data every time (via patient´s password). This is of eminent importance to provide patients in large areas with a small number of physicians.
For Germany there are no national or super national concepts integrating telemedicine into daily practice. Demographic development with a high part of older women and men will push Telemonitoring. The elderly want to stay as long as possible in their homes. Telemonitoring can be used as early warning system and continuously control in their homes. The correct use of telemedicine can save costs in a public health system considerably. The wrong use of telemedicine however can force up costs. Public health organizations hesitate to accept telemedicine. They will be overtaken by the "silver generation", which demand an optimal medical supply. There is a good chance for a broad use of this innovative meaningful new technique.

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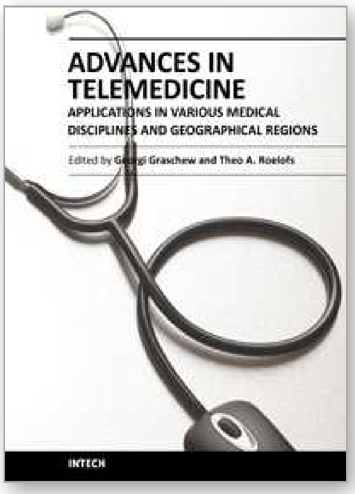

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Innovative developments in information and communication technologies (ICT) irrevocably change our lives and enable new possibilities for society. Telemedicine, which can be defined as novel ICT-enabled medical services that help to overcome classical barriers in space and time, definitely profits from this trend. Through Telemedicine patients can access medical expertise that may not be available at the patient's site. Telemedicine services can range from simply sending a fax message to a colleague to the use of broadband networks with multimodal video- and data streaming for second opinioning as well as medical telepresence. Telemedicine is more and more evolving into a multidisciplinary approach. This book project "Advances in Telemedicine" has been conceived to reflect this broad view and therefore has been split into two volumes, each covering specific themes: Volume 1: Technologies, Enabling Factors and Scenarios; Volume 2: Applications in Various Medical Disciplines and Geographical Regions. The current Volume 2 is structured into the following thematic sections: Cardiovascular Applications; Applications for Diabetes, Pregnancy and Prenatal Medicine; Further Selected Medical Applications; Regional Applications.